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Case Report

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NON-STEROIDAL ANTI-INFLAMMATORY DRUGS INDUCED ACUTE KIDNEY INJURY- A CASE REPORT

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ABSTRACT

NSAIDs are widely used drugs and are generally safe, but their usage should be limited to avoid causing damage to the kidney's structure and potential renal impairment. This case study includes a woman with history of NSAID abuse to alleviate knee pain. She developed AKI due to excessive usage of NSAID. She had hypoalbuminemia, increased ESR, increased serum creatinine levels and increased ESR, decreased GFR and reduced urine output which play a key role in diagnosing AKI along with thorough physical examination. The role of loop diuretics like furosemide to rule out edema and to improve AKI has been discussed. Appropriate treatment strategies to overcome other than performing dialysis, as dialysis shows promising results, but it has its own challenges that need to be overcome.

KEYWORDS: Non-steroidal anti-inflammatory drugs, Acute kidney injury, Serum creatinine levels, Glomerular filtration rate, Furosemide, Antibiotics, Anti-inflammatory medications.

INTRODUCTION

AKI is a medical condition characterized by a sudden reduction in kidney function that occurs within hours, and it includes both injury to the kidney's structure and impairment of its function. Medications can often have harmful effects on the kidneys as they can expose glomerular, interstitial, and tubular cells to significant concentrations of medications and their byproducts.[1] Thus, the diagnosis of AKI is established when the serum creatinine level increases by 0.3 mg/dl or more within 48 hours, or when it rises to at least 1.5 times the baseline value within 7 days. A urine output of less than 0.5 ml per kilogram of body weight per hour for six consecutive hours.[2] Hypoalbuminemia is a recognized risk factor for higher rates of illness and death. It is commonly defined as low levels of serum albumin ($\leq$ 3.5 mmol/L). Moreover, it has been linked to a greater likelihood of developing AKI.[3] Inflammation is a multifaceted biological response that plays a critical role in eliminating microbial pathogens and repairing damaged tissue following various types of injury. AKI has been linked to both local and widespread inflammation in the body.[4] Inflammation can cause an accumulation of excess fluid in the interstitial space, which is known as interstitial edema. This can be caused by increased capillary hydrostatic pressure, reduced plasma oncotic pressure, and increased capillary permeability, all of which may result in an increased filtration of fluid across the capillary membrane, leading to the formation of edema.[5] Non-steroidal anti-inflammatory drugs (NSAIDs) are widely used over-the-counter medications and are recognized to have detrimental impacts on kidney function. Despite their common usage and perceived safety, NSAIDs carry a risk of causing a decline in renal function, even at therapeutic doses.[6]

Pathophysiology involved in NSAID induced AKI:

There are two separate pathological conditions that can result in harmful effects on the kidneys from these drugs. One mechanism through which NSAIDs can cause acute kidney injury (AKI) is by decreasing prostaglandins, which regulate vasodilation at the glomerular level. NSAIDs interfere with the compensatory vasodilation response of renal prostaglandins to vasoconstrictor hormones released by the body. The second mechanism of AKI associated with NSAIDs is acute interstitial nephritis (AIN), which is marked by the presence of inflammatory cells infiltrating the interstitial space of the kidneys. AIN results from an immunological response that occurs about a week after exposure to NSAIDs. Acute interstitial nephritis (AIN) is now acknowledged as a significant cause of drug-induced AKI, contributing to around 15% of cases of unexplained AKI.[6]

Case presentation: A female patient aged 50 years was hospitalized in a tertiary care hospital with complaints of bilateral knee pain for three months, for which she was using NSAID's. She also reported swelling in her lower limbs and redness in her left lower limb associated with pain over the left calf muscle for the past 15 days. Additionally, there were pus-filled discharges and erosions present in her left axillae, ulcers over both the armpits and both inguinal regions for the past 10 days. The patient also experienced a decrease in urine output, weakness in both lower limbs, loose stools, and had a fever. She has a previous history of seizure disorder; she is chronic alcoholic and a chronic smoker.

During the examination, it was observed that the patient had poorly defined erythematous patches with unclear borders, as well as ulcers in the skin folds of the bilateral axilla and inguinal regions. It was observed that she was having bilateral pitting edema and tenderness over the left calf. It was noted that the patient had swelling with the formation of pits when pressure was applied (known as pitting edema) in both legs, and there was also tenderness in the left calf. The patient was found to be conscious, coherent, afebrile, with a blood pressure of 120/70 mmHg, pulse rate of 90bpm, SPO_2- 96% in Radial artery, heart sounds S1S2 were heard.

Laboratory findings were as follows: Her laboratory findings show that she had hypoalbuminemia, raised serum creatinine levels, decreased GFR, decreased urine output and the urine was dark yellow in color and acidic in nature which indicates presence of AKI, increased ESR, which is an indication of inflammation, she was also anemic with hemoglobin level of 6.7g/dl. The detailed information regarding laboratory tests is depicted in the table 1 below,

Table 1: A table depicting the results of laboratory tests.

