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CASE ONE

Acute Kidney Injury from Herbal Medication in a 34 year old Female

SUMMARY

A 34 year old female who presented with abdominal pain and high grade fever of a month's duration, oliguria associated with facial and bilateral leg swelling of a week's duration and jaundice of 5 day's duration. The renal symptoms started one week after taking alcohol based herbal medications for several days. She was managed with dialytic therapy for acute kidney injury.

This case highlights the nephrotoxic potential of seemingly innocuous herbal medicine in causing AKI and management of the condition.

CASE REPORT

A 34 year old female who presented with abdominal pain and high grade fever of a month's duration, oliguria of a week's duration and jaundice of five day's duration. She was apparently well until about a month prior to presentation when she developed abdominal pain. Pain was dull, severe, located in the right hypochondrium and non-radiating. There was associated mild abdominal swelling but no change in bowel habit.

Fever started about the same time with abdominal pain. Fever was high grade, intermittent and temporarily relieved by taking paracetamol. There was no associated headache, cough, breathlessness, dysuria, or urinary frequency. Two weeks after onset of her symptoms, she took alcohol based herbal mixture for several days without improvement in her symptoms. She was not aware of the composition of the herbal medication.

Progressive diminution in urinary output was noticed a week prior to presentation to less than 100 mls of urine daily. There was also progressive bilateral leg and facial swelling.

Jaundice was noticed 5 days prior to presentation which progressively worsened. There was neither associated puritus nor passage of pale bulky stools. There was a change in urine color to dark brown. There was no associated weight loss, history of multiple sexual partners, sharing of sharps, previous blood transfusion or skin scarification. She is not a known sickle cell disease patient. There was no history suggestive of chronic liver disease. She patronizes food vendors and uses pit latrine. There was no recent abdominal surgery. She was not a previously diagnosed hypertensive or diabetic. She has not been diagnosed of any renal disease in the past.

There was no history of irrational behavior, confusion, seizure, breathlessness or bleeding from the orifices. There was vomiting that started five days after onset of oliguria. She had multiple episodes per day and volume of each episode was about 50mls. She initially presented in a private hospital where she was referred to University of Benin Teaching Hospital (UBTH) on account of markedly elevated serum urea and creatinine.

There is no history of hypertension, diabetes mellitus or renal disease in her family. She is married in a monogamous family setting to a commercial motorcyclist with four children. She does not take alcohol or tobacco in any form.

EXAMINATION FINDINGS

Examination showed a young woman who was acutely ill looking with facial puffiness, afebrile (temperature 36.5^0C), not pale, icteric, acyanosed, not dehydrated. She did not have finger clubbing or other peripheral stigmata of chronic liver disease. There was pitting oedema up to the middle third of both legs.

Her pulse rate was 106 per minute, regular, normal volume. Blood pressure was 110/60 mmHg and jugular venous pressure was not elevated. The apex beat was in the 5^{th} left inter-costal space, mid-clavicular line and not heaving. Heart sounds were normal.

The respiratory rate was 22 cycles per minute and her chest was clinically clear.

The abdomen was full, soft moved with respiration with marked right hypochondrial tenderness. The liver was enlarged below the right coastal margin by 6cm. It was firm, smooth and tender. The spleen was not palpably enlarged and the liver span was 16cm. Digital rectal examination was essentially normal. The neurological examination was essentially normal.

Urinalysis showed a dark coloured urine with a pH of 5.0, specific gravity of 1.020, protein, glucose, ketone, blood were all negative.

An assessment of (1) Acute kidney injury secondary to herbal medication

RESULT OF INVESTIGATIONS

Urine microscopy and culture showed few epithelial and pus cells/ hpf with no growth after incubation.

Hepatitis B, C, HIV and Lassa screening were negative.

The total white cell count was 8,500cells/mm^3 with differential of 74.8% granulocyte**,** 7.8% monocyte and 17.4% lymphocyte. Platelet was 183,000 cells/mm^3 and haematocrit was 27.4%.

Peripheral blood film showed mixed deficiency anaemia. Stool examination for ova, cyst and parasites was negative. Urea was 181mg/dl, creatinine was 3.9mg/dl, sodium:126 mmol/dl, potassium:6.3mg/dl, bicarbonate:15mmol/dl and chloride:100mg/dl. Estimated glomerular filtration rate (GFR) at presentation was 17mls/min/1.73m^2

The liver function test showed alkaline phosphatase: 34 I.U/L**,** aspartate aminotransferase: 27 I.U/L**,** alanine aminotransferase: 17 I.U/L**,** total bilirubin 4.0mg/L**,** conjugated: 3.5mg/L, total protein: 6.3g/L, albumin: 3.3g/L, globulin: 3.0g/L. This result was essentially normal.

The abdominal ultrasound report showed that the liver appeared normal in outline and echo texture. There was a solitary hepatic cyst with echogenic debris within the anterior aspect of the right lobe measuring 71cm x 41cm. The spleen, gall bladder and pancreas appeared normal. Both kidneys measured 12.3x4.5x6.0cm and 11.6x6.0x6.0cm on the left and right kidneys respectively. There was normal corticomedullary differentiation and cortical echogenicity. The uterus was normal and adnexia were free.

Based on the ultrasound finding of a solitary cyst on the right hepatic lobe and review by a gastroenterologist, a diagnosis of amoebic liver abscess was made.

TREATMENT

Hyperkalaemia was urgently corrected with 50mls of 50% dextrose with 5 units of soluble insulin and 10 mls of calcium gluconate that was given slowly over 10minutes, while awaiting haemodialysis. She was placed on intravenous metronizadole 500mg 8 hourly which was later converted to tabs metronidazole 400mg tds to complete a 10 day course. Other medications given include diloxanide furoate 500mg bd for 10days, ferrous sulphate 200mg tds, folic acid 5mg daily, viamin b complex 1 tablet tds, and vitamin C 200mg tds. She was placed on high calorie diet and nephrotoxic drugs were avoided.

Her daily fluid regimen was restricted to the previous day output in addition to 1litre. She had three sessions of haemodialysis which were well tolerated. She entered polyuric phase on day 6 which subsequently resolved after day 10. Repeat abdominal ultrasound showed complete resolution of the right hepatic cyst after a 10 days of metronidazole therapy.

She was discharged home at the end of the second week after counseling on the need to abstain from use of herbs and others nephrotoxic agents.

ELECTROLYTE, UREA,CREATININE AND FLUID CHART

	DAY 1	DAY 2*	DAY 3	DAY 4*	DAY 5	DAY 6*	DAY 7	DAY 8	DAY 10	DAY 12	OPD VISIT
Urea	181	178	147	77	129	75	68	39	40	35	38
Cr	3.9	3.3	3.4	1.0	2.5	2.3	1.9	1.7	1.0	0.9	0.8
Na^+	126	135	131	132	142	132	131	137	132	135	138
K^+	6.3	4.4	3.9	4.6	4.4	5.3	6.1	4.2	4.4	4.5	3.9
$HCO3^-$	15	20	20	24	21	27	28	25	24	28	28
Cl^-	100	92	100	104	112	104	96	95	92	96	98
FLUID INPUT	1000	1100	1250	1300	1300	1500	4000	5000	4000	3000	3000
FLUID OUTPUT	100	240	310	270	400	3200	4900	5900	3500	2000	1800

* Post dialysis

DISCUSSION

Acute kidney injury (AKI) is defined by Kidney Disease Improving Global Outcome (KDIGO) as increase in serum creatinine by ≥ 0.3mg/dl within 48 hours; or increase in serum creatinine to ≥ 1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; or urine volume < 0.5mls/kg/hr for a period of 6 hours.[1]

The diagnosis of AKI in the index patient was based on the above criteria which she met. The term AKI has replaced the old term acute renal failure because the former involves a spectrum ranging from renal risk, injury, failure, loss to end stage renal disease. The new nomenclature also helps the physician to identify patients at increased risk, take appropriate preventive and therapeutic measures before allowing a patient to get to the renal failure stage and requiring renal replacement therapy.

The worldwide prevalence and incidence of AKI is not truly known due to under-reporting, regional disparity and differences in definition criteria used in making diagnosis. These problems are even worse in developing countries like Nigeria where patient data are not properly managed. Seedat et al reported the incidence to be 20 cases per million population in South Africa.[2] Noronhaet al reported an incidence of 7.9 cases per 1000 hospital admission in Brazil while Jha et al reported 6.4 per 1000 admissions.[3,4] The incidence of AKI has been on the increase over the last 3 decades.[5]

There are also differences in the epidemiology of AKI in both developing and developed countries. Community acquired AKI occurs more commonly in developing countries than developed countries with associated high mortality. Also, infections, obstetric causes and nephrotoxins are the commonest causes of AKI in the developing countries unlike the developed countries.[6,7,8]

Herbal medication use as a cause of AKI is common in Nigeria as reported in previous studies.[6-9] Nephrotoxins accounted for 13.3% of the cases of AKI over a 5 year period in Osogbo, Osun state. [6] Bamgboye et al also reported a prevalence of 9.5% over a ten year period in Lagos.[7] Emem-Chioma et al reported a prevalence of 11.4% in Port Harcourt and a higher prevalence of 37.5% was reported by Kadiri et al in Ibadan, Oyo state.[8,9] There is also the possibility of an

underestimation of the contribution of herbal medicine to aetiology of AKI in the tropics due to failure to elicit the history due to ignorance of the physician or denial by the patient when the history is being elicited because of fear of social stigmatization The high prevalence of herbal medication induced AKI in Nigeria is however, not surprising because of cultural beliefs of many Nigerians on the potency of these medications.

Herbalists and faith healers use unknown ingredients to prepare these medicines which have not been tested for efficacy and safety. The natural compounds more frequently associated with AKI are impila *(Callilepi laureola),* djenkol beans *(Pithecolobium),* mushrooms (genera *Amanita, Galerina, Cortinarius,* and *Inocybe*), cape aloe, and rawcarp bile.[10,11]

Kadiri et al identified some plant materials such as leaves and bark of mango (Magnifera indica), shoots of cashew leaves (Anacardium occidentale), paw paw leaves (Carica papaya), lime leaves (Citrus aurantifola), Solanium erianthum, Morinda lucida leaves and bark of Azadirachta indica leaves used as traditional herbal preparation which have been implicated in causing acute renal failure in Southwest Nigeria.[12] The identified mechanisms of injury of these plants were intravascular haemolysis, hepatotoxicity and direct nephrotoxicity.[12] Kidneys are particularly vulnerable to toxic injury because of their high blood flow rate, large endothelial surface area, high metabolic activity, active uptake by tubular cells, medullary interstitial concentration, and low urine pH. Renal tubules are involved in active transport and urinary concentration and therefore, the local concentration of toxins is potentially high, leading to direct injury to tubular cells. The nephrotoxic effects of herbal medicines occur through one or more common pathogenic mechanisms which include alteration of intra-glomerular haemodynamics, tubular cell toxicity, inflammation, crystal nephropathy, rhabdomyolysis and thrombotic microangiopathy.

Several factors affect the toxicity and likelihood of kidney injury with herbal medication use. Adulteration of indigenous medicines, incorrect identification by inexperienced personnel may lead to substitution of a medicinal plant with a toxic one such as the substitution of Takaout el badia, a hair dye made from *Tamarix orientalis* seeds, with the toxic Takaout roumia (paraphenylenediamine). Also, incorrect methods of preparation or consumption may cause nephrotoxicity. Examples include consumption of improperly cooked djenkol beans, star fruit, or yam and failure to ingest impila in the prescribed way (with sufficient water, followed by regurgitation soon after consumption). Indirect mechanisms include interaction with metabolism of conventional drugs e.g St. John's wort *(Hypericum perforatum)* increases plasma levels of drugs that are metabolized by the cytochrome P-450 enzyme system. Concomitant administration of other nephrotoxic medicines can also potentiate herbal nephrotoxicity.[10,11]

The patient-related risk factors for drug-induced nephrotoxicity include age older than 60 years, underlying renal insufficiency, GFR less than 60 ml/min per 1.73 m^2, volume depletion, diabetes mellitus, heart failure, and sepsis.[13] These risk factors may also make individuals susceptible to the renal toxicity of herbal medicines.

Kidney injury may either be the sole manifestation or part of a multisystem involvement that includes acid-base disturbances, liver failure, neurologic abnormalities, disseminated intravascular coagulation, or respiratory failure. In the index patient, AKI was the sole manifestation of the toxic effect of the herbal medicine.

Management of AKI from herbal medication is not particularly different from AKI due to other causes as seen in this patient. The herbal medication and other nephrotoxic medication should be discontinued. Electrolyte derangement such as hyperkalaemia should be corrected as done in the patient. Strict fluid management, treatment of any underlying disease and renal replacement

therapy (RRT) when indicated. The mortality associated with AKI is very high especially in developing countries where it ranges between 21.5- 43.5%.[7-9,15,16] Late presentation, unavailability and non-affordability of dialytic therapy contribute significantly to mortality in AKI patients.

Factors affecting survival of AKI patients include severity of disease, availability and affordability of RRT, aetiology of the AKI, age of patient, duration of AKI and illness.[8,14,15]

The index patient had a good outcome probably because of her age, availability and affordability of RRT, short duration of oliguria and absence of co- morbidities. Due to high cost of RRT in developing countries where patients and their relatives bear the cost alone, prevention and early recognition are the realistic way to reduce the burden of AKI. These will involve a multidisciplinary approach involving the government, health care providers, international organizations and the general public.

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CASE TWO

Autosomal Dominant Polycystic Kidney Disease in a 35 year old man

SUMMARY

A 35 year old male who presented with frothiness of urine of a year's duration and malaise of a month's duration. There was associated history of recurrent painless haematuria, bilateral loin pain, fever and dysuria. He was recently diagnosed hypertensive 4 months prior to presentation. Ultrasound confirmed autosomal dominant polysystic kidney disease (ADPKD). He developed end stage renal disease (ESRD) 2 years after the initial presentation and had a successful renal transplant after 2 months on haemodialysis.

This case highlights the presentation, diagnosis and management of autosomal polycystic kidney disease

CASE REPORT

A 35 year old male who presented with frothiness of urine of a year's duration and malaise of a month's duration. He was apparently well until a year before presentation when he noticed frothiness of urine that has been persistent since onset. There were associated episodes of painless total haematuria that were self limiting. There was also history of recurrent episodes of dysuria, urinary frequency and fever that resolved with antibiotics. There was history of occasional bilateral loin pain that was dull and mild in severity. There was no associated swelling or change in usual bowel habit.

Malaise started three months before presentation with associated easy fatigability. There was no breathlessness. There was no history of facial or bilateral leg swelling. He was diagnosed hypertensive 4 months before presentation and had been placed on nifedipine and moduretic with good compliance. He is not a known diabetic. There was no history of chronic use of mercury

containing soaps, cream, herbal medications and analgesics. He was not a known HbSS patient. There was no history of jaundice, snake bite or insect sting. There was no family history of renal disease and no history suggestive of connective tissue disease in him. There was no history of recurrent headaches or palpitation. There was no history of stroke in him or any family member. There was no history of vomiting, puritus, hiccough, irrational behavior or seizures. He presented with an ultrasound report that was done in private hospital where he initially presented to and this showed bilateral multiple cysts in the kidneys.

He is the 4th of 6 children in a monogamous family. There is history of hypertension in his family. He does not take alcohol or tobacco in any of form. He is married but yet to have children after 4 years of marriage.

EXAMINATION

On examination, he was not ill looking, was pale, afebrile, acyanosed, not dehydrated and had no finger clubbing or peripheral oedema.

Pulse rate was 80 per minute, regular, normal volume and blood pressure was 160/100mmHg. Jugular venous pressure was not elevated and apex beat was in the 5th left intercostal space, mid-clavicular line and not heaving. Heart sounds were 1 and 2 only. There were no murmurs.

His respiratory rate was 16 cycles per minute and chest was clinically clear. The abdomen was full, soft moved with respiration. There were no areas of tenderness. Liver and spleen were not palpably enlarged, but both kidneys were palpable. There was no ascites.

Examination of the nervous system was essentially normal. Fundoscopy was normal and revealed no evidence of retinopathy.

Urinalysis showed clear and amber urine with pH of 6.0, S.G of 1.010, proteinuria of 2+, glycosuria of 1+. Blood and leuckocytes were negative

Assessment of chronic kidney disease (CKD) secondary to ADPKD was made.

RESULT OF INVESTIGATIONS

Packed cell volume: 33%, peripheral blood film showed normocytic normochromic anaemia. Total white cell count: 3,800 cell/mm^3 with normal differential count. Platelet count: 200,000 cells/mm^3. Urine microscopy and culture showed 0-1 red cell/hpf, 1-2 cells/hpf, 0-1 epithelial cell /hpf and triple phosphate crystals, but there was no growth of any organism on culture. Hepatitis B, C and HIV screening were negative. FBS: 87mg/dl. Serum urea was 146mg/dl, creatinine was 2.1 mg/dl, sodium was 136 mmol/L, potassium was 6.7 mg/dl, chloride was 100mg/dl and bicarbonate was 16 mmol/dl. The estimated GFR was 46 mls/min/m^2. The total serum cholesterol was 320mg/dl, HDL-C was 52mg/dl, LDL-C was 226 mg/dl and triglyceride was 208mg/dl. Serum uric acid was 11.0 mg/dl. Serum calcium was 7.7 mg/dl and phosphate was 4.9 mg/dl. The liver function tests were essentially normal. The abdomino-pelvic scan showed enlarged kidneys with multiple well defined, but widespread cysts in both kidneys. The right and left kidneys measured 15.1 cm X 6.5cm X 8.9cm and 16.4cm X 8.3cmX 2.8cm respectively. There was loss of corticomedullary differentiation and increase cortical echogenicity. There were no cysts in the liver and pancreas. Chest Xray and ECG were essentially normal. Echocardiography showed concentric left ventricular hypertrophy with no evidence of valvular disease.

