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Gentamicin-Induced Nephrotoxicity in a Patient with Alcoholic Liver Cirrhosis

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Case Report

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Abstract: Gentamicin remains a first line therapy for many severe infections. Its use is associated with a low rate of resistance; moreover, it is inexpensive. Data from medical literature reveal an increase in the incidence of acute renal failure associated with the use of aminoglycosides antibiotics. Presented is a case or a 41-year-old male with a history of liver cirrhosis who developed acute renal failure one week after initiating gentamicin therapy for the management of cellulitis.

Keywords: Aminoglycosides, Gentamicin, Acute renal failure, alcoholic cirrhosis

INTRODUCTION

Aminoglycosides are used for serious gram negative bacillary infections (especially those caused by Pseudomonas aeruginosa). They also possess positive synergism against gram-positive pathogens [1, 2]. Adverse effects of aminoglycosides include ototoxicity, nephrotoxicity, and less commonly neuromuscular blockade [3]. Data from medical literature reveal an increased incidence of acute renal failure associated with the use of aminoglycoside antibiotics [4]. Several factors have been reported to increase the risk of aminoglycoside nephrotoxicity; these include duration of therapy (more than 3 days), administration of high doses, recent use of aminoglycosides, administration of aminoglycosides between midnight and 7AM [1]. Other risk factors include volume depletion, elevated baseline creatinine, concurrent administration of vancomycin, amphotericin B, furosemide, clindamycin, pipracillin, cephalosporins, foscarnet, iodine contrast, advanced age and liver dysfunction (hypoalbuminemia and hyperbilirubinemia, potassium, magnesium depletion) [1, 5-7].

CASE REPORT

A 41 year-old male with a history of alcoholic liver cirrhosis presented to the emergency department with a 1-year history of lower limb edema. The edema was associated with redness and pain on walking since one week. The patient also complained of fever, chills, cough associated with whitish sputum for three days, diarrhea 4-5 times the previous day. His past history included grade II varices, pyloric erosions and dueodenal erosions. He works as a policeman and smokes 4-5 packs a day. His medication history included ranitidine 150mg daily and propranolol 10mg daily. The patient discontinued his medications two months prior to his presentation.

Laboratory Investigations revealed the blood indices (WBC, MCV, MCHC) within normal limits, hemoglobin, hematocrit, MCH were low.

Renal function tests revealed high urea, creatinine within normal limits.

Electrolytes investigation revealed low sodium and chloride.

TCO2 within normal limits.

Liver function tests revealed low albumin and total protein, globulin within normal limits, bilirubin, alkaline phosphatase, SGPT, Gamma GT were elevated.

Occult blood positive.
Coagulations tests revealed elevated PT, APTT, INR and FDP.

Abdominal ultrasound revealed mildly enlarged liver and diffuses alteration in echotexture.

Viral screen revealed VDRL. HIV, HSAg were negative.

Physical examination revealed obese male with marked jaundice, pallor and cyanosis. Abdomen was distended, liver and spleen were not palpable, and ascites was not detected.

Vitals: Temperature 39c, pulse regular 100/min, respiratory rate 22/min, blood pressure 130/80mmHg.
Heart examination revealed S1, S2, no murmurs.

Respiratory system examination revealed clear chest, no crepitation.

CNS examination revealed that the patient was oriented to time, place, and person.
Speech was intact.

Initial management included vitamin k 10mg IV slowly for 4 days, blood transfusion, and vitamin B complex 1 injection daily for 6 days, propranolol and ranitidine were continued. Three days following admission patient developed cellulitis of right lower leg for which gentamicin 80mg IV infusion every 8 hours was initiated. Two days later the trough gentamicin level was 1mg/ml, gentamicin dose was increased to 120mg IV infusion every 8 hours. Five days later the peak gentamicin levels were 3.3mcg/ml, the dose was increased to 160mg IV infusion every 8 hours. The next day, the peak gentamicin level was 8.4mcg/ml, the trough level was 2.2mcg/ml, and urea level was 23.6 micromol/l (normal range 2.9-8.3 mmol/L and creatinine 497unitmol/l (normal range 59.2-104 unitmol/L) His oral intake was 1300ml, output was 1750ml. The diagnosis of non oliguric acute tubular necrosis wasinduced by gentamicin was made. Gentamicin was discontiued and ampicillin, cloxacillin were started. Ultrasound of the kidney revealed normal kidney size, no evidence of hydronephrosis. The patient was placed on hemodialysis, his renal function returned to normal 15 days later.

DISCUSSION

The acute kidney injury induced by aminoglycosides occurs 5-7 days after initiating aminoglycosides therapy. The non oliguric aspect of the renal failure is secondary to loss in renal concentrating ability that may be caused by distal tubular damage. The acute tubular necrosis associated with aminoglycosides therapy is rarely severe with elevations in serum creatinine of 44-177 micromo/L. However, aminoglycosides therapy may be associated with renal toxicity requiring renal replacement therapy in patients who have a history of chronic renal disease. The urine sediment most commonly reveal mild proteinuria, hyaline and granular casts. The fractional excretion of sodium is usually above 10% [8]. Other manifestations of aminoglycosdes toxicity include elevated urea, enzymuria, aminoaciduria, glycosuria and electrolyte disturbances (hypercalciuria, hypermagnesemia, hypocalcemia and hypomagnesemia [9].

Using the Naranjo probability scale for adverse drug reactions the diagnosis of non-oliguric cute tubular necrosis induced by gentamicin is possible. The possibility of concurrently administered drugs causing this adverse reaction was ruled out. The patient was not rechallenged with gentamicin due to the high possibility of this diagnosis.

CONCLUSIONS

This case illustrates non-oliguric acute renal failure possibly induced by gentamicn. A Medline search revealed no cases of adverse reaction reported uptill this date.

Aminoglycosides volume of distribution increase in patients with ascites which results in lower serum levels of aminoglycosides. Therefore, clinicians must be aware of this adverse reaction and be cautious with dosing these drugs in patients with liver dysfunction and dosages must be adjusted carefully. Alterntaive antibiotics should be used if possible.

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