A rare case of cephalexin-induced acute interstitial nephritis with hypokalemic periodic paralysis

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Abstract
Drug-induced acute interstitial nephritis (AIN) is often encountered in clinical practice. Cephalexin is a first-generation cephalosporin with antimicrobial sensitivity ranging from Gram-positive to Gram-negative organisms. Cephalexin-induced AIN presenting with hypokalemic periodic paralysis (HPP) has been rarely reported. A 34-year-old female with recent history of oral cephalexin intake presented with acute onset paraplegia with deranged renal parameters and hypokalemia. She was treated conservatively with mechanical ventilator support. HPP could be a rare clinical presentation for cephalexin-induced AIN.

Keywords:
Acute interstitial nephritis, cephalexin, hypokalemic periodic paralysis

Introduction
Cephalexin is a first-generation cephalosporin with antimicrobial sensitivity pattern ranging from Gram-positive organisms such as methicillin-susceptible Staphylococcus aureus, coagulase-negative Staphylococci spp., penicillin-susceptible Streptococcus pneumoniae, Streptococcus sp. and Gram-negative bacteria like Moraxella catarrhalis, Escherichia coli, Klebsiella pneumonia, and Proteus mirabilis. Like other cephalosporins, bactericidal action of cephalexin is performed through interfering with the later stages of bacterial cell wall synthesis through inactivation of one or more penicillin-binding proteins and inhibiting cross-linking of the peptidoglycan structure.

The usual adult dosage is 0.25–1 g/day given in two to four divided doses depending on the clinical requirements. Up to creatinine clearance of 10–29 ml/min, no dose adjustment is required. Cephalexin is usually well tolerated with few side effects such as neutropenia, thrombocytopenia, eosinophilia, body rashes, deranged liver function tests, and rarely associated to cause interstitial nephritis.[1]

Hypokalemic periodic paralysis (HPP) is an uncommon neuromuscular disorder characterized by transient episodes of flaccid muscle weakness, and exceptionally, respiratory failure, and death. Etiology of HPP can be either of primary, idiopathic, familial or secondary which is mostly acquired as a result of loss of potassium from kidneys, gastrointestinal tract or skin.[2]

However, no case of cephalexin induced AIN with HPP has been reported yet, at best of our knowledge.

Case Report
A 34-year-old female with urban background presented in the emergency room with inability to move all her limbs for the past 24 h. The paresis was acute in onset, rapidly progressive in upward direction.

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Kumar, et al.: Hypokalaemic periodic paralysis secondary to cephalexin induced AIN

Indian Journal of Pharmacology - Volume 52, Issue 3, May-June 2020

with complete paralysis of all four limbs within 24 h. However, the bladder and bowel habits were normal. She was found to be normotensive and normoglycemic. She gave a prominent past history suggestive of upper respiratory tract infection with fever and severe body ache and had taken oral cephalexin 500 mg twice daily as per prescription from elsewhere for the past 5 days. The patient’s condition rapidly deteriorated post admission and required mechanical ventilation. Arterial blood gas analysis revealed severe metabolic acidosis with normal kidney and liver function tests, 19,800 mm³ total leukocyte count, hypokalemia, and normal serum sodium levels. The patient was treated with intravenous sodium bicarbonate infusion, potassium chloride, Piperacillin-Tazobactam and other supporting drugs in the line of septic shock with hypokalemia. Within 48 h, the patient developed severe hypernatremia with hypokalemia and deranged renal parameters. The patient was additionally treated with free water and infusion of dextrose as per recommendations for hypernatremia correction. Gradually, over a period of 3 days, the patient’s hypernatremia, hypokalemia with renal parameters showed normalizing trends with correction of sepsis indicators. This was accompanied with improvement of limb paresis and respiratory drive. The patient was gradually weaned off from mechanical ventilation support as per standard protocols. On 7th day postadmission, the patient showed normal laboratory parameters with full power in all four limbs. Native kidney biopsy was not performed as creatinine improved before extubation and there was no any other indication. The laboratory and imaging parameters of the patient post admission are presented in Table 1.