TREATMENT

Hyperkalaemia was treated with 50mls of 50% dextrose, 5 units of soluble insulin and 10 mls of calcium gluconate was given slowly over 10minute He was placed on tabs vitamin D3 0.5 microgram daily, calcium carbonate 600mg tds, simvastatin 20mg nocte, nifedipine 20mg b.d, moduretic 1 daily, ferrous sulphate 200mg b.d, vitamin c 100mg tds, vit b 1 tds, folic acid 5mg

daily. He was counseled on the nature of disease, likely course of progression and management plan. He was counseled on dietary restriction of fats and potassium containing foods and placed on low salt and protein diet.

He was subsequently followed up for about 2 years as outpatient with regular monitoring of his renal function. His blood pressure was well controlled. He however had a steady decline in his renal function over the 2 year follow-up from 46 mls/ min/1.73m^2 at presentation to 18.6 mls/ min/1.73m^2 despite adequate blood pressure control and adherence to his medications . He had an AV fistula created in anticipation of commencement of haemodialysis. He was placed on 200mg of intraveneous iron sucrose weekly for 5 weeks and mircera 75 microgram twice monthly with improvement in his PCV from 25% to 30%. His siblings who were all above 30 years and mother were counseled and screened for polycystic kidney disease, but none had cyst. He was counseled for renal transplant and his cousin was found to be a suitable donor after screening.

He was commenced on maintenance HD twice weekly when he became uraemic at estimated GFR of 14.2mls/min and was on HD for 2 months before he eventually traveled to India for renal transplantation which was successful. He however continued his post transplant care in Lagos where he lives with his immediate family.

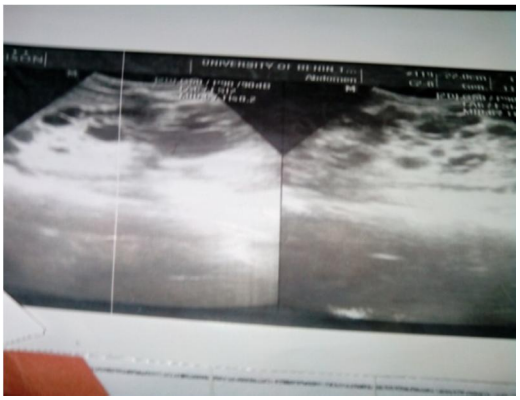

Figure 1: Renal ultra-sound scan showing multiple cysts in both kidneys

DISCUSSION

Autosomal dominant polycystic kidney disease (ADPKD) is a multi-systemic genetic disorder characterized by multiple, bilateral renal cyst and cyst in other organs such as liver, pancreas and arachnoid membrane.[1,2] It occurs worldwide in all races and affects 1 in every 400-1000 population.[1] The percentage of ESRD due to APKD is less among African Americans compared to Caucasians due to higher incidence of other causes in the latter. The disease is more progressive in male than females. [3]

In a 15 year retrospective study done by Chijioke et al in Ilorin, ADPKD accounted for 8% of patients with renal diseases, commoner in males, but females progressed faster to ESRD.[4] In another study in Ilorin, it was found that polycystic kidney disease was the commonest cystic kidney disease seen over a 10 year period, accounting for 53.3% of all the cystic diseases.[5]

Autosomal dominant polycystic kidney disease is caused primarily by mutation in two different genes and is expressed in an autosomal dominant pattern with variable expression. These genes are identified as PKD1 on chromosome 16p 13.3 and PKD2 on chromosome 4q 21. These genes code for tubular proteins; polycystin(PC) 1 and 2 that are responsible for normal phenotypic differentiation of tubular epithelium. Loss of functional polycystin with somatic inactivation of the normal allele which is consistent with a two hit mechanism is required for cyst formation. [2] Cysts have also been shown to occur in individuals without complete loss of these proteins suggesting that multiple genetic mechanism may be involved in development of ADPKD.

The polycystin (PC) 1 and 2 belong to a sub-family of transient receptor potential channels. PC1 has a molecular weight of 460kd. It has a large extracellular N-region end and short intracellular C region. PC1 is found in the primary cilia, cytoplasmic vesicles, plasma membrane at focal adhesions, desmosomes, adherens junction, possibly endoplasmic reticulum and nuclei. It may

regulate mechanical strength of adhesion between cells.[6] PC 2 has a molecular weight of 110 kd, containing a short N and C terminal portion. It is localized predominantly to endoplasmic reticulum, but also to plasma membrane, primary cilium, centrosome and mitotic spindles in dividing cells. Experimental data indicated that the timing of ciliary loss or PKD1 inactivation determines rate of development of cystic disease. Early activation results in actively progressive cystic kidney disease.[7]

The polycystins are involved in cell-cell contacts, cell-matrix contacts and are essential to maintain the differentiated phenotype of tubular epithelium. Reduction in one of the polycystins below a critical threshold results in phenotypic switch characterized by loss of planar polarity, increased rate of proliferation, apoptosis, remodeling of extracellular matrix and expression of secretory phenotype. The mechanisms involved are alteration in intracellular calcium homeostasis, activation of cyclic nucleotide, tyrosine kinase receptor and other intracellular pathways.[2]

Cystic epithelial cells are different from normal cortical collecting duct principal cells because of loss of cell polarity. Chloride ions enter across the baso-lateral NaK2Cl co-transporter driven by the sodium gradient generated by basolateral Na^+,K^+-ATPase, and exits across apical protein kinase A–stimulated cystic fibrosis transmembrane conductance regulator (CFTR). Basolateral recycling of potassium may occur through KCa3.1.[8] In tubular epithelial cells, the primary cilium projects into the lumen and is thought to have a sensory role. The PC1-PC2 complex acts as a sensor on cilia that translates mechanical or chemical stimulation into calcium influx through PC2 channels. This in turn induces calcium release from intracellular stores. It has been suggested that alterations in intracellular calcium homeostasis account for the accumulation of

cAMP, which in turn contributes to the development and progression of PKD by stimulating CFTR-driven chloride, fluid secretion and cell proliferation.

Genic, allelic and gene modifier effects contribute to high phenotypic variability of ADPKD. PKD1 associated disease is more severe than PKD2 due to development of more cysts at an earlier age. Average age at end stage renal disease (ESRD) for PKD 1 and 2 are 54 and 74 years respectively. [3]

This index patient was more likely to have PKD 1 because he had a more severe disease and rapid progression to ESRD in his fourth decade. Hypertension is one of the commonest manifestations of ADPKD and a major contributor to renal disease, cardiovascular morbidity and mortality. Studies have shown that children with borderline hypertension have higher left ventricular mass indices and cardiovascular disease suggesting that target organ damage occurs earlier even in ADPKD, hence antihypertensive medication is indicated earlier in them.[9] About 21% of ADPKD presented with hypertension in a Nigerian study.[4]

Polycystic liver disease is the most common extra-renal manifestation of ADPKD. There is usually preservation of liver parenchyma and function. Female gender and oral contraceptive pill use are associated with more cysts and growth. The abdominal scan in this patient did not show any hepatic cyst and his liver function tests were also normal. The gender of this patient might have been protective. There may be pressure symptoms from cysts. Occasionally, cysts can rupture or become infected. There have been few case report of ADPKD presenting with hepatic encephalopathy.[10,11] The possible cause is the compressive effect of the multiple cysts on the portal vein, leading to portal hypertension which may cause porto-systemic shunting and subsequently leading to hepatic encephalopathy.

Renal size increases with age and enlargement eventually occurs in 100% of patients with ADPKD. It has also been found that severity of structural abnormality correlates with hypertension, pain, and renal impairment by The Consortium for Radiologic Imaging Studies for Polycystic Kidney Disease (CRISP).[12] Loin pain may occur as a result of haemorrhage, infection, development of stones and tumor. Haematuria may be part of the initial presentation in up to 40% of patients as seen in this patient. It may be recurrent and is usually self-limiting.

Nephrolithiasis occurs in 20% of patients. Uric acid and calcium oxalate stones are the commonest types. Risk factors include low urinary pH, hypocitraturia and decrease ammonia excretion. Ultrasonography may be difficult to diagnose stones in them due to cyst wall, but intravenous urography and computed tomography (CT) scan are very sensitive. Urinary tract infection (UTI) is also common in them presenting as cystitis, acute pyelonephritis, cyst infections or perinephric abscess as observed in this patient. Common causative organisms are Escherichia coli, Klebsiella and Proteus. Fluoroquinolones and co-trimoxazole are choice antibiotics because they are lipophilic and can penetrate these cysts. The triple phosphate stone seen in this patient may likely be caused by recurrent UTI he had in the past.

Decline in renal function is usually seen in the 4^{th} and 5^{th} decade of life with an average reduction in GFR by 4.4-5.9 mls/year but ESRD is not inevitable. Risk factor for progression to ESRD are male gender, early onset hypertensive, haematuria, dyslipidaemia and sickle cell trait.[13] This patient had some of these risk factors which were majorly non-modifiable. These might have contributed significantly to the rapid decline of his renal function. Mechanisms of renal failure are interstitial inflammation, apoptosis of tubular epithelial cells, hypertensive glomerulosclerosis and compressive atrophy. The CRIBP study also confirmed that the kidney and cyst volumes are the strongest prediction of renal function decline. [12]

Intracranial aneurysm occurs in about 8% of ADPKD patients. Most are usually asymptomatic. The mean age of rupture of aneurysm is 39 years compared with 51years in general population. Routine screening is not done, but indications for screening include family history of intracranial aneurysm or subarachnoid haemorrhage, previous aneurysmal rupture, high risk occupation like pilot, preparation for surgeries with potential haemodynamic instability, significant anxiety by patient despite adequate information about the risks. [13,14] This patient was not screened because he had a very low risk of aneurysmal rupture. Magnetic resonance angiography is the imaging modality of choice. Other vascular abnormalities that could occur include aortic dissection, cervico-cephalic arterial dissection, coronary artery aneurysm, retinal artery and vein occulsion. Mitral valve prolapse is the commonest valvular abnormality seen in 25% of patients. Others are mitral regurgitation, tricuspid regurgitation, and aortic regurgitation. This patient echocardiogram did not show any valvular abnormality Valvular replacement is rarely required in them.

Cysts could also be found in other organs such as the pancreas, seminal vesicles, arachnoid membrane, epididymis and prostate. Ovarian cyst is not associated with ADPKD. There may also be defective sperm motility but this rarely causes infertility.[15] This patient had infertility which may be partly due to the CKD, but not the underlying ADPKD. The prevalence of duodenal and colonic diverticulum may also be increased. [16]

Renal ultrasound is commonly used for pre-symptomatic testing because of the cost and safety. Ultrasonographic diagnostic criteria for ADPKD1 were established by Ravine et al in 1994. [17]

Ravine's ultranosographic criteria for diagnosis of autosomal dominant polycystic kidney disease.

AGE	POSITIVE FAMILY HISTORY	NO FAMILY HISTORY
< 30years	2 cysts in either kidney	5cysts in either
30-60years	4 cysts in either kidney	5 cysts in either kidney
> 60years	8cysts in either kidney	8 cysts in either kidney.

This patient met the diagnostic criteria for ADPKD type1 because of presence of bilateral multiple cysts in the absence of a positive family history. Genetic testing can be performed when a precise diagnosis is needed and ultrasound result is indeterminate.

Grossly, polycystic kidneys are diffusely cystic and enlarged. They may weigh 4kg with the collecting systems typically distorted. The epithelial lining of the cysts are hyperplastic.

Control of hypertension helps to slow down decline in renal function and extra-renal complications. Modified Diet in Renal Disease (MDRD) study showed delay onset of kidney failure and lower composite outcome of kidney failure and all-cause mortality in those with tight blood pressure (BP) control.[18] Blood pressure target should be between 125/70mmHg and 130/80mmHg using antihypertensive regimen including ACEI or ARB. In those with progressive renal failure, BP should be controlled. Dyslipidaemia, anaemia, calcium and phosphate abnormalities should be treated as in any other case of CKD. This index patient had his blood pressure well controlled. He had dyslipidaemia that was controlled with statin while anaemia was corrected with intravenous iron and long acting erythropoietin.

Outcome of ADPKD on maintenace HD is better than those with ERSD from other causes probably due to higher endogenous erythropoietin and lower co-morbidity. This patient did not

receive blood transfusion while on dialysis, possibly due to the contribution of higher endogeneous erythropeitin that is seen in this group of patients.

Novel therapies for management of ADPKD include use of vasopressin antagonist such as tolvaptan which antagonize the vasopressin activity at V2 receptor in the collecting ducts thereby reducing cAMP that is required for cysts formation. High water intake reduces vasopressin release and has been found to be protective against development of PKD.[2,19] Somatostatin analogue (SST_2) such as octreotide and canreotide have been found to halt cyst expansion in the liver and kidneys by inhibiting cAMP accumulation, though they are still undergoing clinical trials.

Renal transplantation is the treatment of choice for those with ESRD if there are no contr-aindications. Graft survival is similar to other ESRD population. This patient had a successful renal transplantation and continued his follow up care in Lagos where he resides.

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CASE THREE

Acute-on-Chronic Kidney Disease precipitated by NSAID use in a 65 year old Female Diabetic and Hypertensive

SUMMARY

65 year old female, known hypertensive and diabetic for 20 years presented with 2 years history of recurrent body swelling and 2 days history of involuntary jerky movements. There was associated frothiness of urine, nocturia, postural dizziness and paraesthesia. She had been on ibuprofen tablet (400mg thrice daily) for about 3 weeks before onset of involuntary jerking of the hands. She was managed conservatively with significant improvement both clinically and in her biochemical parameters.

This case highlights the importance of identifying factors that could lead to acute deterioration in renal function in patients with CKD and the role of cardiovascular risk factor modification on the course of CKD.

CASE REPORT

A 65 year old female who presented with recurrent facial swelling of 2 years duration and involuntary movement of both hands of 2 days duration. She was apparently well until 2 years ago when she developed recurrent facial swelling. Facial swelling was worse in the morning and regressed during the day. There was associated recurrent bilateral leg swelling. There was no orthopnoea, paroxysmal nocturnal dyspnoea or cough. There was associated nocturia and frothiness of urine. There was no associated haematuria, loin pain or reduction in urine output.

Involuntary movements of both hands were noticed two days prior to presentation. Movements were described as jerky and repeated. No similar movement in any other part of the body.

Movements occurred at rest and with activities such as carrying objects. There was no known aggravating or relieving factors. She had not experienced similar movements in the past.

There were no associated seizures, loss of consciousness, irrational behavior or restlessness. There was no history of hiccups, puritus, vomiting, diarrhea or other history suggestive of uraemia.

She is a known hypertensive and diabetic for about 20 years and claimed good compliance to medications and follow-up clinic visits. She is not a sickle cell disease patient. No history of chronic use of herbal medication, mercurial soaps or creams. There was no previous bee sting, scorpion bite, no history suggestive of connective tissue disease, previous yellowness of the eyes or multiple sexual partners.

There was no history of fever, vomiting, diarrhea prior to onset of involuntary jerky movements of the hands. However, she has been on ibuprofen tablets 400mg thrice daily for about 3 weeks prior to onset of involuntary movements of the hands due to pain in her eyes. There was history of blurring of vision, postural hypotension and paraesthesias.

She is 20 years postmenopausal with no history of postmenopausal bleeding. She had thyroidectomy 10 years ago.

There is history of hypertension and diabetes mellitus in her parents. No family history of renal disease. She is married in a monogamous family setting with 5 children. She does not take alcohol or tobacco in any form. She was on glimepiride 2mg daily, metformin1g b.d, methyldopa 500mg tds, telmisartan 80mg daily.

EXAMINATION

Examination showed an elderly woman who was not in distress but had facial puffiness. She was pale, anicteric, acyanosed, not dehydrated, with no finger clubbing or bilateral pitting oedema.

Her pulse rate was 64 per minute, regular, normal volume and blood pressure was 170/90 mmHg supine and 150/70 mmHg erect. Jugular venous pressure was not elevated and apex beat was in the 6^{th} left intercostal space, lateral to mid-clavicular line and heaving. Heart sounds were S4,S1,S2 and there were no murmurs.

Respiratory rate was 20 cycles per minute and chest was clinically clear. Examination of abdomen was essentially normal and rectal examination showed normal stool.

She was conscious, alert, oriented in time, place and person with no cranial nerve deficits. There was normal tone across all joints and normal muscle bulk globally. Power was 5 in all muscle groups. The reflexes were normal. There was impairment of light touch in both lower limbs up to the ankle and loss of vibration sense. Asterixis was present. Fundoscopy showed features of diabetic maculopathy.

