NJCP_163_11R3

CASE REPORT

Analgesic nephropathy as a cause of end-stage renal disease in a 55 year-old Nigerian

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Abstract

Analgesic nephropathy is a subtle but significant cause of chronic renal failure. There is paucity of data on analgesic nephropathy in Nigeria. This case presentation is to highlight the need to have high index of suspicion in patients at risk of developing analgesic nephropathy. In March 2009 a 55-year-old businessman was referred to the renal unit on account of azotemia by the hematologist who had hitherto managed the patient as a case of refractory anemia. The patient had osteoarthritis for over 10 years and was managed with several analgesic drugs over the same period. He was found to have features suggestive of analgesic nephropathy and had end-stage renal disease. He was commenced on appropriate therapy, and he had a live related kidney transplant six months later. Analgesic nephropathy is preventable and morbidity/mortality can be remarkably reduced with appropriate and prompt intervention.

Key words: Analgesic nephropathy, chronic renal failure, interstitial nephritis

Date of Acceptance: 09-Mar-2011

Introduction

Analgesic nephropathy (AN) is a slowly progressive disease resulting from daily consumption of an analgesic over several years.[1,2] AN is usually preceded by pain that prompts daily use of analgesics or analgesic containing medications. AN is asymptomatic in many patients. Diagnosis is usually late; however, patients can be detected early during screening and occasionally, incidentally while managing other non-renal related ailments.

The frequency of AN in patients with end-stage renal disease (ESRD) varies greatly within and among countries. There is paucity of studies on AN in Africa including Nigeria where it was reported as a rare cause of chronic renal failure (CRF).[2,3]

This case report is to highlight the importance of AN as a cause of CRF and the need to have a high index of suspicion in an at risk patient.

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Case Report

A 55-year old businessman was referred to us by a hematologist on account of azotemia, discovered while being investigated as case of refractory anemia.

He presented with facial swelling of six months, dizziness and weakness of three months' duration.

The facial swelling was of insidious onset, worse on waking up but regressed by mid-day. This was associated with progressive leg swelling. He had oliguria and increased urinary frequency.

Three months later he developed dizziness which was associated with easy fatigability and generalized body weakness. He was anorexic, had abdominal fullness and

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	DOI: ***
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early satiety. There was no associated nausea, vomiting, pruritus, headache, hiccough or seizure. He had dyspnoea on exertion but no orthopnoea, paroxysmal nocturnal dyspnoea, or cough.

There was no past history of jaundice, sore throat, skin rashes or kidney disease. He was receiving treatment for osteoarthritis for over 10 years and for hypertension for eight years. His medications consisted of several mixtures of analgesics for the osteoarthritis; moduratic and alpha methyl dopa for the hypertension. He claimed to be regular with the medication and follow-up, and blood pressure control was good.

He was not a diabetic and did not use mercury-containing soap or cream or herbal concoction.

He was married, and his wife and three children were all alive. There was no family history of hypertension, diabetes mellitus or kidney disease. He neither took tobacco nor ingested alcohol.

He was admitted by the referral team a week prior to referring to us. He had pancytopaenia on blood film and hypocellular bone marrow. He had already received six units of packed red blood cells, and had been reviewed by the orthopedic surgeon.

On examination he was in mild respiratory distress, moderately pale, anicteric, not cyanosed, mildly dehydrated. He had facial puffiness and bilateral pitting pedal edema. The pulse rate was 80 beats per min, full volume and regular. The arterial wall was not thickened. The blood pressure was 150/100 mmHg supine. The jugular venous pressure was not raised. Apex beat was at sixth left intercostal space, anterior axillary line, heaving. Heart sound heard was first and second only, no murmur. He had bilateral basal crepitation. There was no tenderness, ascites or palpable organ in the abdomen. The central nervous system (CNS) was grossly intact, no asterexis. Fundoscopy revealed Grade 2 hypertensive retinopathy. A diagnosis of analgesic nephropathy to rule out hypertensive nephrosclerosis was made. Urinalysis revealed proteinuria+, and specific gravity of 1.010.

Urine microscopy, culture and sensitivity showed pus cells 5 to 10/high power field(HPF) and epithelial cells but no cast, red blood cells, or crystals and there was no significant growth 24-h urine protein was 2.9 g.

Packed cell volue(PCV) was 19% (post transfusion), blood film showed microcytosis, hypochromia, and anisocytosis, total white blood cell count was 6150/mm^{3,} neutrophil was 65%, lymphocyte was 32%, eosinophil was 3%, platelet count was 233,000/mm^3.

