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Case Report

Analgesic Nephropathy due to Diclofenac in a 24-year-old Indian Male Patient: A Case Report

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ABSTRACT

Analgesics are commonly prescribed first line agent for the treatment of rheumatological disorders like rheumatoid arthritis and ankylosing spondylitis. Renal toxicities are known adverse reactions of analgesics, however, acute onset renal injury due to analgesics in rheumatological disorders is not currently known. Here we describe a case of a 24-year-old Indian male patient who was diagnosed with ankylosing spondylitis three years back and was prescribed tablet Diclofenac 150 mg in three divided doses per day. The patient presented with breathlessness, pedal edema and decreased urine output on 24th February 2019. The patient was diagnosed to have bilateral End Stage Renal Disease (ESRD) with small kidneys, pulmonary edema and left ventricular dysfunction using echocardiography. The patient was symptomatically treated and later transferred for renal transplant.

Renal toxicity of analgesics is known but is usually reported after years of exposure. This case is first of the kind of occurrence of ESRD within three years of exposure. This case highlights the need for monitoring in patients who are prescribed analgesics for a long duration especially in patients of rheumatological disorders.

Key words: Diclofenac, Nephropathy, Analgesic, Ankylosing spondylitis, Young.

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BACKGROUND

Ankylosing spondylitis, an autoimmune disease that affects young males more commonly and is seen in patients with HLA-B27. Non-steroidal anti-inflammatory drugs (NSAIDs) form the first line therapy in the management of ankylosing spondylitis. However, NSAIDs are associated with various adverse effects on long term use. Our case report discusses a rare presentation of acute onset analgesic nephropathy in a young adult male patient.

CASE PRESENTATION

A 24-year-old Indian male patient presented in the medicine department on 24th February 2019 with breathlessness, pedal edema, decreased urination and reddish discoloration of urine. The patient was asymptomatic 4 years back when he developed low back pain. The pain was insidious in onset, slowly progressive and relieved by walking. The pain was aggravated during morning hours and relieved by exercise and by evening. The patient was treated symptomatically for 1 year with Diclofenac given 150 mg a day in three divided doses. On 11th August 2016 the patient was diagnosed to be having Ankylosing spondylitis with positive HLA B27. The treatment with Diclofenac 150 mg in three divided doses was continued with an exercise regimen.

After admission of the patient in the medicine department on 24th February 2019, routine investigations were conducted. Urine examination showed the presence of blood and protein in a high amount, signifying glomerular injury. Serum creatinine was found to be 16 mg/dl.

Chest X ray revealed bat-wing appearance signifying pulmonary edema as depicted in Figure 1. USG abdomen revealed smaller size kidney of 69 X 25 mm (Right Kidney) and 51 x 27 mm (Left Kidney) with raised cortical echogenicity and loss of cortico-medullary differentiation. Free fluid was noted in the peritoneal cavity and moderate fluid was noted in the pleural bilaterally. Serum PTH was found to be more than 3 times of the Upper Normal Limit suggesting renal osteodystrophy.

Echocardiography was done on 25th February 2019 revealed LVEF of 35% with global LV hypokinesia, severe mitral regurgitation and RVSP of 42 mm Hg signifying pulmonary arterial hypertension. The patient was diagnosed to be suffering from dilated cardiomyopathy. The patient was treated empirically with Piperacillin-tazobactam, Metronidazole and Azithromycin. Other drugs like heparin, aspirin, clopidogrel, atorvastatin, furosemide, prednisolone, hydroxychloroquine and sevelamer were also prescribed. Emergency hemodialysis was done twice before shifting the patient to the nephrology department with advice for renal transplant.

DISCUSSION

Ankylosing spondylitis (AS) is a disease affecting the joints and back with initial manifestation is around 2nd decade of life with higher male preponderance. NSAID's are the first line agents in the treatment of AS. Recently it has been found out that AS patients also have renal abnormalities,[1] most common being renal amyloidosis.[2,3] Analgesic overuse is notorious for causing serious damage to kidneys by blocking the production of prostaglandins, which play an important role in maintaining homeostasis in kidneys.[4] In a case series it was found that patients with AS have renal vascular abnormality and patients taking NSAIDs should be regularly monitored as it affects the renal homeostasis.[5] There are two forms of analgesic nephropathy, a chronic insidious form of kidney injury that results from repeated consumption of predominantly combination analgesic tablets and an acute kidney injury due to renal vasoconstriction. The risk factors for acute kidney injury are volume depletion, concomitant congestive heart failure, cirrhosis and nephrotic syndrome. Acute kidney injury can occur at any age with