Urinalysis showed straw coloured with a pH: 6.0, S.G: 1.010, proteinuria: 2+, blood, glucose and ketones were negative,

The following assessment were made:

1. Acute-on-chronic kidney disease secondary to diabetic nephropathy precipitated by NSAID (Ibuprofen) use with ? uraemic encephalopathy.
2. Diabetic Neuropathy
3. Diabetic Retinopathy (Maculopathy)

RESULT OF INVESTIGATIONS

Random blood glucose was 205mg/dl. Urine microscopy and culture: No cast or growth after incubation for 24 hours, packed cell volume:23%, 24 hour urinary protein was 1.5g, full blood count: total : 4100cells/mm^3, differential: 78% neutrophil, 15% lymphocytes, others: 7%, platelet

count: 180,000cells/mm^3, ESR: 40mm/hr. Peripheral blood film microcytic hypochromic red cells. Viral screening for hepatitis B, hepatitis C and HIV were all negative.

Electrolyte urea and creatinine: serum urea: 142mg/dl, creatinine: 2.2mg/dl,

sodium: 135mmol/L: potassium: 3.0 mmol/L, bicarbonate: 25 mmol/L, chloride: 100mmol/L.

The estimated GFR by MDRD equation was 23.4mls/min/$1.73m^2$

Fasting Serum Lipid: TC: 168mg/dl, HDL-C: 60mg/dl, LDL-C:88mg/dl, TG:102mg/dl. Liver function test: alkaline phosphatase: 28 I.U/L, aspartate aminotransferase: 16 I.U/L, alanine aminotransferase: 10I.U/L, total bilirubin:0.8mg/dl, conjugated bilurubin:0.6mg/dl, total protein:6.2g/l, albumin:3.6g/l, globulin: 2.6g/l. This was normal. Serum calcium: 8.8mg/dl, serum phosphate: 4.0mg/dl.

Renal Scan showed that the right and the left kidneys were of normal size measuring 11.7cm x 4.9cm and 11.1cm x 4.2cm respectively. There was increased cortical echogenicty with loss of corticomedullary differentiation. Chest Xray showed mild cardiomegaly.

TREATMENT

Both metformin and NSAIDs were discontinued. She was placed on subcut soluble insulin at a dose of 10 units in the morning, 12 units in the afternoon and 8 units in the evening. Tab telmisartan 80mg daily, amlodipine 10mg daily, methyldopa 500mg tds, fersolate 200mg tds, vitamin C 200mg tds, vitamin B 1tab tds, and folic acid 5mg daily.

She had intraveneous iron sucrose 200mg into 200mls of normal saline weekly five times, long acting erythropoietin receptor activator (mircera): 50 micrograms twice monthly.

She was placed on diet low in salt, protein and phosphate.

She was also reviewed and co-managed with the ophthalmology team who made an assessment of diabetic maculopathy and bilateral immature cataract. She was placed on gutt maxidex tds BE, gutt voltaren tds BE and intravitreal triamcinolone injection.

ELECTROLYTE, UREA AND CREATININE CHART

	DAY 1	**DAY3**	**DAY5**	**DAY 7**
Urea (mg/dL)	126	142	63	56
Creatinine (mg/dL)	2.5	2.2	1.8	1.3
Sodium (mmol/L)	138	135	132	130
Potassium (mmol/L)	4.3	3.0	3.8	3.8
Chloride (mmol/L)	106	100	90	102
Bicarbonate (mmol/L)	24	25	25	23

After 5 days on admission, patient was no longer having flapping tremors, blood glucose was well controlled on insulin and was subsequently converted to oral glucose lowering agent; gliclazide 80mg b.d and vildagliptin 50 mg b.d. Blood pressure control was achieved after 7 days on admission. Her estimated GFR improved from 23.4mls/min/1.73m^2 to 49.7 mls/min/1.73m^2 She was discharged after counseling and was followed up in clinic. The erythropoietin was initially reduced, but later discontinued after her packed cell volume was maintained between 33-36% on oral iron tablets only.

DISCUSSION

Diabetes mellitus (DM) is the leading cause of ESRD worldwide [1] while it ranks third after hypertension and chronic glomerulonephritis as a cause of ERSD in Nigeria.[2] The prevalence of

DM is on the increase in Nigeria due to adoption of western lifestyle, hence the incidence of diabetic nephropathy is likely to increase over the next few decades.

About 40% of diabetic patients will develop diabetic nephropathy (DN). Diabetic nephropathy is a preventable complication of DM. The risk factors for DN include black race, male gender, poor glycaemic control, obesity, smoking, family history of renal disease, hypertension, and dyslipidaemia.[3] Poor glycaemic control, hypertension and black race were identified risk factors for DN in this patient. Most of these risk factors are modifiable, hence DN could be delayed or prevented if appropriate measures are instituted to modify these risk factors.

The pathogenesis of DN involves interplay of multiple factors such as hyperglycaemia, hyperfitration, activation of vascular growth factors, renin angiotensin system (RAS) and inflammation. Hyperglycaemia causes stimulation of transforming growth factor-β, insulin-like growth factor-1, nitric oxide and vascular endothelial growth factor that cause vasodilatation, leading to hyperfiltration with subsequent proteinuria. Hyperglycaemia also stimulates an increase in mesangial cells and capillary loops leading to renal hypertrophy through the effects of vascular growth factors and angiotensin II. Activation of RAS in diabetics contributes to haemodynamic alteration, proliferation and hypertrophy of glomerular and tubular cells as well as activation of inflammatory mediators and growth factors. Persistent hyperfiltration will lead to nephron damage and loss which may progress to chronic kidney disease. Inflammatory processes and immune cells are also involved in the development and progression of DN.[4] Glomerular and interstitial infiltration by monocytes, macrophages and activated T lymphocytes have been observed both in human biopsy specimens and in animal models of DN.[4]

The diagnosis is of DN was made in this patient even though she had also been hypertensive for a period of 20 years based on the fact that she had been diabetic for 20 years, had significant proteinuria of 1.5g, diabetic retinopathy, diabetic neuropathy and normal sized kidneys. However, hypertension is also a likely contributor to CKD in this patient.

Factors that could cause acute deterioration in renal function of CKD patients include use of nephrotoxic agents like NSAID, ACEI, radiocontrast agents, herbal medications, fluid or blood loss, infections, accelerated hypertension and obstruction. Identification of precipitants of acute deterioration in kidney function in those with pre-existing kidney disease requires a thorough history and physical examination. Ibuprofen was identified as the acute precipitant in this patient. Risk factors for deleterious effects of NSAIDS on the kidneys are congestive cardiac failure, liver cirrhosis, nephritic syndrome, diabetes mellitus, nephrotic syndrome, preexisting renal disease and elderly.[5] NSAIDS could cause acute deterioration in renal function especially in those with pre-existing renal disease through various mechanisms. They inhibit prostaglandin mediated glomerular vasodilatation especially in those with activated vasomotor system with subsequent deterioration in renal function.[5,6] This vasomotor acute kidney injury is not associated with histopathological changes in the kidneys, therefore it is fully reversible within days of discontinuing the NSAID as seen in this patient. [5,6] Other mechanism of renal injury include interstitial nephritis which is immunologically mediated. The likelihood of this was remote in this patient because of absence of other features such as fever, rash and athralgia. They also cause salt and water retention and this might have also contributed to uncontrolled hypertension in the patient. Other renal effects are hyperkalemia especially in those on potassium sparing medications, chronic tubular obstruction, though this was not seen in the patient. It may also cause nephrotic syndrome after prolong use.

The DCCT, Kumamoto and UKPDS trials have shown that stricter glycaemic control significantly reduces development of microvascular complications including diabetic nephropathy.[7,8,9] The ADVANCE study confirmed that there was reduction in new onset microalbuminuria and nephropathy in patients with nearly normal glycaemic control.[10] This index patient had poorly controlled diabetes at presentation. Her medications were adjusted to achieve good glycaemic control.

Blood pressure control is critical for both primary and secondary prevention of renal disease and cardiovascular complications in DM. At any given level of GFR, BP tends to be higher in diabetics compared to non-diabetic CKD because they are more prone to fluid and salt retention. According to KDIGO guidelines, the blood pressure target in diabetic CKD should be ≤140/90 mmHg for those with urine albumin excretion of < 30mg/24 hours and ≤130/80 mmHg for those with urine albumin excretion of ≥ 30mg/24 hours.[11] Multiple antihypertensive drugs are usually required to achieve blood pressure control in diabetics. [12] Irbesartan in diabetic nephropathy trial showed that ARB extended the time required for diabetics to require dialysis.[13] The first line antihypertensive in diabetics is either ARB or ACEI unless there is contraindication to their use.[11] The index patient had uncontrolled blood pressure at presentation, but target blood pressure was achieved after adjustment of her antihypertensive and inclusion of a calcium channel blocker.

Dyslipidaemia may damage glomerular capillary endothelium, mesangial cells and podocytes by enhancing recruitment of macrophages which infiltrates the glomerulus, becoming foam cells that also release cytokines. Lipid variables are associated with progression of diabetic kidney disease. [14] It was reported that statins reduce cardiovascular risks and rate of decline in GFR in

patients with DN. [15,16] It was noted that this index patient did not have have dyslipidaemia, hence she was not placed on a statin.

Anaemia occurs at an earlier stage of CKD in diabetic patients and is more severe at any level of GFR compared to non-diabetic CKD patients.[17] The reasons include microvascular damage to bone marrow, effect of systemic inflammation and hepcidin causing bone marrow hyporesponsiveness and reduced intestinal iron absorption in diabetics. Anaemia is also a risk factor for all adverse cardiovascular outcomes as well as mortality in those with DM and CKD.[18] Anaemia predicts faster decline in GFR and CKD progression. The use of ibubrofen in this patient may have contributed to the anaemia she had by causing gastritis and subtle gastrointestinal bleeding, even though there was no melaena stool when a digital rectal examination was done for her. She had improvement in her PCV with EPO and haematinics after weeks of therapy.

Dietary protein restriction improves prognosis in type 1 diabetic patients with progressive diabetic nephropathy in addition to the beneficial effect of antihypertensive drugs.[19] Small trials have also shown that low protein diet of about 0.8g/kg per day significantly reduced proteinuria in diabetic patients.[20] The index patient was also placed on low protein diet which might have also contributed to the sustained improvement in her renal function.

Diabetics are prone to having adynamic bone disease which is a recognized risk factor for cardiovascular calcification especially in the presence of hypercalcaemia and hyperphosphataemia. The serum calcium and phosphate in this patient were normal, but she was still placed on diet low in phosphate.

Diabetics tend to commence RRT at earlier GFR compared to non-diabetics because they tolerate uraemia poorly and are frequently affected by salt and water overload.[21] Death rate of diabetics on dialysis has significantly reduced but is still higher than non-diabetics.[21] Higher rate of co-morbidities have been shown to predict mortality in them.[22] Diabetics with ESRD of all age groups significantly benefit from kidney transplantation. Although, only a minority of older diabetics will be eligible for transplantation because of the presence of cardiovascular morbidities in them. [23] Finally, there is evidence that ESRD rates may be stabilizing in diabetics and that efforts to reduce progression may start to show benefits.[24]

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CASE FOUR

Sickle Cell Nephropathy in a 37 year old man

CASE SUMMARY

A 37 year old sickle cell disease patient who presented with 6 weeks history of facial and bilateral leg swelling with associated frothiness of urine and nocturia. He was found to be hypertensive at presentation with deranged renal function and severe anemia.

This case highlights the importance of early diagnosis of sickle cell nephroapthy and challenges in the management of sickle cell nephropathy.

CASE REPORT

A 37 year old businessman who was referred from sickle cell clinic on account of a 6 week history of bilateral facial and leg swelling. He was apparently well until six weeks prior to presentation when he developed bilateral leg swelling that was insidious in onset, painless and progressively worsened. There was no cough, effort intolerance, orthopnoea or paroxysmal nocturnal dyspnoea.

Facial swelling started about same time, worse in the morning and regressed later in the day. There was associated frothiness of urine, but no haematuria. There was history of nocturia that was noticed about four months prior to presentation. There was no history of diminution in urine output.

He is a known sickle cell anaemia patient who had been apparently stable. His last hospital admission and vaso-occlusive crisis was 12 years prior to presentation. He was not a previously diagnosed hypertensive or diabetic. There was no preceding history of sore throat, skin rash prior

to onset of symptoms. There was no history of chronic use of mercurial soaps, cream or analgesics. There was no history of snake bite, bee or scorpion sting. There was no family history of renal disease, exposure to multiple sexual partners or history suggestive of recurrent urinary tract infections.

There was no history of chronic leg ulcer, blurring of vision or gait abnormality. There was history of recurrent jaundice in the past. There was no history of puritus, hiccough, nausea, vomiting, diarrhea, chest pain, seizures or irrational behavior since onset of symptoms.

He had cholecystectomy 5 years prior to this index illness. He had blood transfusion in childhood. His stable packed cell volume was 18%. He was on folic acid, vitamin B and paludrine but not on hydroxyurea.

He is the 4th of 6 children in a monogamous family. He is married but yet to have children. He does not take alcohol or tobacco in any of form.

On examination, he was a young man who was not in distress, had prognatism and peri-orbital oedema. He was pale, anicteric, acyanosed, not dehydrated and had bilateral pitting oedema up to the knee.

His pulse rate was 90 per minute, blood pressure was 150/70mmHg and jugular venous pressure was not elevated. The apex beat was in the 5th left intercostal space, lateral to mid-clavicular line and heaving. First and second heart sounds only were heard and there was no murmur.

Respiratory rate was 20 cycles per minutes and breath sounds were vesicular without any added sounds. Abdomen was full, moved with respiration. It was soft with no area of tenderness. There

was hepatomegaly with a span of 14 cm. The spleen and kidneys were not palpably enlarged. The neurological examination was essentially normal.

Urinalysis showed amber coloured urine with a pH of 6.0, specific gravity of 1.010. There was ++ proteinuria. Blood, bilirubin and urobilinogen were negative.

An assessment of CKD secondary to sickle cell nephropathy was made.

RESULT OF INVESTIGATIONS

Result of 24 hour urinary protein estimation was 2.5grams, packed cell volume was 15%, the white cell and platelet counts were essentially normal. Peripheral blood film showed a mixed picture of both iron and vitamin B12 deficiency. Hepatitis B, C and retroviral screenings were negative. Serum urea: 60mg/dL, creatinine: 1.5mg/dL, sodium: 140mg/dL, potassium:4.5mmol/dL, chloride:100mg/dL and bicarbonate:22mmol/dL. His estimated GFR using MDRD formula was 63.7 mls/min/1.73m^2. Serum calcium was 8.5mg/dL, phosphate of 5.6mg/dL. Results of fasting serum lipid profile were TC:216 mg/dL, HDL-C:58mg/dL, LDL-C:120mg/dL, TG:190mg/dL. Serum albumin was 3.3g/L, globulin 2.2g/L, and uric acid was 9.1mg/dL. Chest Xray showed cardiomegaly with clear lung fields. ECG showed left ventricular hypertrophy. Renal ultrasound showed enlarged kidneys measuring 13.4cm by 7.4cm and 13.9 cm by 8.cm on the left and right respectively with increased cortical echogenicity and partial loss of cortico-medullary differentiation.

TREATMENT

He was placed on oral lisinopril 2.5 mg o.d, hydroxyurea, vitamin D3 0.5 microgram and calcium carbonate 600mg tds, furosemide 40mg b.d, simvastatin 20 mg nocte, vitamin B complex 1 tablet tds, folic acid 5mg daily, intraveneous iron sucrose 200mg weekly for 5 doses,

subcut erythropoietin (EPO) 4000 units twice weekly. He was also referred to the haematologist for co-management.

He was been followed up in clinic with monitoring of his renal function for about 4 weeks when he later presented in emergency room on account of progressively worsening effort intolerance with associated generalized body weakness. There was no associated jaundice or fever. Examination showed severe pallor, raised jugular venous pressure, first, second and third heart sounds, bi-basal crepitations, tender hepatomegaly with a span of 20cm and ascites. An assessment of sickle cell nephropathy in anaemic heart failure was made. PCV was 8%.

He was admitted and co-managed with haematology unit. He had peripheral blood film that showed paucity of red cells, moderate hypochromia, left shift in the granulocytes with toxic granulations, adequate number of lymphocytes and increased number of platelets. The impression was sepsis with severe anaemia. White cell count was 5000 cells/mm^3 with normal differential counts. He was placed on intravenous ceftriaxone 1g daily for 10days after samples were collected for sepsis work-up and was transfused with two units of packed cells. Blood culture, urine and sputum were taken for MCS and all were negative. He had treatment for malaria with arthemeter-lumefantrine combination following a positive malaria parasite test.

However, his PCV remained persistently below 12% despite the above treatments and he was transfused with 8 units of blood while on admission. He also had his EPO increased stepwisely from 8000 to 18000 units weekly without improvement after completion of antibiotic therapy and the repeated peripheral blood film did not show signs of infection.

