Paroxetine-Induced Acute Pancreatitis: Case Report

Paroksetine Bağlı Akut Pankreatit

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Geliş Tarihi/*Received:* 02.07.2008
Kabul Tarihi/*Accepted:* 08.01.2009

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ABSTRACT Acute pancreatitis is a severe disease with considerable morbidity and mortality rates. Drug induced acute pancreatitis, after gallstones and alcohol use, is one of the most common causes of acute pancreatitis. Paroxetine inhibits neuronal reuptake of serotonin and is frequently used in the treatment of major depression. We present a case of a young man with acute pancreatitis induced most likely by oral paroxetine therapy that had been started to eliminate depression. Taking the potential severity of this disease and the widespread use of paroxetine into account, the association between them should always be kept in mind when investigating possible causes for acute pancreatitis.

Key Words: Paroxetine; pancreatitis, acute necrotizing

ÖZET Akut pankreatit yüksek morbite ve mortalitesi olan bir hastalıktır. İlaçlar, safra taşı ve alkolden sonra akut pankreatite yol açan en sık nedenlerden biridir. Paroksetin, serotonin geri alımını inhibe eden ve genellikle major depresyonda kullanılan bir ilaçdır. Bu yazıda depresyon tedavisi için paroksetin kullanmaya başlayan ve sonrasında bu ilaca bağlı akut pankreatit geliştiği düşünülen bir erkek hasta sunulmuştur. Hastalığın ciddiyeti düşünüldüğünde ve paroksetin kullanımının yaygınlığı dikkate alındığında, akut pankreatitli hastalarda neden araştırılırken bu ilacın kullanımınında akılda tutulması gerektiğine dikkat çekilmiştir.

Anahtar Kelimeler: Paroksetin; akut pankreatit

Turkiye Klinikleri J Gastroenterohepatol 2009;16(2):84-7

Acute pancreatitis is a severe disease with considerable morbidity and mortality rates. The overall mortality rate of patients with acute pancreatitis is 2-9%.[1] In patients with severe disease (necrosis and/or organ failure), the mortality rate is approximately 30%.[2,3] Many risk factors are causally related to acute pancreatitis. Gallstones and alcohol consumption are the most important risk factors. Other risk factors include drugs, endoscopic retrograde cholangiopancreaticography (ERCP), trauma, infections, hereditary pancreatitis, hypertriglyceridemia, hypercalcemia, developmental abnormalities of the pancreas, tumors that cause an obstruction of the pancreatic ductal system, toxins, postoperative and vascular abnormalities.[2-4] Drug induced acute pancreatitis approximately constitute approximately 2% of all acute pancreatitis. Over one hundred drugs have been implicated as causes of pancreatitis.[5,6]

Paroxetine hydrochloride is an orally administered psychotropic drug. It is generally used in the treatment of major depressive disorder, social anxiety disorder, obsessive compulsive disorder, panic disorder, generalized anxiety disorder, and posttraumatic stress disorder. According to the information provided by the manufacturer, acute pancreatitis is included in the post marketing voluntary reports of adverse events but may have no causal relationship with the drug.[7] We present a case of a young man with acute pancreatitis associated with oral paroxetine therapy for depression.

CASE REPORT

A 23-year-old male presented to the emergency department with complaints of nausea, vomiting, severe epigastric and left upper quadrant pain radiating to his back. His symptoms started 36 hours prior to his admission. He was diagnosed with depression by his psychiatrist and had been taking oral paroxetine HCl (Paxil®, GlaxoSmithKline) 40 mg once a day for approximately one week. He has no history of a previous illness or medication or alcohol consumption.

His vital signs were normal. He was alert. His respiratory and cardiovascular examination was normal. His abdominal examination was significant for a mildly distended abdomen with mild epigastric and left upper quadrant tenderness. There was no muscular guarding and his bowel sounds were normal. There were no palpable abdominal masses. His laboratory parameters are shown in Table 1.

There were no remarkable signs on his chest x-ray and plain abdominal graphy. His abdominal USG showed no evidence of gallstones or biliary sludge. His abdominal computerized tomography revealed enlargement of the pancreas tail. Pancreas head and corpus were normal, pancreatic parenchyma was homogeneous, there was no sign of pancreatic necrosis, or peripancreatic fluid collections (Figure 1). Other abdominal organs were normal. According to Balthazar-Ranson classification it showed grade B pancreatitis. CT Severity Index Scoring System (CTSI) score was calculated to be 1, in the absence of necrosis. His Ranson score was 1 and his APACHE II score was 3. He had mild pancreatitis according to Atlanta Classification.