Serum electrolyte and creatinine was sodium 127 mmol/l, potassium 6.0 mmol/l, bicarbonate 15 mmol/l, Chloride 100 mmol/l, Urea 364 mg/dl (60.7 mmol/l), creatinine 10.8 mg/dl (950 umol/l), calcium 7.8 mg/dl, and phosphate 7.9 mg/dl. Creatinine clearance (measured) 6.3 ml/min.

Total protein was 6.5 g/dl, albumin 2.2 g/dl, globulin 4.3 g/dl, Bence Jones protein negative, serum protein electrophoresis was normal.

Renal scan showed bilaterally shrunken kidneys with the right measuring 7.35 × 3.42 cm and the left measuring 7.06 × 3.77 cm. The kidney outline was irregular and the corticomedullary differentiation was lost. The analgesic and alpha methyl dopa were discontinued.

He was rehydrated with 5% dextrose saline. Ten milliliters of 10% calcium gluconate and 50 ml of 50% dextrose were given. He also received two units of packed red blood cells.

He was commenced on tablet lisinopril 5 mg daily, and continued on the tablet moduratic, multivitamins and hematinics. He commenced hemodialysis; and subsequently continued on twice weekly maintenance hemodialysis.

He received intravenous iron dextran 500 mg (after a test dose). He was commenced on erythropoietin given subcutaneously at a dose of 4000 i.u twice weekly. Arteriovenous fistula was later created for the maintenance hemodialysis.

Tabs doxazocin and nifedipine were later added for better blood pressure control. He improved and was discharged six weeks after admission with a PCV 31%, serum creatinine 3.0 mg/dl (264 umo/l), serum urea 69 mg/dl (11.5 mmol/l), potassium 4.3 mmol/l, sodium 132 mmo/l, bicarbonate 22 mmo/l, and chloride 105 mmol/l.

He was regular for follow-up, hemodialysis and medications. He had a live related kidney transplant six months later, and he is doing well.

Discussion

Analgesic nephropathy is a non-specific, potentially preventable, and slowly progressive chronic renal disease.

The prevalence varies from 1% in the United States to 22% in South Africa.[1,2] The prevalence in Nigeria has not been documented but Akinsola *et al*., classified AN as among the rare causes of CRF.[3] Underestimation of prevalence is likely because of lack of well-defined criteria of diagnosis. But the prevalence of AN varies inversely with CRF of unknown origin.[1,4,5] This could explain the paucity of reports of

AN in Nigeria where the cause of CRF is not known in a significant number of patients.[3] Thus the importance of this case report highlighting the need for a high index of suspicion of AN as a cause of CRF in patients at risk.

The patient in this report is a middle-aged male, however, AN is more common in women and in the fourth to seventh decade. Usually, there is a preceding history of back or hip pain as in our patient or headache, which leads to the daily use of analgesic. AN was initially thought to result mainly from either the use of phenacetin or phenacetin-containing drugs, but since the use of phenacetin was banned in many countries there was no significant reduction in the prevalence of AN in these countries. Many analgesics, especially NSAIDs have been implicated directly or indirectly as a cause of AN.[6-8] Our patient had taken various types of analgesics in various combinations.

Most patients are asymptomatic and diagnosis is usually incidental as in our patient, thus the need for the medical personnel to have a high index of suspicion. Common presentations of patients with AN include flank pain, hematuria, anemia, hypertension, and atherosclerotic changes. Urine is usually bland or shows non-nephrotic proteinuria, hematuria, and pyuria which are usually sterile. The kidneys are often bilaterally shrunken with irregular contours and have papillary calcifications.[1,5,9]

The diagnostic criteria for AN are:[5]

- History of daily use of analgesic for over five years.
- Renal imaging showing small kidneys/bumpy kidneys/papillary calcifications.
- Proteinuria less than 3 g/day.
- Sterile pyuria.

Three parameters in the presence of a strong history of analgesic use make a diagnosis. The case reported had all the four diagnostic parameters, thus making AN a more likely diagnosis rather than hypertensive nephrosclerosis.

The pathogenesis of AN is not well established. Initially, there is thickening of the vasa recta and necrosis of their endothelium leading to tubular necrosis. This is followed by swelling of the papillae, necrosis and detachment of the fornices, necrosis and calcification of the papillae. There is usually infiltration of the interstitium by inflammatory cells leading to fibrosis and subsequent shrinkage of the kidneys. There may be associated cortical injury and glomerular damage.[5,10,11] The kidneys in AN are initially normal in size and architecture, but later there is thickening and sclerosis of the tubular epithelium revealing onion skin-like arrangement on microscopy. The interstitium is usually thickened and there is precipitate of calcium salt in the tubular cells. There may be areas of focal glomerular sclerosis, atrophy and collapse.