On the 4^{th} week of admission, he had a bone marrow biopsy that showed mixed deficiency anaemia. He also had other investigations done: Serum ferritin 546.2ng/L (16-220), serum iron:

35.1 microgram/dl (12-30 microgram/dl), Serum transferrin 1.7 microgram/dl (2.0-3.6 microgram/dl), Serum EPO 63.9 IU(16-220 IU), transferrin saturation was 17.4%. Oral iron supplement was added to his medication and the PCV increased to 20% after 2 weeks. His EPO dose was reduced to 4000 units thrice weekly and subsequently discharged. He was followed up in the outpatient clinic with improvement in his renal function from a GFR of 63.7mls/min/1.73m^2/ to 87.3mls/min/1.73/m^2. He also had sustained improvement in his PCV to a value of 18-20%.

DISCUSSION

Sickle cell nephropathy (SCN) is one of the end-organ complications that may occur in patients with sickle cell disease. Platt et al reported that 18% of deaths could be ascribed to chronic end-organ involvement which predominantly is of renal cause.[1] The prevalence of CKD among SCA patients was reported to be 35.7% by Arogundade et al.[2] This prevalence is likely to increase because SCA patients now survive longer due to availability of better health care services which has led to improvement in their care. The mean age of SCA patients with CKD was reported to be 32.6±3 years by Abdul et al [3] and this was similar to the age of this index patient.

The hallmark of sickle cell nephropathy is a combination of impaired renal concentrating capacity and normal diluting capacity. [4,5] This index patient had a specific gravity of 1.010 which could be explained by impaired concentrating ability. The relative hypoxia and hypertonicity in the renal medulla favour sickling of red cells in the vasa recta. This causes formation of intravascular microthrombi and obstruction of blood flow through the vasa recta; hence, there is impairment of the counter current exchange mechanism.

There is also defective urinary acidification and potassium excretion in the distal tubules probably due to failure to maintain the electrochemical and hydrogen gradient along the collecting ducts resulting from impaired medullary blood flow and hypoxia. There is increase in renal plasma flow and to a lesser extent in GFR due to release of vasodilators such as nitric oxide and prostangladin. The hyperfiltration in the glomeruli leads to glomerulomegaly which causes glomerular injury when it is sustained, resulting in the characteristic focal segmental glomerulosclerosis (FSGS).

Focal segmental glomerulosclerosis was reported as the commonest biopsy proven glomerular disease in SCA patients by Maigne et al, but Arogundade et al reported mesangioproliferative glomerulonephritis (GN) as the commonest glomerular disease in south-west Nigeria[6,2]. Others are thrombotic microangiopathy and less commonly minimal change disease. The classical mesangioproliferative GN is an immune complex disease that is associated with hypocomplementaemia, but this is different from the type found in SCA patients. Fragmented red cells lodge in the glomerular capillaries and they become phagocytosed by the mesangium which leads to mesangial expansion and duplication of the basement membrane.[7] Chronic use of analgesics to relieve pain during vaso-occlusive crises may also contribute to renal disease in them. Sickle cell anaemia patients receive frequent transfusions on account of severe anaemia during periods of crises and these expose them to hepatitis B and C infections which could also contribute to glomerular disease.

The clinical manifestations of sickle cell nephropathy include haematuria, proteinuria, nephrotic syndrome and hypertension. Abdul et al reported haematuria and proteinuria in 27% and 28% of SCA patients respectively while Aleem et al reported a higher prevalence of proteinuria of 41%, but a lower prevalence of haematuria of 8.5% in similar study.[3,8] The causes of non-glomerular

haematuria in SCA patients include papillary necrosis, rupture of congested veins in the renal medulla and rarely, renal medullary carcinoma.

The pathogenesis of albuminuria is not well understood, but it is believed that it may be related to hyperfiltration and subsequent glomerulosclerosis. The severity may range between microalbuminuria to nephrotic syndrome, though the latter is not common. This index patient did not have haematuria but had significant proteinuria of 2.5 g in 24 hour urinary estimation. Hypertension is not a common feature of SCA with or without renal disease. Blood pressure in these patients has been found to be lower than age and sex matched controls without SCA. [9-11] Hypertension is a late feature in the course of sickle cell nephropathy and its presence may signal the onset of severe renal damage. Vasodilatation from release of nitric oxide and prostaglandin, salt and water wasting due to medullary defect and reduced vascular reactivity which occur in SCA account for relative resistance to development of hypertension in them. This patient presented with hypertension which may be explained by the presence of chronic kidney disease .

Serum creatinine is not a reliable marker for evaluating renal function in SCA patients because they have reduced muscle mass and also have significant tubular secretion of creatinine, hence it overestimate glomerular filtration rate when used. The estimated GFR in this patient was 63.7 mls/min/1.73m^2 at presentation, which may actually be an overestimation of the true GFR. Cystatin C may be a more reliable marker for assessing glomerular filtration rate in them, though this is not yet validated, not readily available and very expensive.

The management of CKD in SCA patients is similar to CKD from other causes except for anaemia management. The use of ACEI or ARB in combination with low dietary protein and salt

are renoprotective just like in other causes of proteinuric CKD. Hydroxyurea has been found to prevent worsening proteinuria when used in combination with ACEI.[12,13] Arogunadade et al reported a reduction in proteinuria and improvement in GFR in SCA patients after treatment with telmisartan which is an ARB without compromising the blood pressure.[14] This may also be a pointer to the fact that glomerular hypertension may be one of the pathogenetic mechanism to development of albuminuria and progressive renal damage in this patients. This patient had improvement from an initial GFR of 63.7mls/min/1.73m^2 to 87.3mls/min/1.73m^2 after about 3 months of therapy with lisinopril and hydroxyurea.

Management of anemia in sickle cell nephropathy may be challenging as seen in this index patient. The target goal for anaemia treatment in SCA patients is to achieve the stable haemtocrit before the onset of CKD which is usually less than 30% compared to 33-36 % in ESRD from other causes. The treatment goal is usually difficult to achieve due to the presence of ineffective erythropoiesis seen in SCA patients. Sickle cell anaemia patients with normal renal function have been found to require higher doses of erythropoietin in range similar to that required in ESRD from other causes. [14] This index patient required higher dose of erythropoietin before achieving the target packed cell volume. Erythropoeitin has been found to be useful in anemia treatment of SCA patients with renal failure.[15] This index patient had functional iron deficiency suggested by high ferritin level with reduced transferrin saturation which responded to oral iron supplements.

Renal transplant is a viable treatment option for SCA patients with ESRD. It has been reported that SCA patients who had renal transplant had better survival rate than those on chronic dialysis.[16] Both graft and patient's survival compare favorably after transplant in patients with

ESRD from sickle cell anaemia and other causes.[17] The prevalence of vaso-occlusive crises may also increase in post-renal transplant SCA patients due to increase in haematocrit value.

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CASE FIVE

Central Venous Catheter Infection in a 68 year old Diabetic patient on Maintenance Haemodialysis

CASE SUMMARY

A 68 year old diabetic Filipino female on maintenance haemodialysis presenting with one week history of high grade fever associated with vomiting. There was no associated cough, chest pain, dysuria, urinary frequency or discharge from her catheter exit site. She has been using a tunneled catheter for dialysis after a failed arteriovenous fistula creation for about 4 months. She had a positive catheter blood culture and improved with antibiotic therapy.

This case highlights the importance of care of central catheters in CKD patients, early diagnosis and treatment of catheter related infections in preventing associated morbidity and mortality.

CASE REPORT

A 68 year old female Phillipino patient who has been on maintenance haemodialysis for 4 months complained of fever of a week duration. She was apparently well until one week before she presented with high grade fever, associated with chills and rigor. Fever was relieved by taking paracetamol. Fever was noticed to start about one hour into commencing dialysis. There was associated vomiting of recently ingested food. She had similar presentation in her last two dialysis sessions. There was no similar experience of fever in other patients on dialysis in the same dialysis unit during this period. There was no history suggestive of previous reaction to dialyzer or blood line in the past. There was no headache, body aches, but there was associated malaise. There was no history of cough, breathing difficulty or pleuritic chest pain. There was no

associated dysuria, urinary frequency or loin pain. There was no abdominal pain or passage of watery stool. There was no pain in any of her joints. There was no sore throat or pain with swallowing.

She has been using a tunneled catheter in the right internal jugular vein as vascular access for haemodialysis for about 4 months after a failed attempt at creation an AV vistula. There was no purulent discharge from the catheter or around the exit site. She was not on antibiotic lock after dialysis, but used mupirocin cream over the exit site.

She is a known diabetic of about 25 years and hypertensive of 10 years duration. She is not on any form of immunosupressants. There was no history of catheter infection in the past. She claimed that she adhered strictly to instructions given concerning care of her tunnel line.

There was no history of easy fatigability, orthopnoea or paroxysmal nocturnal dyspnoea since onset of fever. There was no history of blurring of vision, noticeable swelling on her fingers since onset of her symptoms.

She does not smoke or take alcohol. She was compliant with her antihypertensive medications. Her glycaemic control has been good since commencement of dialysis without using glucose lowering agents which were discontinued on account of recurrent hypoglycaemia. There is no previous history of allergy in her or family history of atopy.

EXAMINATION

Clinical examination revealed an elderly woman, who was acutely ill looking, febrile and had temperature of 39^0 C, not pale, anicteric, acyanosed, not dehydrated. There was no finger

clubbing or generalized lymphadenopathy. She had mild bilateral pitting oedema up to the middle of her legs. Examination of the mouth did not show inflammed tonsils.

There were no sign of inflammation or discharge around the exit site of the central catheter.

Her pulse was 104 beats per minutes, regular, normal volume. Jugular venous pressure was not elevated, apex beat was at the 6^{th} left intercostal space, lateral to mid clavicular line, heaving. She had first, second and fourth heart sounds. There was no murmur.

Respiratory rate was 24 cycles per minute and breath sounds were vesicular in all lung zones. The abdomen was full, moves with respiration. There was no area of tenderness and organs were not palpably enlarged. Neurological examination was essentially normal.

An assessment of Sepsis ? focus in a patient with ESRD was made.

RESULT OF INVESTIGATIONS

Blood film for malaria parasite was negative, full blood count showed a total white cell count of 15,300 cells/mm^3 (with differential of 88.7% granulocytes, 2% monocyte and 9.3% lymphocyte), heamatocrit of 33.8%, platelet count of146,000 cells/mm^3 and ESR was 110mm/hr. Peripheral blood film showed numerous toxic granulations with a left shift. Urine and sputum culture did not yield any growth.

Chest Xray showed normal lung fields, aortic unfolding and cardiomegaly

She was commenced on Ceftriaxone 1g daily, metronidazole 500mg 8 hrly while awaiting the results of blood culture. Blood culture of central catheter blood yielded significant growth of Staphyloccocus aureus that was sensitive to vancomycin. The blood culture from peripheral vein

did not yield any growth. Following further review with blood culture results, a diagnosis of central venous catheter infection was made.

Echocardiography was done and showed a large heart with an ejection fraction of 55%. There was concentric left ventricular hypertrophy with thickened pericardium. There were no valvular abnormalities or vegetations.

She was commenced on intravenous vancomycin 1g in the last l hr of haemodialysis session for the first dose and 500mg in subsequent doses. This was combined with 1g of intravenous ceftazidine after each session of dialysis. She had the antibiotic therapy for 3 weeks with improvement evidenced by improvement in clinical state, resolution of fever, reduction of ESR from 110 mm/hr to 40 mm/hr, reduction in total white cell count from 15,300 cells/mm^3 to 7400cells/mm^3 and a repeat blood culture that was negative. Central venous catheter salvage was achieved in this patient and her subsequent dialysis sessions were without fever, chill and rigor. She is presently in Philippines for a renal transplant.

DISCUSSION

Infection is the second commonest cause of morbidity and mortality in ESRD patients on haemodialysis after cardiovascular disease.[1] Central catheter related infection is a major source of infection in these group of patients. In Nigeria, the major vascular access for haemodialysis in ESRD patients are both the temporary and permanent catheters,[2] hence the burden of catheter related infections is likely to be high in our patients even though no study has been done in this area .

Awobusyi et al found that the C-reactive protein was significantly elevated in ESRD patients on chronic haemodialysis compared to normal controls with infections as a probable contributor to

inflammation.[3] It was reported that patients with central venous catheters have an increased relative mortality risk of 3.4 compared with patients with AVfistulas. [4] Switching from central venous catheters to AV fistulas decreases the relative mortality risk to 1.4. [4] The most likely explanation for this increased mortality risk is infection and sepsis related to the central venous catheter, including exit site infection. Typical infection rates are 3 episodes of infection per 1000 tunneled catheter–days and these are higher with non-tunneled catheters.[5] The prevalence of haemodialysis catheter infections was reported to be 19.3% in a prospective study by Nabi et al while Dahlberg et al reported a lower prevalence of 9.4%.[6,7]

The major route of central catheter infection is through the catheter hub and lumen. When these catheters are inserted, there is formation of fibrin in the lumen and external surface of the catheter to which microoraganisms attach, hence establishing colonization. Some microbes such as staphylococcus aureus and candida form a layer of slime over it known as biofilm which serves as a protective barrier from the effects of antibiotic therapy.

Factors that predisposes to catheter infections in renal failure patients are uraemia, DM, immunosuppressive therapy, malignancy, prolonged stay of catheters, nasal carriage of staphylococcus by patients and attending health workers, poor hygiene in patients, non compliance to aseptic technique during catheter insertion and use, type of catheters and the location of the catheters. The possible predisposing factors in this index patients are DM, elderly age, non- use of antibiotic lock solutions after each session of dialysis.

The clinical manifestations of catheter-related blood stream infections are fever, redness, tenderness at catheter site, features of systemic inflammatory response and in some severe cases, septic shock. This index patient had history of fever with associated tachycardia and tachypnoea which usually started few hours into dialysis and get relieved by taking paracetamol. There was

no similar history in other patients who were on dialysis in the same unit and she has been dialysing in the unit for about four months without similar complaints. The history in this patient supported a probable line infection and not contaminated dialysis water or allergic reaction to dialysate, dialyzer or blood line. Other common source of infections like UTI, cellulitis, and pneumonia were also ruled out.

The common organisms implicated in haemodialysis catheter infections are staphylococcus aureus, staphylococcuc epidermidis, gram negative bacillus like eschericia coli and candida species. Patil et al reported stapyloccoccus epidermidis as the commonest isolate in patients with central catheter infections admitted into intensive care unit.[8] Staphylococcus species were the commonest isolate in a similar study conducted on haemodialysis patients.[6] Marcos et al reported that the prevalence of gram negative organism increased significantly from 4.7% to 40.2 % between 1991 and 2008 in patients with central catheters.[9] Abdul Gafor et al reported gram negative bacteria and staphylococcus species as the commonest isolate in HD catheters.[10] Catheter colonization could occur in HD patients without clinical manifestations and this was seen in between 21.6% of HD catheters.[7]

The diagnosis is based on presence of infection in a patient that has a central venous catheter where other possible sources of infection have been ruled out in the presence of a positive blood culture. Method of diagnosis includes catheter tip culture, quantitative blood cultures and differential time culture of the catheter and peripheral site. Two paired samples from catheter and peripheral sites should be taken as done in this index patient. The catheter blood culture yielded growth of Staphylococcus aureus sensitive to vancomycin.

Management of catheter related blood stream infection involves timely commencement of broad spectrum antibiotics to cover both gram negative organism and methicillin resistant staphylococcus specie while awaiting culture result. The type of antibiotic to be used could also be guided by centre based local experience of antibiotic sensitivity pattern. The index patient was placed on vancomycin and ceftazidime for 3weeks. The duration of the antibiotic treatment is 2-3 weeks for uncomplicated infection and may be up to 6 weeks in the presence of complications like septic arthritis or infective endocarditis. Catheter removal is also recommended in the presence of severe infection, complications like abcesses and in severely ill patients. Catheter salvage was achieved in this index patient probably because of early diagnosis and institution of treatment, absence of complications and good response to treatment.

Central catheter related infections may lead to various complications in HD patients such as infective endocarditis, septic pulmonary embolic, osteomyelitis, metastatic abscesses to distant organs like brain, kidneys, liver, lungs, spleen and bones. The index patient was assessed for some of these complications which were absent.

Significant reduction in HD central catheters related infections could be achieved through strict adherence to aseptic technique in handling these catheters, use of antibiotic solution lock, preferential use of 2% chlorhexidine in skin preparation. [11,12] Nabi et al reported that the nasal carriage rate of staphylococcus aureus in HD patients was 35%.[6] Boelaert et al reported eradication of staphylococcus aureus in 96.3% of patients with nasal carriage following the use of mupirocin ointment and a four-fold decrease in the incidence of Staphylococcus aureus bacteraemia.[13]

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CASE SIX

Obstructive Nephropathy secondary to Uterine cancer a in 61 year old female

SUMMARY

A 61 year old female who presented with abdominal pain and swelling of 4 weeks duration, oliguria of a week duration. There was associated weight loss. She was not previously diagnosed hypertensive or diabetic. A diagnosis of obstructive nephropathy secondary to uterine cancer was made. She was co-managed with urology team with improvement of her renal function after nephrostomy was done without requiring dialytic therapy.

