

A Case Report of Metronidazole-Induced Pancreatitis

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E-mail: cristina_corsini@hotmail.com**Submitted:** 01 May 2018; **Accepted:** 07 May 2018; **Published:** 25 May 2018**Abstract**

Case Summary: A 23-year-old African-American female came to the emergency department with sudden onset epigastric pain associated with nausea having begun one day before presentation. Her symptoms started after the third dose of Metronidazole therapy for treatment of bacterial vaginosis. Clinical examination showed moderate epigastric tenderness. Lipase was 771 IU/L on admission. CT abdomen showed mild haziness of peripancreatic fat, which was suggestive of inflammation and diagnosis of acute pancreatitis was made. A detailed history and biochemical evaluation excluded pancreatitis-gallstones, recent increased alcohol intake, ERCP, hypercholesterolemia, hypercalcemia or viral infections. Symptoms resolved quickly upon discontinuation of metronidazole. We conclude therefore that Metronidazole was thought the most probable etiological factor.

Discussion: The proportion of cases of Metronidazole-induced pancreatitis occurs in less than 1% in the general population, and the mechanism of action is not well known. Overall has a benign clinical course when assessed and treated appropriately.

Conclusion: There are only 15 previous case reports of Metronidazole-induced pancreatitis in the literature to our best knowledge. Identification of Metronidazole as the causative agent is the key to recovery, and physicians should discontinue metronidazole in patients with pancreatitis of no identifiable source to ensure proper healing.

Keywords: Drug-induced pancreatitis, metronidazole, bacterial vaginosis

Introduction

Metronidazole belongs to the 5-aminoimidazole group of antibacterial medications used mainly in the treatment of infections caused by anaerobic bacteria which can cause bacterial vaginosis. It is also used in management of Crohn's disease, c. difficile colitis, necrotizing pancreatitis, gastritis, and protozoa infections, among others. Metronidazole is one of the most frequently prescribed antibiotics worldwide.

The adverse side effects of Metronidazole include gastrointestinal upset, urticaria, headache, drowsiness, metallic taste, peripheral neuropathy. Notably, in less than 1% of the patients, it has been associated with pancreatitis [1].

Pancreatitis is an acute inflammatory process of the pancreas. It is clinically characterized by the onset of persistent, severe epigastric abdominal pain. In some patients, the pain may be in the right upper quadrant, or rarely, confined to the left side. Approximately 90 % of patients have associated nausea and vomiting which may persist for several hours. Alcoholism and biliary tract stone disease account for 95% of cases, especially in the U.S.

The diagnosis of drug-induced acute pancreatitis often is difficult to establish, and there are at least 15 reported cases of Metronidazole-induced pancreatitis in the English language literature to date in the PubMed database.

We report a case of acute pancreatitis associated with three days of Metronidazole therapy prescribed for bacterial vaginosis.

Case Report

A 23-year-old African-American female came to the emergency department with sudden onset epigastric pain associated with nausea having begun one day before presentation. The pain was sharp, 10/10 intensity, radiated to the back and aggravated with food. She had a similar episode one year before and was diagnosed with alcohol-induced pancreatitis.

On this occasion, symptoms started after the third dose of Metronidazole therapy prescribed by the patient's PCP for treatment of bacterial vaginosis. The patient denied diarrhea, bloating, fever or chills; denied alcohol intake for the past two months. She is a nonsmoker. No other concurrent medications. No known drug allergies and no history of any autoimmune disease in the family. No relevant surgical history.

Clinical examination showed moderate epigastric tenderness. The patient was tachycardic but afebrile and not jaundiced. She had normal heart and chest examinations. Lipase was 771 IU/L on admission. CT abdomen showed mild haziness of peripancreatic fat, which was suggestive of inflammation. Right upper quadrant ultrasound ruled out gallstones as the cause. Triglyceride levels were normal at 119 mg/dl.

A detailed history and biochemical evaluation excluded pancreatitis-gallstones, recent increased alcohol intake, ERCP, hypercholesterolemia, hypercalcemia or viral infections. Metronidazole was thought the most probable etiological factor.

Supportive management with IV fluids, analgesia, antiemetics and immediate discontinuation of Metronidazole was the primary therapy initiated by the treatment team.

Her clinical course was uncomplicated, and lipase returned to normal (63 mg/dl) on day three post-admission. She tolerated diet and was discharged home to close follow up with her primary care physician.

Discussion

Although more than 100 drugs have been implicated in causing acute pancreatitis, Metronidazole-induced pancreatitis occurs in less than 1% of the cases [2]. There is a documented increased incidence in high-risk populations such as HIV positive patients and children [3].

To make a proper diagnosis, common etiologies must first be excluded. The starting date of treatment correlated with the onset of symptoms and documentation of the response upon discontinuation of the drug are the basis for the identification of the disease. Mallory et al. in 1980 defined those as specific criteria, also including drug rechallenge in their diagnosis criteria.

Our patient developed pancreatitis after the third dose of Metronidazole, and no other etiology was identified. Her symptoms rapidly resolved upon discontinuation of the drug. Although there are only 15 previous case reports of Metronidazole-induced pancreatitis in the literature, the drug meets the above criteria, making a strong association with the onset of acute pancreatitis in our patient. Metronidazole can be identified as the probable causative agent in this case.

A rechallenge occasionally is recommended, but due to the potential side effects, morbidity, and complications especially in a young population, this sometimes goes against patient safety [4].

The mechanism of action of Metronidazole-induced pancreatitis is not well known, but several studies have proposed a possible redox cycling leading to hydrogen peroxide and other free radicals which are toxic to the pancreatic beta cells to induce acute inflammation [5]. It is interesting that even with good penetration of Metronidazole in the pancreas; this is still a rare complication. Idiosyncrasy may play a role.

Like any other drug-induced reaction, Metronidazole associated acute pancreatitis requires a quick withdrawal of the offending agent. Acute pancreatitis overall has a benign clinical course when assessed and treated appropriately.

Conclusion

The incidence of Metronidazole-induced pancreatitis is relatively rare; however it can cause serious morbidity in patients with minimal exposure. Identification of Metronidazole as the causative agent is the key to recovery.

Physicians should discontinue metronidazole in patients with pancreatitis of no identifiable source. Early diagnosis and supportive care will lead to a successful recovery in the majority of cases.

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