Name of the diagnostic procedure	Abnormal values	Standard values
Radiometer ABL 800 blood gas analyzer results:		
1. pH	7.488	7.350-7.450
2. pCO2	28.3mmHg	32.0-45.0 (mmHg)
3. HCO3	20.2mmol/L	22-32mmol/L
Complete Blood Picture:		
1. White blood cells	29,030 UL	4,500-11,000 UL
2. Red blood cells	34,70,000 UL	47,00,000-61,00,000 UL
3. Platelets	7,41,000 UL	1,50,000-4,50,000 UL
4. Hemoglobin	6.7 g/dl	11.6-15 g/dl
5. Hematocrit value (HCT)	25.8%	36-48%
6. Mean corpuscular volume (MCV)	74.4 FL	80-100 FL
7. Mean corpuscular hemoglobin (MCH)	22.2 Pg/cell	27-31 Pg/cell
8. Mean corpuscular hemoglobin concentration (MCHC)	29.8 g/dl	32-36 g/dl
9. Serum creatinine levels	1.4 mg/dl	0.59-1.04 mg/dl
10. Albumin levels	2 g/dl	3.5-5.5 g/dl

Inflammatory arthritis with AKI caused by the excessive use of NSAIDs was diagnosed through a comprehensive analysis of the patient's indications, physical examination, and laboratory test results. The treatment pattern followed is as mentioned below,

Treatment: She was prescribed with an antibiotic piperacillin tazobactam (2.25mg) IV TID to rule out any bacterial infections as she was having erythema, Inj. Lasix was administered to reduce pitting edema, T. Sporolac was given to relieve loose stools, T. Levipil and T. Lorazepam were prescribed as she had seizure disorder, to alleviate arthritis T.HCQ was prescribed, as she has AKI it is not recommended to prescribe steroids to alleviate arthritis and reduce inflammation, piperacillin tazobactam was found to be ineffective so it was replaced with another antibiotic T. Doxycycline 100 mg PO BD, Inj. MVT and Inj. Thiamine are given as nutritional supplements. Table-2 gives us basic information regarding medications used.

Table 2: List of medications prescribed.

S. No	Brand name	Generic name	Dose	Frequency	Route of administration
1.	Inj. Piptaz	Piperacillin+ Tazobactam	2.25g	TID	IV
2.	Inj. Lasix	Furosemide	40mg	BD	IV
3.	T. Sporolac	Lactic acid DS	120M	TID	PO
4.	Inj. MVT	Multivitamin	1 ampoule	OD	IV 1-unit N.S
5.	T. Levipil	Levetiracetam	500mg	BD	PO

6.	Inj. Pan	Pantoprazole	40mg	OD	IV
7.	Inj. Zofer	Ondansetron	4g	BD	IV
8.	Inj. Thiamine	Vitamin- B1	1 ampoule	OD	IV 1-unit N.S
9.	T. Lorazepam	Lorazepam	2mg	OD	PO
10.	T. HCQ	Hydroxychloroquine	200mg	BD	PO
11.	T. Doxy	Doxycycline	100mg	BD	PO

DISCUSSION

Presently, methods for diagnosing AKI involve an extensive review of the patient's medical history and a comprehensive physical examination. The laboratory assessment comprises testing for serum creatinine (S. Cr), urea, and electrolytes. Additionally, urine analysis and microscopic examination, along with urinary chemistries, may provide valuable insights into the underlying cause of AKI.[7] Monitoring of serum albumin levels can assist in identifying patients who are at a higher risk of developing AKI and may benefit from early intervention to correct hypoalbuminemia.[3] Hypoalbuminemia is caused by a combination of factors including the loss of albumin through urine due to proteinuria, inadequate production of albumin by the liver to compensate for the loss, and potentially an increase in the breakdown of albumin.[8] Referring and intervening in nephrology at an early stage is expected to lead to better results. A delay or lack of referral in nephrology has been linked to increased mortality, dependence on dialysis, and a longer duration of hospitalization. Our recommendation is to discontinue the use of all nephrotoxic medications, except when necessary for critical medical situations. AKI can be reversed early by discontinuing the drug that caused it.[9] In this case furosemide was the loop diuretic which was utilized to treat edema and to eliminate excess fluids from the body. In AKI patients, a higher than usual dose of diuretics may be necessary to achieve diuresis. Additionally, it is widely believed that a continuous infusion of loop diuretics may be more effective than intermittent boluses.[10] A comprehensive clinical evaluation of fluid and volume levels is crucial for immediate resuscitation with normal saline, eliminating nephrotoxic substances, and offering early and sufficient enteral nutritional support. These are the fundamental measures for preventing and treating AKI [9]. Increased understanding of the potential hazards associated with the use of NSAIDs may lead to a decrease in the occurrences of nephrotoxicity.[6]

CONCLUSION

In this case study the patient had been inappropriately using NSAIDs to alleviate knee pain, which resulted in an adverse outcome of AKI. The diagnosis was confirmed based on elevated Sr. Cr levels, hypoalbuminemia, decreased GFR and reduced urine output and thorough physical examination. Edema has been ruled out and the patient appropriate renal function test values, her serum creatinine levels have become normal with appropriate treatment strategies without performing dialysis. Although NSAID's are not very harmful their misuse can lead to impairment of renal function and may cause structural damage within the kidney. Proper monitoring is necessary to prevent the abuse of NSAID's. It is crucial to use NSAID's with caution to avoid the development of AKI.

List of Abbreviations:
AKI- Acute kidney injury
NSAID- Nonsteroidal anti-inflammatory drugs
AIN- Acute interstitial nephritis
GFR- Glomerular filtration rate
ESR- Erythrocyte sedimentation rate
Sr. Cr- Serum creatinine
SPO2- Oxygen saturation
PCO2- Partial pressure of Carbon dioxide
HCQ- Hydroxychloroquine

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