This case highlights the importance of early diagnosis and intervention in the management obstructive nephropathy.

CASE REPORT

A 61year old female who m n presented with abdominal pain and abdominal swelling of 4 weeks and one week history of oliguria. She was apparently healthy until when abdominal pain started 4 weeks prior to presentation. Pain was colicky and located in the lower abdomen. Pain was moderate in severity, radiating to the waist. There was no pain in the other part of her body. There was no associated aggravating or relieving factors.

Progressive abdominal swelling started about the same time. There was no vomiting or change in her usual bowel habit. There was associated anorexia and weight loss. There was no associated vaginal bleeding either spontaneously or following coitus. There was however, history of foul smelling vaginal discharge that occured occasionally.

Progressive diminution in urine output started a week prior to presentation with associated bilateral leg swelling. Her urinary output was less than 200mls at the time of presentation despite

adequate water intake. There was no history suggestive of fluid loss prior to onset of oliguria. There was no facial swelling, frothiness of urine or haematuria.

She was not a previously diagnosed hypertensive or diabetic. She was not a known SCA patient. There was no history of chronic use of analgesics, herbal medications, mercury containing soaps or cream. There was no associated cough, breathlessness, jaundice or right hypochondrial pain. There was no history of puritus, hiccough, irrational behavior or seizures following onset of oliguria. She had 10 deliveries by spontaneous vaginal delivery in the past. There was no previous history of cancer in her or her family members. There was no history of oral contraceptive pill use. She does not take alcohol or tobacco in any form. She was not on any medication for any medical nor surgical condition.

EXAMINATION

Examination showed an obese middle aged woman, not in distress, afebrile, pale, anicteric, acyanosed, dehydrated. She had bilateral pitting ankle oedema.

Pulse rate was 98 per minutes, regular, normal volume. Blood pressure was 170/100 mmHg, jugular venous pressure was not elevated. Apex beat was in the 5^{th} left intercostal space and not heaving. Heart sounds were 1 and 2 only.

Respiratory rate was 20 cycles per minute and chest was clinically clear.

Abdomen was distended, soft and moved with respiration. There was lower abdominal tenderness. There was a pelvic mass measuring about 12cm by 6cm. It was firm, nodular. Liver, spleen and kidneys were not palpable. There was ascites.

Rectal examination was normal. The vulva and vagina, cervix were grossly normal and pouch of Douglas was free.

Neurological examination was essentially normal and there was no asterixis.

Urinalysis showed pH of 6.0, S.G of 1.010. Proteinuria, haematuria and glycosuria were negative.

Assessment of acute kidney injury secondary to obstructive nephropathy from a ? pelvic malignancy and moderate hypertension were made.

RESULT OF INVESTIGATIONS

Urine microscopy only showed few epithelial cells/hpf. Packed cell volume:24%, total white blood count of 10,100cells/mm^3 with differential of 60% granulocyte and 40% lymphocyte. platelet count:226,000cells/mm^3 , peripheral blood film showed normochromic normocytic anaemia. Hepatitis B, C and HIV screening were negative. Random blood sugar:108mg/dL

Electrolyte, urea and creatinine result done: serum urea 183mg/dL, creatinine 3.3mg/dL, sodium: 136mmol/L, potassium 6.5mmol/L, chloride 110 mmol/L, bicarbonate 18mmo/L. Estimated GFR at presentation was 18.3mls/min/m^2. TC:141mg/dL, HDL-C:46mg/dL, LDL-C 71mg/L, TG: 119mg/dL.

Abdomino-pelvic ultrasound showed enlarged uterus measuring 15.1x8.6x12.1 cm containing a heterogeneous mass measuring 12.1x6.8cm. Both kidneys were enlarged measuring 14.5x6.8cm and 13.7x6.8cm for the right and left kidneys respectively with evidence of hydronephrosis. Both kidneys showed increase echogenicity and loss of cortical medullary differentiation. There was gross ascites and other organs were normal. The ultrasound conclusion was uterine mass ? malignancy with evidence of obstructive uropathy.

ECG and Chest Xray were essentially normal. Cytology of ascitic fluid showed haemorrhagic smear containing clumps of atypical polygonal epithelial with large pleomorphic nuclei.

Pelvic computed tomography scan showed enlarged para-ortic lymph nodes, ascites, uterine masses with malignant features.

TREATMENT

She had urgent correction of hyperkalaemia with 50 mls of 10% dextrose with 5 units of soluble insulin infusion after giving 10mls of 10% calcium gluconate slowly over 10 minutes. The repeat electrolytes showed normal serum potassium. She was also transfused with 2 units of packed red cells. She was placed on antihypertensive; amlodipine 10mg daily. She was co-managed with urologist and gynaecologist.

She had percutaneous nephrostomy done by urologist on the second day of admission under ultrasound guidiance. She had post-obstruction diuresis after the nephrostomy tube was passed. Fluid input and output were strictly monitored. Daily fluid intake was restricted to 1.2 litres in addition to previous day's output. There was a steady improvement in her renal function without dialytic intervention.

	DAY 1	DAY1*	DAY2	DAY 3	DAY 5	DAY7	DAY9
Urea (mg/dl)	183	180	163	100	50	40	43
Creatinine (mg/dl)	3.3	3.2	2.8	1.8	1.1	0.8	0.7
Sodium (mmol/L)	136	135	137	136	140	138	135
Potassium (mmol/L)	6.5	4.0	3.8	4.0	3.7	3.9	3.5
Chloride (mmol/L)	110	100	96	102	100	98	99
Bicarbonate (mmol/L)	18	25	28	23	25	28	29
Input (ml)		2000	1300	5000	4400	4000	3000
Output (ml)		170	5650	4100	3250	2100	1550

* After correction of hyperkalaemia

She had explorative laparotomy on the 14th day of admission and subtotal hysterectomy was done. Intra-operative findings were enlarged multinodular uterus with necrotic debris, poorly defined ovaries and tubes. There were obvious tumour nodules on the mesentery, bladder, liver, spleen and parietal peritoneum. Histology of uterine tissue showed features of adenocarcinoma. She was subsequently discharged and referred for follow-up radiotherapy treatment.

DISCUSSION

Obstructive uropathy refers to structural or functional changes in the urinary tract that impede normal urine flow. Obstructive nephropathy refers to the renal disease caused by impaired flow of urine or tubular fluid. Hydronephrosis refers to dilatation of urinary tract and it is not synonymous to obstructive uropathy as it can be present without a functional obstruction. Likewise, there can be obstruction without hydronephrosis. It is the fourth common cause of CKD in Nigeria after chronic glomerulonephritis, hypertension and diabetes mellitus [1,2] It is the leading cause of ESRD in paediatric age group in North America. [3] In Europe, obstructive uropathy accounts for 3-5% of ESRD in patients older than 65 years, with prostatic disease accounting for majority of cases.[4] It occurs across all age group, but its aetiology and frequency vary with age and gender. The prevalence of hydronephrosis at autopsy was found to be between 3.5-3.8% in a study done by Bell. [5] It is commoner in females in the middle age group where pregnancies and gynaecologic malignancies are the leading causes as seen in this index patient. Other causes of obstructive uropathy are stones, blood clot, neurogenic bladder, vesicoureteral reflux, diabetes mellitus, Parkinson disease, retroperitoneal fibrosis, lymhomas fungal balls, infections such as schistosomiasis, tuberculosis. Obstructive uropathy can be further classified into complete or partial, lower or upper, congenital or acquired, intrinsic or extrinsic.

Obstruction along the urinary tract causes profound functional and structural changes in the kidney.[6] Initially, changes are functional and potentially reversible, but may progress to structural changes that are irreversible if underlying cause is not addressed. Obstruction in the kidney affects both glomerular haemodynamics and tubular function.[7]

Glomerular filtration rate declines progressively after the onset of complete ureteral obstruction. Following obstruction, there is an increase in proximal tubular pressure and at the same time,

vasodilatory substances such as prostaglandin E2 and prostacyclin are released leading to efferent arteriolar dilatation. The increase in the glomerular pressure is not sufficient to overcome the tubular pressure, hence GFR declines. Intra-renal angiotensin II generation occurs secondary to an increase in renin release either through reduced delivery of sodium chloride to the distal nephron or through reduction in transmural pressure at the barroreceptor as a consequence of prostangladin dependent afferent arteriolar dilatation. Intra-renal vasoconstriction occurs due to generation of angiotensin II, thromboxane A2, antidiuretic hormone and decreased nitric oxide production. Angiotensin II and thromboxane A2 may also reduce ultrafiltration coefficient.[7,8]

Early tubular change that occur in obstructive uropathy is loss of ability to concentrate urine due to loss of medullary tonicity from reduced medullary blood flow, overall decrease in GFR and reduced expression of sodium transporter.[9] This might account for the low specific gravity of 1.00 seen in this patient. There is also decrease in the response of collecting ducts to antidiuretic due to reduced expression of aquaporins that results from cyclooxygenase activity and angoitensin II. [10,11]

Acidification of urine is also affected because of the defects in bicarbonate absorption in proximal tubules and or defect in hydrogen ATPase activity of the alpha intercalated cells that follow ureteral obstruction resulting to hyperkalaemia. This could have also contributed to severe hyperkalaemia seen in this patient.

The clinical features depend on the site, degree and duration of obstruction. Pain may occur in acute urinary obstruction or may be due to underlying cause like stones. The abdominal pain in this index patient was most likely due to the pelvic tumour she had. Lower urinary tract symptoms such as poor stream, intermittency, hesistancy or nocturia occur in bladder neck

lesions. Urinary tract infection may occur due to urinary stasis and if this become recurrent in the presence of urease producing organisms such as Proteus mirabilis, staghorn stones may be formed in the renal pelvis. There were no signs of UTI or stones in this patient probably because the obstruction was not so prolonged. Haematuria may occur due to aetiology of obstruction such as stones and malignancy. Changes in urinary output such as oliguria or anuria in complete obstruction and polyuria in partial obstruction usually occur. This patient had oliguria which was suggestive of complete or bilateral obstruction.

Blood pressure changes also occurs in obstructive uropathy. Hypertension may result from impaired sodium excretion, volume expansion and increase renin release. This could possibly explain or contribute to the new onset hypertension in this patient. Hypotension may be seen in partial obstruction where polyuria has led to volume depletion and severe dehydration. Secondary polycythemia may occur in obstructive nephropathy due to increased erythropoietin production. This patient was anaemic with the peripheral blood film suggestive of anaemia of chronic disease. The underlying uterine malignancy may be responsible for the anaemia in this index patient.

Prompt diagnosis of obstructive uropathy is essential in order to prevent irreversible damage to the kidneys. High index of suspicion based on the history and physical examination of the patient are essential. Ultrasound is the most widely used imaging modality. It defines renal size and is able demonstrate calyceal dilatation as seen in this patient, however it is operator dependent. It is preferred in children and pregnant woman where radiation should be avoided as much as possible. Its sensitivity for diagnosis in obstructive uropathy can be improved by measuring the resistive index with colour doppler ultrasound.[12] A value greater than 0.7 reflects increased vascular resistance present in obstruction and effectively discriminate between obstructed and

non obstructed kidneys. Computed tomography and magnetic resonance imaging are useful in accurate diagnosis of the site and cause of obstruction, but availability, cost and expertise are major constraints in our environment. This patient had a pelvic CT scan that was helpful in diagnosing the cause of the obstruction and planning of the definitive treatment which was surgical. Other useful investigations are intravenous urography, plain abdominal Xray, retrograde pyelography, diuresis renography and urodynamic and pressure flow studies.

Choice of treatment depends on the location, aetiology of obstruction and severity of renal impairment if present. Early relief of obstruction is key to restoration and preservation of renal function. This patient had percutaneous nephrostomy done by the urologist and she had improvement in her renal function. Renal replacement therapy may be indicated in severe renal impairment, but this patient responded well with conservative treatment. Hyperkalaemia is a common electrolyte abnormality in patients with obstructive uropathy due to associated type 4 renal tubular acidosis, hence this should be corrected urgently to prevent cardiac arrest. This patient had severe hyperkaelemia that was also urgently corrected with dextrose insulin infusion. Postobstructive diuresis commonly follows relief of obstruction if it is bilateral and this is rarely seen in unilateral obstruction.[13] There is need for anticipated and careful monitoring with adequate fluid repletion if this occurs. The index patient had postobstructive diuresis and subsequently had adequate fluid repletion. However, overzealous fluid administration should be avoided because it may prevent the kidney from recovering its concentrating ability.

Definitive treatment involves removal of the cause of the obstruction as done in this patient who had subtotal hysterectomy and subsequently regained her renal function.

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CASE SEVEN

Lupus Nephritis in a 20 year old Female

SUMMARY

A twenty year old female who was referred to renal clinic with suspicion of systemic lupus erythematosis (SLE). She developed new onset hypertension, nephrotic range proteinuria and deranged renal function while on follow up. A diagnosis of lupus nephritis class III was made following renal biopsy. She was treated for proliferative lupus nephritis with achievement of remission.

This case highlights the need for regular monitoring of renal function in apparently clinically stable lupus patients and the role of renal biopsy and immunosuppressants in management of lupus nephritis.

CASE REPORT

A 20 year old female student who was referred to the renal clinic from the general practice clinic on account of recurrent joint pains of four months duration. She was apparently well until 4 months before presentation when she developed joint pains affecting the fingers, wrist, elbows and knees bilaterally. There was associated joint swellings but no joint deformities. There was associated low grade fever which was relieved by taking paracetamol. There was no preceeding history of trauma to the affected joints

There was no history of headaches, seizures or irrational behavior in the past. There was no history of facial rash, photosensitive rash or hair loss. There was history of recurrent mouth ulcers. There was no history of chest pain, breathlessness or easy fatigability. There was no

history of facial puffiness, leg swelling, frothiness of urine, nocturia or haematuria. There was no history of easy bruising or recurrent sore throat.

There was no family history of similar condition. She had been amenorrhoeic since onset of her symptoms, however she was not sexually active. She does not smoke or take alcohol. She is not a sickle cell disease patient.

She took analgesics to relieve her joint pains, but the improvement was short lived. She presented in general practice clinic where lupus erythematosus (LE) cells was found to be positive and she was subsequently referred to the renal clinic.

Examination showed a young female, who was not in distress, afebrile, pale, anicteric, acyanosed. There was no peripheral lymphadenopathy, finger clubbing or pedal swelling

Joint examination showed swollen, tender wrist joints with no differential warmth or deformity. Her pulse rate was 92 per minutes, regular, normal volume. Jugular venous pressure was not elevated and blood pressure was 120/70 mmHg supine. The apex beat was in the 5^{th} left intercostal space, mid-clavicular line, non-heaving and heart sounds were normal. Respiratory rate was 20 cycles per minute and chest was clinically clear.

The abdomen was full, soft, moved with respiration with no area of tenderness. The liver, spleen and kidneys were not palpably enlarged. The neurological examination was essentially normal.

Urinalysis showed amber coloured urine with a pH of 6.0, specific gravity of 1.020, albumin: negative, glucose: negative, blood: negative.

An assessment of SLE was made.

RESULT OF INVESTIGATIONS

Result of investigations showed total white cell count of 3,400 cells/mm^3 with normal differential count, packed cell volume of 29%, platelet count of 20,200 cells/mm^3 . Serum urea was 23mg/dl, creatinine was 1.1 mg/dl with normal electrolytes. LE cell was positive. Anti-nuclear antibody was positive with a speckled pattern of appearance and anti-double stranded DNA was also positive. Corrected serum calcium was 7.9mg/dl and phosphate was 4.1mg/dl Total serum protein was 7.7g/l, albumin was 4g/l, globulin was 3.7g/. Total bilirubin was 1mg/dl, aspartate transaminase was 7IU/l, alanine transaminase 40IU/l and alkaline phosphatase was 37 IU/l. This liver function test was essentially normal.

The renal ultrasound scan showed normal sized kidneys with normal cortical echogenicity and cortico-medullary differentiation. The right kidney measured 10.0 cm by 4.5 cm while the left kidney measured 10.3cm by 5.0cm

She was placed on tab prednisolone 30mg daily, azathioprine 50mg daily, hydroxychloroquine 100mg BD, and a short course of diclofenac. She was followed up in clinic and the prednisolone was tapered down to 10mg daily and also her normal menstrual cycle started again. However, she developed blistering rash over the face and was subsequently reviewed by the consultant rheumatologist who made an assessment of Rowell syndrome. Dapsone was added to her medications with improvement.

After about 1 year of follow up, she was noticed to be having persistent proteinuria and elevated blood pressure of 150/100mmHg. Spot urinalysis showed proteinuria and haematuria. A 24-hour quantification of urinary protein showed 4g / 24 hours. Serum urea was 55mg/dl and creatinine was 1.5mg/dl with normal electrolytes. An assessment of lupus nephritis was made. She was

worked up for renal biopsy which showed focal and segmental proliferative lesion. There were also focal areas of mild to moderate chronic inflammatory cell infiltrate in the interstitium. A diagnosis of lupus nephritis class 3 was made.