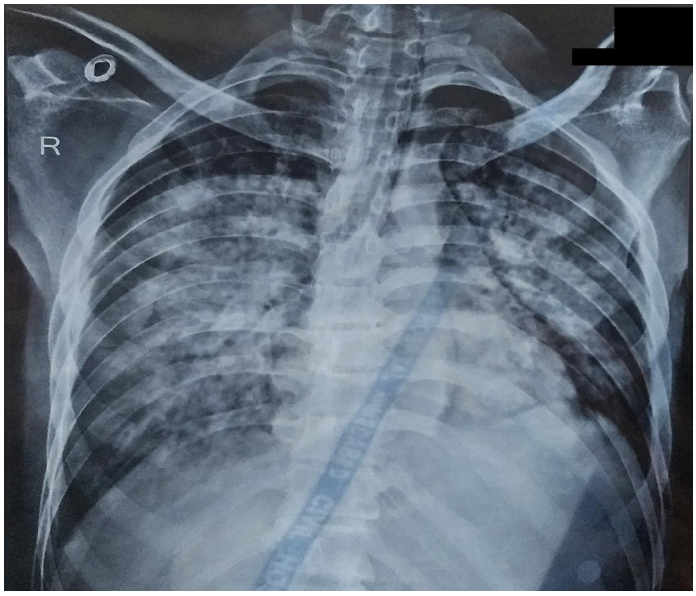

Figure 1: Chest X-Ray of the patient showing bat wing appearance signifying the presence of pulmonary edema.[6]

excessive consumption of NSAIDs, however, it is not associated with reduced kidney size which is characteristically found in chronic kidney disease (CKD).[7] Analgesics or NSAIDs exert their anti-inflammatory, analgesic and anti-pyretic property by suppression of prostaglandins, which also play a crucial role in renal homeostasis. NSAIDs cause renal damage by causing glomerular injury.

The glomeruli of humans express chemokine's like monocyte chemoattractant protein-1 (MCP-1). This MCP-1 is attributed to the monocyte/macrophage infiltration into glomeruli and the renal interstitium.[8,9] Cytokines and growth factors cause meningeal cell proliferation and MCP-1 release,[10] while Prostaglandin (PGE)[11] reduces the glomerular MCP-1 expression. Since in glomerulonephritis there is meningeal cell proliferation and monocyte infiltration, it is suggested that endogenously formed prostaglandins have a role in preventing glomerulonephritis. All NSAIDs augment the glomerular production of MCP-1 which plays an important role in glomerular injury.[12] Increase monocyte and macrophage infiltration were seen in animal models treated with indomethacin signifying the role of prostaglandins in suppressing renal inflammation.[13] Pro-inflammatory agents like interleukin-1ß[14] and lipopolysaccharide (LPS)[15] induce PGE2 by COX-2 indicating that COX-2 generated PGE2 plays an important role in suppression of renal inflammatory processes, such as glomerulonephritis.[16,17] In experimental models it was found that PGE decreases kidney damage through the reduction of glomerular immune complex formation, by reducing inflammatory cell infiltration and deposition of extracellular matrix products.[18] The experimental study concluded that prostaglandins have a role in the clearing of monocyte/macrophage and the healing process in glomerulonephritis.[19,20] However, the exact pathophysiological mechanism of analgesic nephropathy especially in acute kidney injury by NSAIDs is not well understood.

The cause of unusually rapid renal failure in this young patient can be possibly due to two causes: the presence of renal amyloidosis, which may have affected renal homeostasis and the use of NSAIDs affecting the protective mechanism of prostaglandins. Further, the patient might have developed left ventricular systolic dysfunction due to acute kidney disease.[21] This case report suggests that it is prudent to monitor the patients on long term analgesic therapy as rheumatological disorders may themselves cause systemic abnormalities which can increase the likelihood of renal toxicities by NSAIDs.

It is known that NSAIDs do not affect the disease progression of Ankylosing spondylitis and provides symptomatic benefit. However, controlling disease progression by the use of Disease modifying anti rheumatic drugs (DMARDs) is prudent. Judicial use of NSAIDs may help to prevent such occurrences.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

ESRD: End Stage Renal Disease; **NSAID:** Non steroidal Anti Inflammatory Drugs; **PTH:** Parathyroid Hormone; **LVEF:** Left Ventricular Ejection Fraction; **RVSP:** Right Ventricular Systolic Pressure; **LV:** Left Ventricle; **AS:** Ankylosing Spondylitis; **CKD:** Chronic Kidney Disease; **MCP:** Monocyte Chemo attractant; **PGE:** Prostaglandin E; **LPS:** Lipopolysacchride; **COX:** Cyclooxygenase; **DMARD:** Disease Modifying Anti Rheumatic Dru.

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