



A Case of Azathioprine Induced Acute Pancreatitis in Post Renal Transplant Patient

Authors

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Abstract

Acute pancreatitis, the sudden inflammation of the pancreas is characterized by elevated levels of pancreatic enzymes such as amylase and lipase. Acute pancreatitis present as sudden onset of pain in the upper abdomen which may spread to the back side and vomiting. The most common cause of acute pancreatitis is gallstone, metabolic causes such as hypercalcemia, hypertriglyceridemia, infections and the drugs such as thiopurine (azathioprine, 6-mercaptopurine (6-MP)), corticosteroid, metronidazole and biological agents. Among them azathioprine mainly causes acute pancreatitis. Here we present a case on azathioprine induced acute pancreatitis.

Introduction

About 1-5 % of the patients after organ transplantation suffers from acute pancreatitis.¹The common etiological factors in post renal transplant patients include biliary tract disease, alcohol intake, viral infection, hypercalcemia, hyperparathyroidism, hypertriglyceridemia, uremia, hypertension and drugs.² Drugs such as thiopurine (azathioprine, 6-mercaptopurine [6-MP]), corticosteroid, metronidazole and biological agents can lead to acute pancreatitis. A purine analogue, Azathioprine is used as an immunosuppressant which prevent graft rejection of transplanted organ.³

Acute pancreatitis is confirmed by any of the two criteria such as abdominal pain, serum amylase or lipase greater than three times the upper limit of normal and characteristic findings from abdominal imaging.⁴ The following criteria determine the

drug induced acute pancreatitis: (1) The time sequence between the drug administration and acute pancreatitis development. (2) Improvement of clinical status after drug withdrawal. (3) There is re-appearance of symptoms, after re-exposure.⁵ Management of acute pancreatitis include Intravenous fluid resuscitation which is titrated according to urine output and comorbidities of patient, electrolyte replacement, analgesia and treatment of underlying causes and complications of acute pancreatitis. Withdrawal of drug is essential in case of suspected drug induced acute pancreatitis.⁶

Case Report

A 49-year-old post renal transplant female patient who presented to emergency department of our hospital with complaints of pain in the left hypochondric and epigastric region radiating to the back associated with 3-4 episodes of vomiting

and one episode of loose stool. On physical examination she was conscious and oriented, Blood Pressure: 120/80 mmHg, Pulse:80 bpm, Respiratory rate: 20 breath per min, the abdomen was soft and no tenderness was present. She had undergone renal transplant surgery in 2020 and was taking Azathioprine 50 mg twice a day for last two weeks. On laboratory tests, Hb: 12 g/dl, Total Leucocyte Count: 11690 c/cumm, platelet: 164000 c/cumm, Total RBC: 4.16 million c/cumm, CRP:217.86 mg/L, Hematocrit: 37.6%, blood urea: 24 mg/dl, serum creatinine: 0.9 mg/dl, serum sodium: 146 mEq/L, serum potassium: 3.5 mEq/L, serum calcium:8.7 mg/dl, serum chloride: 110 mEq/L, serum phosphate: 3.9 mg/dl, SGOT: 59 U/L, SGPT: 63 IU/L, ALP: 60 U/L, GGTP: 146 U/L, total bilirubin:1 mg/dl, direct bilirubin:0.5 mg/dl, total protein: 5.8 g/dl, serum albumin: 4.1 g/dl, serum globulin: 2g/dl, A:G ratio: 1.9, serum amylase: 3040 IU/L, serum lipase: 5630 IU/L, Non Contrast Computerized Tomography was performed which showed bulky pancreas with indistinct margins and peripancreatic fat stranding. USG abdomen and x-ray abdomen shows no significant findings.

In view of above lab values the patient was diagnosed as acute pancreatitis and undergone supportive management. At the time of admission, patient was on Prednisolone 5 mg/day, Azathioprine 100 mg/day, Tacrolimus 3 mg/ day, Sulphamethoxazole/Trimethoprim 800/160 mg/day. To control diabetes mellitus and hypertension, Linagliptin 5mg/day and Metoprolol 12.5 mg/day were taken respectively. Work up for abdominal pain was done in which her amylase and lipase were found to be raised. Renal function and urine output was continuously monitored. By excluding the other causes of acute pancreatitis, drug induced acute pancreatitis was diagnosed. Causes such as gallbladder stone, alcohol, hypercalcemia, hypertriglyceridemia was ruled out in our patient. On the second day of hospital admission, drug azathioprine was discontinued as it is a major factor for inducing acute pancreatitis and started conservative management. From the

third day onwards, we noticed improvement in the clinical status of the patient and hence we concluded it as a case on azathioprine induced acute pancreatitis. On the fourth day, symptoms such as pain and vomiting subsided with conservative management thereby patient's condition improved. Patient was discharged on the next day and called for follow up.

Discussion

Acute pancreatitis is the severe inflammatory clinical condition with high mortality of 1-30%. In transplant patients, azathioprine may be implicated as a major cause of drug induced acute pancreatitis.¹ However, the exact mechanism of drugs induced acute pancreatitis is unknown. The cytotoxic effect of drugs that are caused by mechanisms such as biliary constriction, accumulation of toxic metabolites and hypersensitivity, may be the reason for acute pancreatitis. From the literature reports, the risk of getting acute pancreatitis is eight times higher in patients taking azathioprine.⁷ Upon withdrawal of the offending drug, all the signs and symptoms disappear over a period of 1-11 days in case of drug induced acute pancreatitis, which is benign course whereas in post-transplant immunosuppressed patients it may be severe or lethal course.^{8,9,10} In our patient it took 3 days to recover from signs and symptoms. The incidence of pancreatitis is higher in post-transplant patients than non-transplant patients (20-30%). The mortality in immunocompromised patients ranges from 50-100%, whereas only 5-10% of mortality rate is in non-immunosuppressed patients.¹⁰⁻¹⁴

Our patient undergoes renal transplantation since one year and was on mycophenolate mofetil 360 mg twice a day. Later patient came in out-patient department and prescribed azathioprine 500 mg twice a day. The diagnosis of drug induced acute pancreatitis is made by excluding other clinical causes.⁷ Causes such as gallbladder stone, alcohol, hypercalcemia, hypertriglyceridemia was ruled out in our patient.^{1,15} After two weeks of azathioprine administration, patient admitted with

complaints of abdominal pain, vomiting and loose stool. Acute pancreatitis was detected after two weeks of azathioprine course, hence this drug was stopped on the second day of hospitalization and managed with conservative therapy.

In conclusion, patients with azathioprine induced acute pancreatitis, azathioprine is contraindicated and should not be used. In case if patient develops severe symptoms of acute pancreatitis, immediate medical care should be taken. Patients who are taking azathioprine should be closely monitored for the manifestations of acute pancreatitis, as azathioprine frequently causes acute pancreatitis. Rechallenge in our case could not be done as azathioprine is contraindicated in patient with azathioprine induced acute pancreatitis.

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