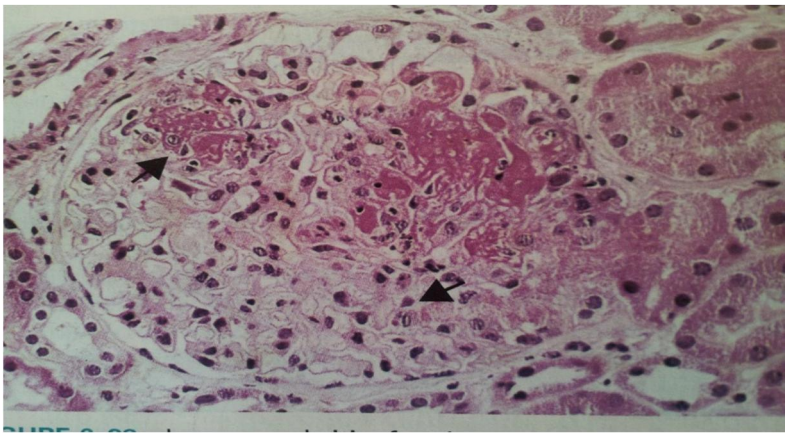

Figure 2: A micrograph showing focal proliferative lupus nephritis (x100)

She was counseled along with her parents on the diagnosis, course of disease and treatment options available. She was commenced on tab mycophenolate mofetil 1g BD, lisinopril 5mg, prednisolone 50mg daily, rabeprazole 20 mg daily after anti-helminthic therapy with tab mebendazole 100mg BD for 3 days. She was placed on low protein and salt diet. She was followed up with fasting blood glucose, full blood count and urinary protein estimation on a monthly basis. She achieved remission at 4th month of the induction phase with a reduction in 24 hour urinary protein to a value of 420 mg and a reduction in serum urea and creatinine to 40mg/dl and 0.9mg/dl respectively. The prednisolone was tapered down to 10 mg daily and she had 50mg of azathioprine added as maintenance therapy while mycophenolate mofetil (MMF) was discontinued. She is presently being seen on follow up clinic.

DISCUSSION

Systemic lupus erythematosus is a complex autoimmune disease that is characterized by multi-systemic manifestations and varied laboratory test abnormalities. Adelowo et al reported that SLE was not as rare in black African as formerly thought.[1] They reported the prevalence of SLE to be 5.3% out of a total of 1250 cases seen in a rheumatologic clinic in Nigeria and a male to female ratio of 1.2:9 [2]

The pathogenesis is not completely understood, but it is multi-factorial and involves the interplay of genetic predisposition, race, environmental factors such as ultraviolet rays and drugs. These provoke excessive apoptosis or defective clearance of apoptotic bodies and release of nuclear antigens from the host cells. This creates an enabling environment for excessive nuclear antigens to drive autoimmune responses and create pathogenic circulating immune complexes.

Lupus nephritis (LN) is a common and serious feature of SLE. The incidence and prevalence of LN are influenced by age, gender, ethnicity, geographic region, diagnostic criteria employed and method of ascertainment. The kidneys were found to be the second commonest organ affected in admitted cases of SLE in Ogun State, southwest Nigeria with most occurring 2-5 years after diagnosis of SLE.[3] The prevalence of biopsy proven LN in United Kingdom was found to be 4.4/100,000 population and it was five times commoner in females compared to males.[4] Lupus nephritis is more severe in children and men. The other risk factors are family history of SLE, longer duration of disease, presence of more American College of Rheumatology (ACR) criteria, younger age and hypertension. Arogundade et al reported that the mean age of patients with LN in Nigeria was 28.73±11.78 years while Ayodele et al also reported a similar mean age of

31.6±11.78 years in South Africans with LN.[5,6] In agreement with above reports, this index patient was 21 year old.

The diagnosis of SLE is based on the presence of four or more criteria defined by the ACR.[7] These include malar rash, discoid rash, photosensitivity, oral ulcers, non-erosive arthritis, serositis, renal disease, neurologic, haematological disorder (haemolytic anaemia, leucopenia, thrombocytopenia), immunological disorders (anti-double stranded DNA, anti-Sm antibody) as well as antinuclear antibodies (ANA). This index patient met four out of the 11 criteria, hence diagnosis of SLE was made.

The pathogenesis of LN involves formation of auto-antibodies that are directly pathogenic or formation of circulating antigen-antibody complexes that deposit in the kidneys to incite inflammatory responses through complement-mediated damages, activation of pro-coagulant factors, leukocyte infiltration and release of proteolytic enzymes. Intra-glomerular hypertension and activation of coagulation cascade also contribute to glomerular injury. The localization of immune complex in the glomerulus is influenced by the size, charge, avidity, clearing ability of the mesangium and local haemodynamics. The immune complex hence could be sub-epithelial or sub-endothelial in location. In addition to glomerular injury, there could also be tubulointerstitial disease or rarely necrotizing vasculitis.

The clinical manifestations of LN are proteinuria in 100%, haematuria in 60%, cellular cast in 30%, reduced renal function in 40-80%, hypertension in 15-50%, hyperkalaemia in 15% and tubular abnormalities in 60-80% of patients.[8] This index patient presented with proteinuria, hypertension and reduced renal function. About 30-50% of SLE patients will develop clinically evident renal disease at presentation while 60% will develop renal complication on follow up. [8,9]

This index patient developed LN about a year after being diagnosed of SLE. Systemic lupus erythematosus can affect any part of the kidneys, but the glomerulus is the most studied component. The glomerular lesion that is predominant may also transform with time.

Anti-Sm antibodies are strongly associated with the diagnosis of LN, but only present in 25-30% of patients. The titres of dsDNA antibodies can be used to follow the course of LN. AntiC1q antibodies are more closely associated with activity of LN than anti-dsDNA antibodies and may play a prognostic role in follow up of LN patients.[10] Due to financial constraint in this patient , only ANA and Anti-dsDNA were done in this index patients and these serology markers were not used to follow up her treatment for LN.

The World Health Organization classification for LN was used for many years, but this has been replaced by the International Society of Nephrology/Renal Pathology Society classification (ISN/RPS) which has refined and clarified some of the deficiencies of the former.[11] It is based on light microscopy, immunofluorescence and electron microscopy findings. Inter-observer reproducibility and the predictive value has also been improved.[12] It has been shown that the glomerular lesion correlates well with the presentation, course and treatment. In this index patient a proliferative LN was suspected on clinically before a biopsy was done because the patient had hypertension, nephrotic range proteinuria, haematuria and reduced renal function and this was also confirmed on renal biopsy.

ISN-RPS 2004 classification is shown below:

Class I : Minimal mesangial LN; normal glomeruli on light microscopy, but mesangial immune deposit by immunoflourescence

Class II: Mesangial proliferative LN; mesangial hypercellularity with mesangial immune deposit

Class III: Focal LN

IIIA: Purely active lesion

IIIA/C: Acute and chronic lesion

III C: Chronic inactive lesion

Class IV: Diffuse LN

IVA: Purely active lesion

IVA/C: Acute and chronic lesion

IV C: Chronic inactive lesion

Class V: Membranous LN

Class VI: Advanced sclerosing LN

Treatment of proliferative LN as seen in this patient involves 2 phases; induction and maintenance phases. The induction phase involves the use of high dose steroid which is tapered off over the months as used in this index patient in combination with either cyclophosphamide or MMF. The aim of induction therapy is to achieve remission which is defined as reduction of proteinuria to < 1g/ 24 hours or reduction in serum creatinine. There have been studies that compared the efficacy of cyclophosphamide and MMF as induction therapy and also to compare oral and intravenous cyclcophophamide using various treatment regimens.[13,14] The cumulative dose in oral regimen is more compared to the parenteral regimen and the outcome with low dose cyclophosphamide is as good as the high dose regimen.[13] It was found that MMF was not superior to cyclophosphamide in the management of LN. [14] MMF was preferentially used in this

index patient because it had a better safety profile compared to cyclophosphamide, even though more expensive. Common side effects of MMF are gastrointestinal symptoms which were not seen in the index patient. Houssiau et al reported that early response to immunosuppressive therapy predicts good renal outcome in LN in the follow up of Euro-Lupus Nephritis Trial.[13] The overall renal outcome of this patient is likely to be good because she achieved remission at the 4th month of induction phase. Rituximab has been found to be useful in achieving remission in those that have failed with both cyclophosphamide and MMF.[15]

Drugs useful in the maintenance phase of treatment are azathioprine, MMF, cyclophosphamide. Azathioprine was used in this patient because of cost, good safety profile and efficacy. Monthly full blood count was used to monitor this patient for leucopenia and macrocytosis which could occur with long term treatment on azathioprine. Azathioprine does not have teratogenic effects, hence it is the preferred option in women with lupus who are in child bearing age like this patient or desirous of pregnancy.

Other medications given to this index patient include lisinopril which had both antihypertensive and anti-proteinuric effects which were desired in this patient. Blood pressure control was an integral part of management of this index patient and the aim was a target blood pressure of 130/80mmHg which was achieved in this patient. A regular fasting blood glucose was done for this patient to detect steroid-induced hyperglyaceamia which did not occur in her.

End-stage renal disease has been shown to occur in about 10-15% of patients with lupus nephritis and outcome of those on dialysis is comparable to those with ESRD from other aetiologies.[16] Arteriovenous fistula and graft of LN patients with antiphospholipid syndrome are prone to thrombosis, hence they may require high doses of anticoagulant therapy.[17]

Renal transplantation is a treatment option in LN patients but this is delayed till 6-12 months after commencement of dialysis to ensure that lupus is not active during transplant. The risk of graft loss from recurrence of lupus is low. The index patient and her parents were counseled and reassured that pregnancy outcome in patients with LN who have normal renal function or mild renal impairment is good as reported in previous studies. [18,19]

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CASE EIGHT

Early Post-Transplant Erythrocytosis in a 30 year old Man

SUMMARY

A thirty year old male post-transplant patient who presented with one week history of blurring of vision, headache that was associated with dizziness. He had sudden loss of vibration in his arteriovenous fistula (AV) about 4 weeks prior to onset of his symptoms. He was managed for post-transplant erythrocytosis with sessions of phlebotomies and ACEI.

This case highlights the risk factors and management of an uncommon complication in post-transplant patients that was initially thought to be benign.

CASE REPORT

A 30 year old male post-transplant patient who was being followed up in clinic presented with one week history of blurring of vision and headache . He was apparently well until a week prior to presentation when he developed blurring of vision which was intermittent. There was no associated redness of the eyes. Each episode lasted few minutes and was self limiting. There was no known aggravating or relieving factor. About the same time, he developed headache which was frontal in location, dull aching with no radiation to any other part of the head. There was no associated nausea, vomiting, photophobia or phonophobia, There was associated dizziness that was not related to posture. Severity of headache was not increased by straining or during any particular time of the day.

About 4 weeks prior to presentation, he noticed that there was loss of vibration in the fistula he had on his left forearm. There was no preceding history of trauma to his hand. There was no

associated swelling, pain, discoloration or numbness on the digits. However, he was not bothered because he was not presently using the fistula. There was no history suggestive of transient ischaemic attack, chest pain, breathlessness, calf pain, cough or haemoptysis

He is a known hypertensive for 6 years, but not diabetic. He was diagnosed of ESRD secondary to chronic glomerulonephritis about a year ago prior to this index presentation and commenced on haemodialysis. His PCV range during haemodialysis was between 20-24%. He had a living donor renal transplant 7 months after commencement of haemodialysis and native kidney nephrectomy was not done. His post-transplant follow up had been uneventful prior to this event. He did not have any episode of transplant rejection and had good graft function. His serum creatinine value has been between 1.2-1.4 mg/dl post-transplant. His medications are tacrolimus, mycophenolate mofetil, prednisolone, metoprolol, prazocin and amlodipine . His packed cell volume was noted to be on a steady rise in the last two clinic visit. The last value about a week prior to this index presentation was 52%.

He does not smoke cigarette or take alcohol.

EXAMINATION

Examination showed an anxious young man who was not in distress. He was not pale, anicteric, acynosed ,well hydrated, afebrile, had no finger clubbing and there was no pedal oedema

His pulse rate was 75 per minute, regular with normal volume. There was absent thrill over the left forearm AV fistula. Blood pressure was 120/90 mmHg, jugular venous pressure was normal. Apex beat was in the 5^{th} left intercostal space, lateral to mid-clavicular line and it was heaving. First, second and fourth heart sounds were heard. Respiratory rate was 22 cycles per minute and chest was clinically clear

The abdomen was full, soft moved with respiration and there was no area of tenderness There was no palpably enlarged liver or spleen, but the allograft was palpable in the right iliac fossa. There was absence of bruit over the allograft.

The neurological examination was essentially normal.

Urinalysis showed pale yellow urine with specific gravity of 1.020, p H of 6. Protein, glucose, ketones were all absent.

An assessment of ? post-transplant erythrocytosis (PTE) complicated by possibly left AV graft thrombosis was made.

RESULT OF INVESTIGATIONS

Urgent full blood count result showed a total white cell count of 8,000 cells/mm^3 with differential of 56.6% neutrophil, 36.6% lymphocyte, 5.8% monocyte and 1% eosinophil. Packed cell volume of 58%, platelet count of 128,000 cells/mm^3. This full blood count confirmed the diagnosis of PTE. Results of other investigations showed erythrocyte sedimentation rate of 2mm/hr. Serum urea was 40mg/dl, creatinine was 1.28mg/dl, the electrolytes were essentially normal. Lipid profile result; TC: 169 mg/dl, HDL-C : 46 mg/dl, LDL-C: 111mg/dl, TG: 118 mg/dl and uric acid: 7.6 mg/dl,

Ultrasound scan of the transplant kidney showed that it measured 106mm by 46mm with a smooth outline and uniform parenchymal echogenicity. There was no evidence of calyceal dilatation, hydronephrosis or calculi. The doppler flow showed normal flow pattern in the intra-renal artery with a restive index of 0.67-0.70. The ultrasound of both native kidneys showed bilaterally shrunken kidneys without any cyst.

TREATMENT

He had a session of phlebotomy with plasma expansion using normal saline weekly for 3 weeks while monitoring his full blood count. He had 5mg of ramipril added to his medications, while amlodipine was reduced from 10mg to 5 mg.

FULL BLOOD COUNT CHART

	WEEK 1 before treatment	WEEK 2 after 1st phlebotomy	WEEK3 after 2nd phlebotomy	WEEK 4 After 3rd phlebotomy	WEEK 6	WEEK10	WEEK 14
PCV	58%	54%	52%	48%	47%	48%	45%
WBC	8000	8500	7600	6900	7400	5900	6300
Platelet	128,000	123,000	140,000	134,000	138,000	129,000	140,000

He had relief from all his symptoms after 3 sessions of phlebotomies. He is still on follow up as a post-transplant patient and his haematocrit has been between 45-48%.

DISCUSSION

Post-transplant erythrocytosis is defined as persistently elevated haematocrit to a level of greater than 51 % after renal transplantation. This index patient had haematocrit value of 55% with symptom attributable to the erythrocytosis at the time of diagnosis. The prevalence of PTE varied from different studies between 7.5-37.3% .[1-5] This varied prevalence is due to the different cut-off values used in the definition of PTE and mode of diagnosis such as the use of isotopic method to exclude spurious cases of erythrocytosis. PTE as a form of erythrocytosis is

differentiated from polycythemia rubra vera by the absence of splenomagaly, leukocytosis and thrombocytosis that are present in the latter. In this index patient, poycythemia rubra vera was ruled out by the absence of splenomegaly, thrombocytosis and leukocytosis.

Most cases of PTE occur between 8 months and 2 years after renal transplant, though it may occur earlier. The index patient developed PTE at about 6 months post-transplant, a time much earlier than previous reports. Prakash et al however, reported early PTE in a patient 3 months post-transplant.[6] PTE has not received the much needed attention because it was thought to be a benign condition that is rarely characterized by thrombo-embolic complications. Wickre et al reported that about 20% of renal transplant patients who had PTE developed thrombo-embolic complications after being followed up for over 3.5 years compared to absent complications in matched controls who also had renal transplant but did not have PTE.[7] This finding was also supported by Hestin et al [8] This patient also had a sudden loss of function of his AV fistula around the time of presentation and this could have been due to thrombosis of the fistula. However, a confirmatory doppler scan was not done due to financial constraints. The features of PTE like headache, dizziness, malaise, lethargy , plethora are only seen in 60% of affected patients, hence a high index of suspicion is required so as not to miss the diagnosis.[9] This patient had headache, malaise and blurring of vision which could be attributed to erythrocytosis. PTE may be transient or may persist for several years if treatment is not instituted, but spontaneous remission may occur in up to 25% of affected patients.[9]

The pathogenesis of PTE is not well understood, but suggested pathogenic mechanisms include defective feedback regulation of EPO metabolism, increased production of EPO, increased sensitivity of the erythroid stem cells to EPO, direct stimulation of erythroid precursors by angiotensin II, and abnormalities in circulating insulin-like growth factor 1 levels. Although

increased EPO production has been reported after transplantation, erythrocytosis is not directly related to EPO levels. It may be low or even undectectable in some cases. This further supported that other mechanisms may contribute to PTE.