Table 1: Laboratory parameters of the patient

| Parameters                          | Day 1     | Day 2     | Day 3     | Day 4     | Day 5     | Day 6     | Day 7     |
|------------------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| Hb (g/l)                           | 12.1      | 11.1      | 10.7      | 9.3       | 9.7       | 9.8       | 10.5      |
| TLC (mm³)                          | 19,800    | 24,500    | 27,500    | 17,500    | 13,200    | 12,600    | 11,400    |
| Urea (mg/dl)                       | 41        | 48        | 76        | 73        | 71        | 65        | 50        |
| Creatinine (mg/dl)                 | 0.8       | 0.9       | 1.7       | 1.6       | 1.4       | 1.3       | 1.2       |
| Sodium (mmol/L)                    | 140       | 143       | 170       | 165       | 161       | 151       | 144       |
| Potassium (mmol/L)                 | 1.9       | 2.2       | 2.7       | 4.2       | 4.2       | 4.3       | 4.7       |
| Liver and thyroid function test    | Normal    | Normal    | Normal    | Negative  | Normal    | Negative  | Positive  |
| ANA                                | Normal    | Normal    | Normal    | Negative  | Normal    | Negative  | Normal    |
| Serum protein electrophoresis      | Negative  | Negative  | Negative  | Negative  | Negative  | Negative  | Negative  |
| Serum ACE                          | Normal    | Normal    | Normal    | Normal    | Normal    | Normal    | Normal    |
| Anti R/Li                          | Positive  | Positive  | Positive  | Positive  | Positive  | Positive  | Positive  |
| Urine for eosinophils              | Right kidney: 8.4x4.5 cm, Left kidney: 8.4x4.2 cm | Increased echogenicity indicating medical renal disease | Normal echogenicity and corticomedullary differentiation | No Hydronephrotic changes | No Hydronephrotic changes |
| NCCT KUB                           | Normal echogenicity and corticomedullary differentiation | No Hydronephrotic changes | No Hydronephrotic changes | No Hydronephrotic changes | No Hydronephrotic changes |

Discussion

Drug-induced AIN is secondary to immune response in humans. It is dose independent, occurs only in a miniscule proportions of people taking the drug and recurrence of the adverse reactions on re-exposure to the same drug or a closely related one. Studies of experimental models of AIN have shown that their induction can involve either cell-mediated immunity or antibody-mediated immunity, and in some cases, the same antigen can even trigger either type of immune response depending on the species.[3] Analyses of human renal biopsy tissue and of kidneys taken from animals with experimental AIN have shown that acute interstitial inflammatory reactions are associated with damage to tubular cells. The lesions are multifactorial and are due to direct interactions between inflammatory cells and tubular epithelial cells, to the release of soluble molecules by inflammatory cells, or to the activation of the complement cascade. On the basis of both animal and human studies, pathogenesis of hypokalemia nephropathy is presumed to be due to renal vasoconstriction, reduced medullary blood flow, and impaired renal angiogenesis. There is evidence of progressive capillary loss, reduced endothelial cell proliferation, and loss of vascular endothelial growth factor expression.[4]

Hypokalemia nephropathy occurs in renal diseases associated with renal potassium wasting conditions such as in Fanconi syndrome, renal tubular acidosis, cystinosis, and diuretic abuse.[5]

In the present case scenario, it is strongly postulated that cephalexin induced renal tubular injury and acute
interstitial inflammation led to potassium wasting and renal tubular acidosis. This eventually induced secondary HPP in the patient prompting mechanical ventilation support. Correction of acidosis along with sodium replacement led to hypernatremia. Progressive stabilization of serum electrolytes along with renal parameters improved the paresis of the muscles. Subsequently, the patient showed dramatic improvement of general condition.

Conclusion

Extensive literature searches in renowned scientific platforms have revealed few cases of cephalexin induced AIN. Past literatures have also reported cases of primary and secondary HPP. However, this was the first clinical case reported for cephalexin induced AIN with associated secondary HPP and renal tubular acidosis. This has prompted the current authors to highlight the details of the case for future medical references and further documentations.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understand that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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