The classical picture of AN can be obscured by complications frequently associated with AN and analgesic use like hypertension, pyelonephritis, anemia etc. This can lead to misinterpretation and mismanagement of the actual clinical condition as occurred in this case report.[12,13]

Early detection of AN and discontinuation of analgesic use stabilizes or improves renal function and occasionally reverses renal functional impairment, however, diagnosis is usually delayed because of the subtle presentation of AN. Continuous use of analgesic, need for renal replacement therapy, patients aged above 60 years and presence of other analgesic-related complications like urothelial malignancy are poor prognostic indicators in AN.[10,11,14] Though our patient was younger than 60 years and had no other detectable analgesic-related complication, he presented late in ESRD and was still using analgesic at presentation.

Analgesic nephropathy contributes significantly to the burden of chronic kidney disease. There is a need to prevent or ameliorate the morbidity of AN through the following.

- Combinations of analgesics should be restricted and at-risk patients appropriately educated on the proper use of analgesic.
- Avoid further intake of analgesic.
- Avoid dehydration by ensuring that the patient takes over 2000 ml of fluid unless the patient is fluid-overloaded.
- Control hypertension.
- Treat infection.
- Maintain fluid and electrolyte balance.
- Correct anemia. Commence renal replacement therapy when it is indicated as in our patient.

References

1. Drukker W, Schwarz A, Vauher-wehem JL. Analgesic Nephropathy: An under estimated cause of end stage renal disease. Int Artif Organs 1986;9:216-43.
2. Klag MJ, Wheton PK, Reoneger TV. Analgesic and chronic renal disease. Curr Opinion Nephrol Hypertens 1996;5:236-41.
3. Ojo OS, Akinsola AA, Nwosu SO, Odesanmi WO. The pathological basis of chronic renal failure in Nigerians. An autopsy report. Trop Geogr Med 1992;44:42-6.
4. Elseeviers MM, DeBroe ME. Analgesic nephropathy in Belgium is related to the sales of particular analgesic mixtures. Nephrol Dial Transplant 1994;9:41-6.
5. Elseeviers MM, Bosteels V, Cambier P, De Paepe M, Godon JP, Lins R, *et al*. Diagnostic Criteria of analgesi nephrotoxicity in patients with end stage renal failure, results in Belgian study. Nephrol Dial Transplant 1992;7:479-86.
6. Perneger TV, Welton PK, Klag MJ. Risk of kidney failure associated with use of acetaminophen, aspirin, and non steroidal anti inflammatory drugs. N Engl J Med 1994;331:1675-9.
7. DeBroe ME, Elseeviers MM. Compound analgesic mixtures. N Engl J Med 1998;338:446-52.
8. Pommer W, Bronder E, Greiser E, Helmert U, Jesdinsky HJ, Klimpel A, *et al*. Regular analgesic intake and the risk of end - stage renal failure. Am J Nephrol 1989;9:403-12.
9. Pinter I, Martyns J, Czégány Z, Harsányi J, Homoki M, Kassai M, *et al*. Analgesic nephropathy in Hungary: The HANS study. Nephrol Dial Transplant 2004;19:840-3.
10. Gamber SL, Mirochunk Y, Anuda JA, Dunea G. Evolution of experimentally induced papillary necrosis to focal segmental glomerulosclerosis and nephrotic proteinuria. Am J Kidney Dis 1999;33:1033-9.
11. Murray TG, Goldberg M. Analgesic associated nephropathy in the USA. Epidemiologic, clinical and pathogenetic features. Kidney Int 1978;13:64-71.

12. Kincaid–Smith P, Nanra RS. Chronic effects of analgesics on the kidney. Prog biochem pharmacol 1972:7:285 – 323.
13. Nanra RS, Stuart–Taylor JM, de Leon AH, White KH. Analgesic nephropathy: Etiology, clinical syndrome, and clinicopathologic correlation in Australia. Kidney Int 1978;13:79-92.
14. Gault MH, Wilson DR. Analgesic nephropathy in Canada: Clinical syndrome, management, and outcome. Kidney Int 1978;13:58-63.

How to cite this article: ???

Source of Support: Nil, **Conflict of Interest:** None declared.