Studies have identified risk factors for PTE which have been found to be consistent over the years. These are male gender, smoking, hypertension, DM, short duration on dialysis prior to transplant, high pre-transplant haematocrit value, use of cyclosporine and diuretics, reduced frequency of episodes of acute rejection, excellent graft functions, retention of native kidneys, ADPKD as aetiology of CKD.[5,10,11] Patients with PTE usually have a combination of these risk factors. The possible risk factors in this patient were presence of hypertension, retention of native kidneys, good graft function, absence of episodes of acute rejection and short duration on dialysis before he had renal transplantation.

Cyclosporine predisposes to PTE by inhibiting interleukin 2 which is an inhibitor of erythroid precursors as well as causing vasoconstriction of the renal artery and subsequent ischaemia which is a stimulus for EPO production. Diuretic therapy causes plasma depletion and dehydration which may lead to increase PCV.[12] Polyuria from the effect of uncontrolled DM may also have similar effect of PCV. Acquired cystic disease in native kidneys may contribute to PTE by increased production of EPO.

Post transplant erythrocytosis may be a manifestation of transplant renal artery stenosis which may have other clinical features like hypertension, allograft bruit, oedema and acute decline in renal function. Hence , patients with PTE should be evaluated for transplant renal artery stenosis through doppler ultrasound scanning of the allograft. This patient was evaluated for transplant

renal artery stenosis which was ruled out by the presence of normal transplant renal artery blood flow by doppler scan, absence of bruit, oedema and worsening hypertension.

Treatment should be instituted when the PCV is greater than 55% because there is increased risk of developing complications or in the presence of symptoms even when the PCV is not greater that 55%. Renin-angiotensin system inhibitors such as ACEI or ARB have been found to be effective in the treatment.[4,13] The mechanism of action is not completely understood, but may be related to the induction of erythroid precursor apoptosis and reduction of insulin like growth factor 1. Drugs that block renal adenosine A2 receptor such as theophylline are also effective in the treatment of PTE, though less tolerated compared to ACEI or ARB.[14] Phlebotomy is the treatment modality of choice in symptomatic patients or females who are willing to get pregnant because ACEI is contraindicated in them due to its teratogenic effects. [15] Ahmed et al reported that 70% of patients with PTE required phlebotomies with ACEI for effective treatment. [2] This patient had a combination of ACEI and phlebotomy. He had 3 sessions of phlebotomies because he was symptomatic and the haematocrit was greater than 55% with good response clinically and by the follow up haematological indices. Phlebotomy should be done cautiously and slowly to avoid complications like acute myocardial infarction, hypotension, cardiovascular collapse and death in those with pre-existing cardiovascular disease which is common in renal disease patients.[16] Native nephrectomy could be performed if these other treatment modalities are ineffective in the presence of suspected renal lesion like acquired or hereditary cystic kidney disease.[15] This was not considered in this patient because the ultrasound of the native kidneys did not show cyst or suspicious lesion. He also had good response to ACEI and phlebotomy. There is a negative association between the use of sirolimus and development of PTE, however the use of sirolimus to prevent or treat PTE is yet to be determined.[9]

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CASE NINE

Massive Pericardial Effusion in a 54 year old Man with End Stage Renal Disease

SUMMARY

A 54 year old man who presented with one month's history of cough, progressive breathlessness. There was associated left sided pleuritic chest pain, orthopnoea, paroxysmal nocturnal dyspnoea. He is a known ESRD patient who has been on maintenance HD for 8 months with poor compliance prior to onset of his symptoms. He had pericardiostomy on account of massive pericardial effusion with clinical improvement

This case highlights the risk factors, significance and management of pericardial disease in CKD patients

CASE REPORT

A 54 year old man who presented with one month's history of cough and breathlessness. He was apparently well until one month prior to presentation when he developed cough. Cough was initially dry and later became productive of whitish sputum. There was no haemoptysis or weight loss. There was associated left sided pleuritic chest pain. Pain was not affected by his posture. There was no history of fever or drenching night sweating. There was no history of recent contact with someone with chronic cough.

Breathlessness started a month prior to presentation and progressively worsened. There was associated orthopnoea, paroxysmal nocturnal dyspnoea and associated bilateral leg swelling. There was no abdominal swelling or early satiety.

He has been hypertensive for 10 years, but not diabetic. He is known ESRD patient who has been on maintenance haemodialysis for about 8 months. He has not been able to comply with

thrice weekly dialysis on account of financial constraints, but dialyses about 1-2 times weekly. He has also been having recurrent unexplained intra-dialytic hypotension since onset of his symptoms despite having normal or even elevated blood pressure at the commencement of his dialysis sessions. There was no history of similar presentation in the past. There is no known family history of cardiac disease. His PCV was between 22-25% and no history of frequent transfusion since commencement of dialysis. He does not take alcohol or use tobacco. He has been compliant with his medications.

EXAMINATION

Examination revealed acutely ill-looking man that was dyspnoeic, pale, anicteric , acyanosed, not dehydrated and afebrile. He had bilateral pitting oedema up to the middle of the legs.

Cardiovascular examination showed a pulse rate of 90 per minute, regular, normal volume and blood pressure was 160/100 mmHg. He had elevated jugular venous pressure and apex beat that was in the 6^{th} left intercostal space lateral to mid-clavicular line. His heart sounds were S1,S2, S3 but were distant. There was no murmur.

Respiratory rate was 24 cycles per minute, trachea was central and breath sounds were vesicular with fine bibasal crepitations. Abdomen was slightly distended and moved with respiration. The liver was enlarged 4 cm below the costal margin. It was smooth, soft and tender with a span of 14cm. The spleen and kidneys were not palpably enlarged. Ascites was present.

Neurological examination did not show any abnormality and there was no asterixis..

An diagnosis of congestive cardiac failure secondary to uncontrolled hypertension in patient with ESRD was made.

RESULT OF INVESTIGATIONS

PCV: 22%, total white cell count : 3600 cell/mm^3, differential: 31.5% lymphocyte. 9% monocyte, 59.5% granulocyte, platelet count : 176,000 cells/mm^3

ESR : 55mm/hr, mantoux test: negative, prothrombin time 14seconds (control was 10 seconds), partial thromboplastin 50 seconds (control was 45 seconds) .

Peripheral blood film showed iron deficiency anaemia. The retroviral, hepatitis B and C were negative. The serum urea was 109mg/dl, creatinine: 3.1 mg/dl, sodium: 131mmol/l, potassium: 3.3mmol/l, chloride: 110mmol/l, and bicarbonate: 13 mmol/l. Serum calcium: 9.3mg/dl, phosphate: 4.8mg/dl and serum uric acid: 2.3mg/dl. Fasting serum lipid profile; TC: 223mg/dl, HDL-C : 49mg/dl**,** LDL-C: 129mg/dl and TG: 227mg/dl

Chest radiograph showed massive cardiomegaly. Echocardiography showed an enlarged heart with dilated right ventricle. There was marked snowing motion of the heart with hyperdynamic ventricles. The ejection fraction was 50%. Colour doppler echocardiography demonstrated mild tricuspid regurgitation, mild aortic stenosis and mitral regurgitation. There was massive pericardial effusion with a 3 cm echo free space. A diagnosis of massive pericardial effusion was made.

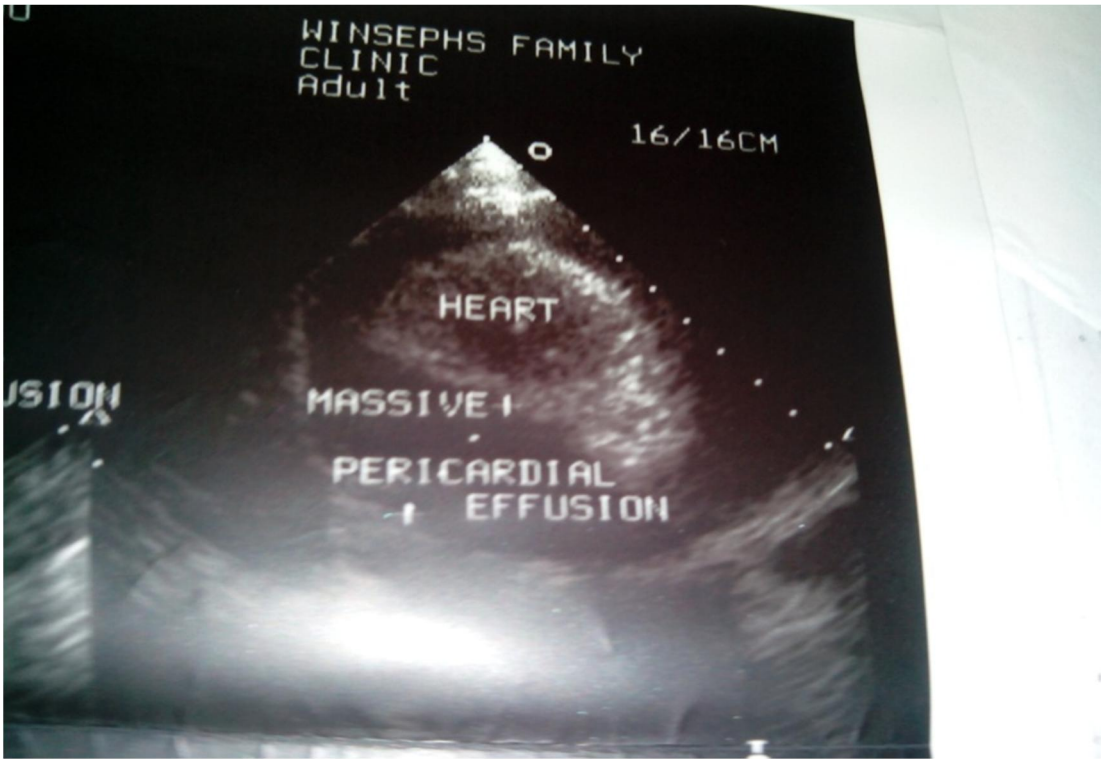

Figure 3: Echocardiographic image showing Massive Pericardial effusion

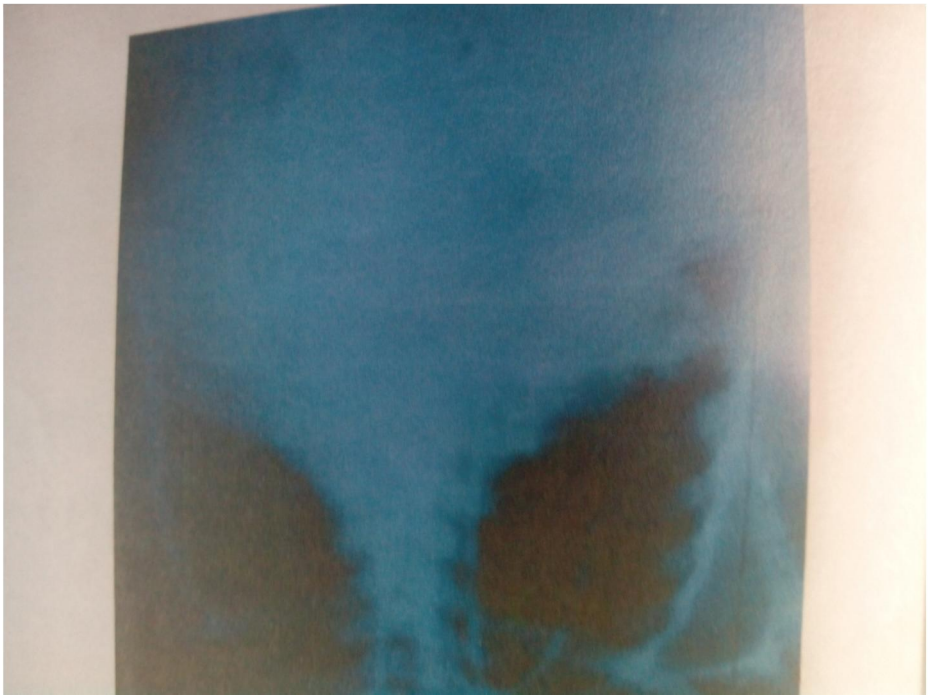

Figure 4: Chest Xray showing cardiomegaly and pleural effusion

TREATMENT

He was co-managed with the cardiologist and cardiothoracic surgeon. He was placed on oxygen at rate of 5L/minute, intravenous furosemide 80mg 12hrly, tabs lisinopril 10mg daily, moduretic 1 tablet daily. He was dialysed for longer duration at reduced blood flow rate of 150-200 mls per min. His heparin dose was also reduced to 2000 IU during dialysis to reduce the risk of haemorrhagic transformation and cardiac tamponade.

He was transfused with 2 unit of blood intraoperatively and had pericardiostomy. Intra-operative findings were bulging pericardium and 700mls of serous fluid which was drained. The pericardial effluent acid and alcohol fast stain was negative and cytology did not show any malignant cell. His clinical condition improved significantly after surgery and he is presently being worked up for a renal transplant.

DISCUSSION

Cardiovascular disease is the leading cause of hospitalization and death in CKD patients at all stages and accounts for 50% of mortality in this group of patients.[1,2] In the United States, the all-cause mortality rate of prevalent dialysis patients in 2006 was 221 deaths per 1000 patient-years and 41% of these mortality was attributable to cardiac causes.[3]

Pericardial disease is one of the cardiovascular complications that could occur in CKD patients. The common aetiologies of large pericardial effusion are neoplasia, ureamia and idiopathic.[4] The presentation of pericardial disease in CKD patients includes ureamic pericarditis, dialysis pericarditis, pericardial effusion and pericardial thickening. Ureamic pericarditis can predispose to life threatening arrhythmias, effusion, tamponade and constrictive pericarditis.[5] Early

detection and treatment of pericardial disease in CKD patients will reduce the high cardiovascular morbidity and mortality associated with this disease.

Pericardial disease is not uncommon in CKD patients.[6,7] Ijoma et al reported that 15.9% of CKD patients had pericardial effusion, 29.5% had pericardial thickening and 10.2% had both pericardial thickening and effusion.[8] Pericardial effusion is commoner in ESRD patients on maintenance haemodialysis compared to those on peritoneal dialysis.[7] The major cause of pericardial effusion in ESRD patient is inadequate dialysis which is the most likely cause in this index patient.

The normal pericardial space contains 15-50mls of pericardial fluid which is a plasma ultrafiltrate secreted by the mesothelial cells that lined the visceral pericardium. At low intra-pericardial volume, a small increase in volume leads to only a small rise in pressure. However, when the intra-pericardial volume expands beyond a critical level, a dramatic increase in pressure is incited by the non-distensible sac such that even a minor increase in volume can lead to a larger compressive force on the heart with subsequent haemodynamic compromise.

Factors that determine the presentation of patients with pericardial effusion are the volume of the effusion, rate of fluid accumulation and the compliance characteristics of the pericardium. The rate of accumulation of effusion in this index patient was likely to be gradual because he had a large volume without going into cardiac tamponade .

Ijoma et al reported a positive correlation between pericardial disease and systolic blood pressure, diastolic pressure, serum calcium and a negative correlation with haematocrit.[8] These factors which were associated with pericardial disease in this study are cardiovascular risk factors that are highly prevalent in CKD patients, hence adequate control of these factors may prevent pericardial disease and subsequent cardiovascular morbidity and mortality in them.

The result of studies on association between aetiology of renal disease and prevalence of pericardial effusion has not been consistent. Ijoma et al did not find any association while Nasir et al found that there was significant association between pericardial effusion and chronic glomerulonephritis[8,9]. The latter finding may be explained by the predominance of chronic glomerulonephritis as aetiology of renal disease in the population studied. Qian et al reported that pericardial effusion was more prevalent in ADPKD, well tolerated and clinically insignificant even in those with moderate to large effusion.[10] The pathogenesis of pericardial effusion in ADPKD is uncertain, but may reflect a defect in the structure and function of connective tissue and extracellular matrix which also underlies the other extra-renal manifestation of the disease. [10]

The clinical features of pericardial disease are similar in patients with and those without CKD except that chest pain is usually milder in the CKD patients.[7] This is because ureamia is associated with autonomic neuropathy which may blunt the feeling of pain. Other symptoms of pericardial disease are palpitations, cough, breathlessness, hoarseness of voice and hiccough. The examination findings may include Beck's triad which consists of hypotension, jugular venous distension and muffled heart sounds if there is associated cardiac tamponade. Other physical signs are pericardial friction rub, Ewart's sign, hepatosplenomegaly, and weak peripheral pulses. Chest pain, breathlessness, distended neck veins, and distant heart sounds were present in the index patient.

Pericardial disease is a risk factor for intra-dialytic hypotension which was frequently encountered in this patient. The massive pericardial effusion in this patient could be responsible for the inability to tolerate haemodialysis well and the repeated episodes of hypotension he experienced during dialysis. His dialysis prescription was adjusted by reducing the blood flow

rate and increasing the duration of dialysis in order to reduce the occurrence of hypotension which might further compromise effective clearance of uraemic toxins. The intra-dialytic hypotension in this index patient could have also put him at risk of complications like seizures, arrhythmias, myocardial ischaemia and cerebrovascular accident. Intra-dialytic hypotension has been shown to be an independent risk factor for mortality in ESRD patients on maintenance dialysis.[11]

Computed tomography is a well established method used to detect the presence and severity of pericardial effusion, although it is less sensitive than echocardiography in assessing its haemodynamic effects.[12-14] Echocardiography was used to confirm the diagnosis in this patient because it was cheaper and more sensitive as noted earlier in the diagnosis of pericardial effusion.

Treatment of pericardial effusion in CKD patients could be medical and or surgical. Some patients may respond to adequate dialysis while others may require surgical intervention as seen in the index patient. Indications for surgical treatment includes the presence of massive pericardial effusion or imminent cardiovascular collapse. Heparin dose should be reduced in patients with pericarditis or pericardial effusion undergoing haemodialysis in order to prevent haemorrhagic transformation and cardiac tamponade. This precaution was taken in the index patient.

Zack et al in a comparative study between the use of pericardiocentesis and surgical pericardiotomy in treatment of pericardial effusion in CKD patients in United States reported that in-patient mortality was significantly higher with the former while morbidity and resource utilization was higher with the latter.[15] The index patient was co-managed with cardio-thoracic

unit and had pericardiostomy done with drainage of 700mls of serous fluid intra-operatively. There was significant improvement in his clinical state after the surgery.

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CASE TEN

Nephrotic Syndrome in a 20 year old Man

SUMMARY

A 25 year old male who presented with 6 months history of generalized body swelling with associated nocturia and reduced urinary output. He had a renal biopsy that showed focal segmental glomerulosclerosis (FSGS). He achieved remission with high dose steroid.

This case highlights the fact that FSGS is increasingly becoming prevalent as a cause of nephrotic syndrome in the black and factors that determine the renal outcome.

CASE REPORT

A 25 year old male artisan who presented with 6 months history of generalized body swelling

He was apparently well until 6 months prior to presentation when he noticed body swelling that started with early morning facial swelling that regressed during the day. The swelling became progressive to involve the whole body including the abdomen and both legs. There was associated frothiness of urine, but no nocturia or haematuria. There was reduction in urinary output over the last few weeks before presentation which also coincided with worsening body swelling. There was mild bilateral loin pain that was dull and was not radiating. The pain was not associated with urinary frequency or dysuria.

There was no history of cough, breathlessness, or easy fatigability. There was no history of jaundice, puritus, change in colour of urine or faeces.

There was no history of recent sore throat or skin rash prior to onset of generalized body swelling. He did not have history of habitual use of pain relieving medications or substance abuse. He was not a known hypertensive or diabetic. His genotype is AA. There was no history history of renal disease in him or any family member prior to this index presentation. There was

no history of use of herbal medications, mercury containing creams or soap. He did not have history of indiscrimate use of sharps, previous blood transfusion or scarification. He denied history of multiple sexual partners. He is not a known asthmatic and there is no history suggestive of atopy in him or his family members.

There was no history of fever, pleuritic chest pain, painful leg swelling or sudden onset breathlessness since the onset of his symptoms. There was no history of irrational behavior, hiccups, vomiting or diarrhea. He neither takes alcohol nor use tobacco.

He had presented in a peripheral hospital at the onset of his symptoms where he was given some unknown medications without significant improvement in his condition.

Examination showed a young man that was chronically ill looking with anasarca and was not in distress. He was pale, anicteric , afebrile, well hydrated, had leukonychia but did not have finger clubbing.

His pulse was 80 beats per minutes, regular , normal volume. The blood pressure was 110/70 mmHg supine, jugular venous pressure was not elevated, apex beat was in the 5^{th} left intercostal space, in the mid-clavicular line and not heaving. Heart sounds were S1,S2 and were normal.

The respiratory rate was 20 cycles per minute, trachea was central and there was resonant percussion notes in all the lung zones with normal hepatic and cardiac dullness. Breath sounds were vesicular in all lung zones. The abdomen was distended. There were no palpably enlarged, but ascites was demonstrated by fluid thrill. He was conscious, alert, oriented in time, place and person.

There was no asterixis or neurological deficit.

Urinalysis showed amber coloured urine, pH was 5.5, specific gravity was 1.020, 3^{+} proteinuria, 1^{+} haematuria.

An assessment of nephrotic syndrome ? cause was made.

RESULT OF INVESTIGATIONS

Urine microscopy showed few red cells, granular cast, numerous pus cells/ hpf. Urine culture yielded escherichia coli that was sensitive to ciprofloxacin and gentamycin. Twenty- four urine protein was 3.5 grams. The packed cell volume was 33%, total white cell count was 5,100 cell/mm^3. Differential white cell count showed that neutrophil was 60.7%, lymphocyte was 36.4% was, eosinophil was 2.1% and basophil was 0.8%. Peripheral blood film showed iron deficiency anaemia. The retroviral, syphilis, hepatitis B and C screenings were all negative.

The total serum protein was 5.0g/l; albumin was 3.0g/l while globulin was 2.0g/l, aspartate transaminase was 45 unit/l, alanine transaminase was 60unit/l, total bilirubin was 0.8 mg/dl. The liver function test was essentially normal except serum albumin which was low.

Serum urea was 18mg/dl, serum creatinine was 0.5mg/dl and electrolytes were normal. The TC was 230 mg/dl, HDL-C was 35mg/dl, LDL-C was 156mg/dl and TG was 135 mg/dl.

The chest X-ray was essentially normal. The renal scan showed that the right kidney measured 12.1cm by 5.0 cm by 3.0cm and the left measured 12.0cm by 4.3cm by 3.0cm. Both kidneys had slightly increased cortical echogenicity and preservation of the normal cortico-medullary differentiation.

TREATMENT

The patient was offered admission but refused on account of finanacial constraint, hence he was managed as an out-patient. He was commenced on furosemide tablets120 mg B.D, spironolactone 50 mg daily, lisinopril 2.5 mg daily, artovastatin 20mg daily, ferrous sulphate 200 mg TDS, ciprofloxacin 500 mg B.D for 10 days. He was seen on a weekly appointment with regular weighing and measurement of abdominal girth. Hydrochlorthiazide was added and the

dose of spironolactone was doubled 2 weeks after therapy was commenced because the rate of diuresis was not adequate. His repeat mid-stream urine microscopy did not show any sign of infection at the end of 2nd week.

He was booked for renal biopsy 4 weeks after his first clinic visit. The coagulation screen that was done showed normal results: prothrombin time was 15 seconds (control was 12 seconds) activated partial thromboplastin time was 44 seconds (control was 48 seconds) and INR was 1.25. The result of the biopsy showed 26 glomeruli with 7 showing focal segmental sclerosis which was in keeping with FSGS.

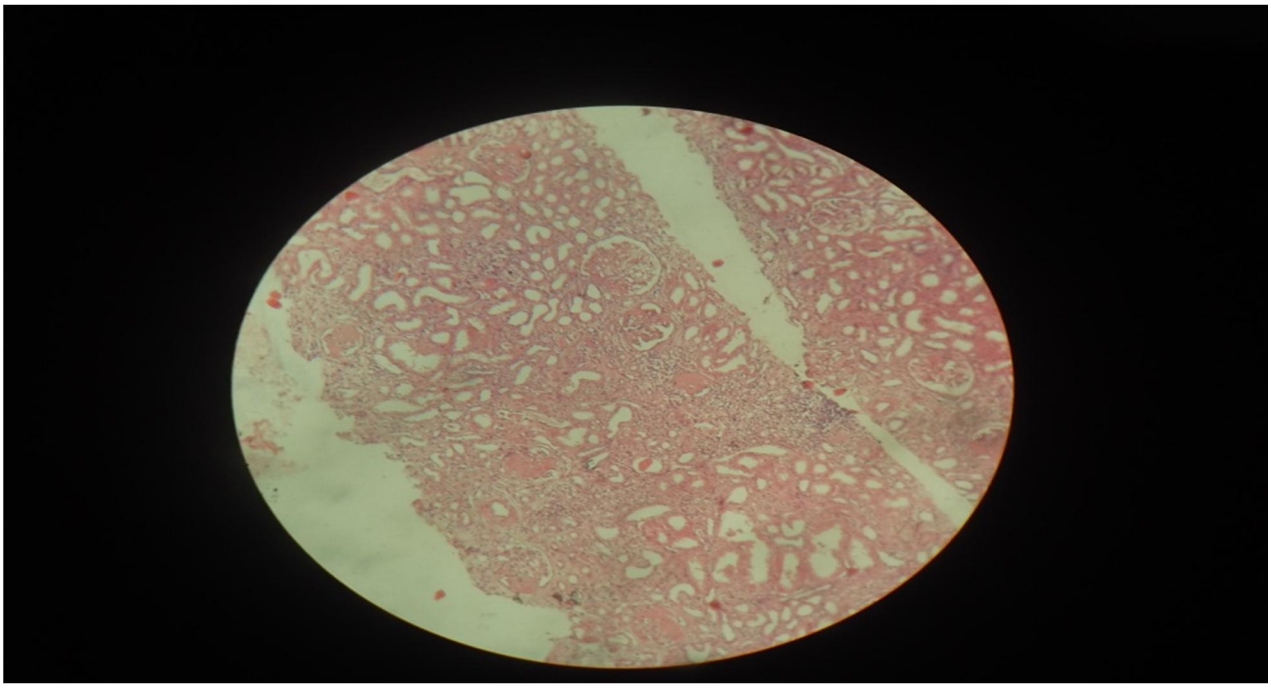

Figure 5: Micrograph showing FSGS (X 100)

He was commenced on tab prednisolone 60mg daily, rabeprazole 20 mg daily after a course of anti-helminthic therapy with tab mebendazole 100mg BD for 3 days and low salt diet. He was followed up in clinic with serial urinalysis, fasting blood glucose, serum electrolyte, urea, creatinine and weight monitoring. His diuretic therapy was also reduced after significant diuresis was achieved.

Remission was achieved after 11 weeks of steroid therapy defined by reduction in 24 hour urine protein to 400mg and increase of serum albumin to 3.6g/l. The prednisolone was tapered down to 5mg daily over a period of 6 months and he is being followed up regularly in clinic. His renal function has remained normal and already off diuretics as at the last clinic attendance.

DISCUSSION

Focal segmental glomerulosclerosis is a form of glomerular injury that belongs to the family of podocytopathy characterized by focal glomerulosclerosis involving a segment of the glomerular tuft. However, this becomes more diffuse and global as the disease progresses. It is a common cause of nephrotic syndrome in adults compared to children. Oviasu et al reported that FSGS accounted for 26.3% of adult nephrotic syndrome in Benin while Chijoke et al reported a prevalence of 19% in a study done in Ilorin.[1,2] . It was the commonest cause of adult nephrotic syndrome in Zaire with a prevalence of 41%.[3] In the US, the prevalence of FSGS as a cause of glomerulonephritis and ESRD has increased especially in the last 20 years and has been found to be commoner in the blacks.[4]

The pathogenesis is not well understood, but podocyte injury plays a central role. [5] This injury promotes altered cell signaling, reorganization of actin cytoskeleton leading to foot processes effacement. Critical levels of injury causes podocyte depletion through detachment or apoptosis. There is also spread of this injury to adjacent podocytes through loss of supportive factors like nephrin signaling.

There is a close association between minimal change disease and FSGS. It is believed that both disease entity are the two extremes of a spectrum of a related disease referred to as podocytopathy. Some researchers have shown that multiple biopsies in allograft that had

recurrence of FSGS actually showed earlier changes that were similar to minimal change disease.[6]

There are certain genetic mutation and polymorphisms which have been found to predispose certain races to FSGS. Individuals with myosin heavy chain 9 are more likely to develop FSGS when exposed to risk factors like obesity, hypertension and viral infections such as HIV.[7] G1 and G2 mutations in apolipoprotein gene on chromosome 22 which were found to be protective against African trypanosomiasis in people of African ancestry have also been found to predispose them to FSGS.[8] Genetic studies were not done in this patient due to absence of such diagnostic facility in our hospital, financial constraints and absence of family history of renal disease. Focal segmental glomerulosclerosis can be primary (idiopathic) or secondary. Common secondary causes are infections like HIV, cytomegalovirus, drugs like heroin, pamidronate, hypertension, obesity, SCA, reflux nephropathy and anabolic steroids. There are certain genetic mutations affecting the podocyte proteins such as nephrin, podocin, alpha-actinin 4 which also lead to FSGS. The index patient was evaluated for common secondary causes such as SCA, retroviral infection, history of substance abuse and they were all absent in the patient.

The proteinuria in FSGS is usually non-selective unlike what is seen in minimal change disease. Protein selectivity was not assessed in this patient because of absence of diagnostic facility and the outcome will not change the modality of management of this patient. It may present with different range of proteinuria ranging from sub-nephrotic range to severe nephrotic range. Hypertension only occurs in 30-50% of affected individuals while microscopic haematuria may be seen in up to 75% of patients. Impaired function may be seen at initial presentation in 20-30 %. of patients.[9] The serum complement levels are usually normal. This index patient presented with nephrotic range proteinuria and hypoalbuminaemia. Hypertension and impaired renal

function were absent in him, but he had microscopic haematuria. This patient also had mild anemia and hypocalcaemia which are not unusual in patients with nephrotic syndrome because they lose protein in urine which includes transferrin and vitamin D3 binding protein.

Minimal change disease and membranous nephropathy may present clinically like FSGS and only renal biopsy findings could differentiate them. Due to the focal pattern of glomerular disease in FSGS, the defining features may be confined to the deeper juxtamedullary glomeruli especially in early disease, hence good core of tissue with at least 20 glomeruli may be required to make a diagnosis. The renal biopsy samples in this patient had 26 glomeruli which were sufficient to make a diagnosis of FSGS confidently.

There are five different types of histological variants of FSGS; tip variant, collapsing, cellular, peri-hilar and classical variant also referred to as not otherwise specified (NOS). These histological variants have some differences in clinical presentation, response to treatment and prognosis. The collapsing variant presents with more severe proteinuria, impaired renal function, rapid progression to ESRD and has the worst prognosis.[10] There are also some differences in presentation and histologic findings in primary and secondary FSGS. The latter especially in post-adaptive cases presents with milder proteinuria , hypoalbuminaemia, lesser degree of foot processes effacement and respond well to treatment compared to the former. Spontaneous remission of proteinuria is seen in only 5-25% of patients with FSGS.[11]

Predictors of progressive renal disease in FSGS are black race, massive proteinuria, hypertension, elevated serum creatinine, reduced creatinine clearance at presentation and failure to achieve either partial or complete remission, poor histologic features on biopsies which include presence of tubulointerstitial fibrosis and collapsing variant. [5,9,12] This patient had

reduced risk of progression to ESRD because of absence of hypertension, normal renal function and less severe proteinuria and early onset remission he had. The biopsy did not also show collapsing glomerulopathy which has a worse prognosis.

Treatment of FSGS depends on the clinical presentation either as nephrotic syndrome or sub-nephrotic range proteinuria. Both will require use of low protein and salt diet, blood pressure control, ACEI or ARB and statins if there is dyslipidaemia. This patient received these treatments as well as definitive treatment because he had idiopathic FSGS. The definitive treatment of idiopathic FSGS is the use of corticosteroids and immunosuppressant therapy. Kidney Disease Improving Global Outcome (KDIGO) recommended high dose steroid of 1mg/kg body weight daily with a maximum of 80 mg daily or alternate day steroid therapy with 2mg/kg body weight with maximum of 120 mg daily for a minimum of 4 weeks and maximum of 6 months before tapering down the dose over months. Dose reduction of steroid could be done earlier if remission is achieved or the high dose is not well tolerated. The recommended second line drugs are calcineurin inhibitors like cyclosporine that are used for those who relapse, fail to achieve remission or steroid dependent. These immunosuppresants could be used as first line therapy in those who have contraindication to steroid therapy such as those with diabetes mellitus and severe osteoporosis. Immunosuppresants are not recommended in treatment of secondary FSGS where treatment is directed towards the underlying cause and use of other supportive therapy. [13]

This patient had complete remission at about 3months of steroid therapy and was subsequently tapered off from the high dose of 60mg of prednisolone to 10 mg daily. This patient did not get prophylaxis for anticoagulation because he had low risk of thrombotic complications in the absence of previous history of thromboses, severe hypoalabuminaemia and proteinuria. He was

followed up with urinalysis, serum electrolytes, urea, creatinine and fasting blood glucose to detect complications of steroid therapy or relapse.

In those who failed to respond to treatment, 50% of them will progress to ESRD in 10 years. Matalon et al reported that the renal survival is significantly better in those who had partial remission compared to those who did not have remission.[14]

Novel therapy in treatment of FSGS include the use of pirfenidone, an oral transforming growth factor-β inhibitor which reduces fibrosis and also decline in renal function without having effect on BP or proteinuria.[15] Galactose, a monosaccharide have been found to be useful in treatment of FSGS.[16] It has high affinity for permeability factor, hence reducing the level in the plasma and subsequently reducing proteinuria. [16]

Transplantation could be done for patients with FSGS who progress to ESRD, however there is increased risk of recurrence of the primary disease and subsequent lost of renal allograft. Risk factors for recurrence of disease in the graft are heavy proteinuria, rapid progression to ESRD, previous history of recurrence and presence of circulating permeability.[17] The use of plasmapheresis and rituximab prior to transplantation in those with circulating permeability factor reduces the incidence of disease in graft and subsequent allograft lost in transplanted patients. [17]

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