We eliminated the most common etiological factors of acute pancreatitis and therefore we were left with either idiopathic or drug induced pancreatitis. When the patient was admitted to the hospital, paroxetine use was interrupted. After that,

TABLE 1: Patient's laboratory parameters and reference ranges.

Laboratory parameters (reference range)	Day of admission
Serum amylase (U/L; reference range: 28-100)	972
Serum lipase (U/L; reference range: 13-60)	360
Blood glucose (mg/dL; reference range: 70-110)	128
Serum aspartate aminotransferase (U/L; reference range: 0-40)	35
Serum alanine aminotransferase (U/L; reference range: 0-40)	36
Serum alkaline phosphatase (U/L; reference range: 35-129)	118
Serum total bilirubin (mg/dL; reference range: 0.0-1.0)	0.98
Serum calcium (mg/dL; reference range: 8.8-10.2)	9.2
Serum total cholesterol (mg/dL; reference range: 110-200)	133
Serum triglycerides (mg/dL; reference range: 50-200)	71
Serum blood urea nitrogen (mg/dL; reference range: 5-25)	20
Serum creatinine (mg/dL; reference range: 0.5-1.2)	0.9
Hemoglobin (g/dL; reference range: 11.5-18.0)	16.7
Hct (%; reference range: 37-50)	48
White blood cell count (cells/mm3; reference range: 4,000-11,000)	12400
Platelet (cells/mm3; reference range:150000-400000)	183000
Serum LDH (U/L; reference range: 240-480)	415
PT (seconds; reference range: 11-15)	12.5
APTT (seconds; reference range: 25-38)	26.2

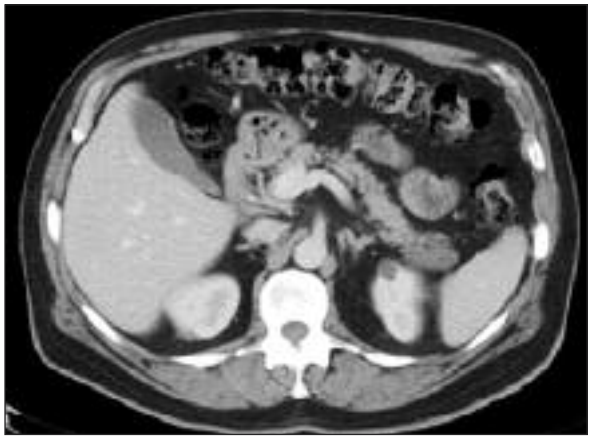

FIGURE 1: Abdominal CT imaging of our patients with a mild acute pancreatitis.

the patient had an uneventful recovery, the symptoms remitted and the serum amylase level returned to normal on day three. Management was mainly supportive; he was treated conservatively by restricting oral intake and with administration of IV fluids, pain control, and observation. There was no need for antibiotics. Oral intake was started on day three and the patient was discharged on day five. He was advised to avoid using paroxetine and his antidepressant therapy was changed by the psychiatry department.

DISCUSSION

The diagnosis of acute pancreatitis in this patient was made according to American College of Gastroenterology's Practice Guidelines in Acute Pancreatitis. According to this guideline diagnosis of acute pancreatitis requires two of the following three features: 1) abdominal pain characteristic of acute pancreatitis, 2) serum amylase and/or lipase ≥3 times the upper limit of normal, and 3) characteristic findings of acute pancreatitis on CT scan.[1] Our patient had met all three criteria and his abdominal CT scan also showed pancreatitis.

Proposed criteria for classifying drugs as having an association with pancreatitis [8,9] include the following: 1) pancreatitis develops during treatment with the drug; 2) other likely causes of pancreatitis are not present; 3) pancreatitis resolves upon discontinuing the drug; 4) pancreatitis usually recurs upon re-administration of the drug. Drugs are classified as having either a definite, probable or possible association with pancreatitis based on the degree to which these criteria are met. Proving a definite association requires that all the criteria mentioned above are met. An association is considered as probable if some but not all of the above mentioned criteria are met. In our case we eliminated the most common etiological factors of acute pancreatitis using history or laboratory tests or imaging and are therefore left with either idiopathic or paroxetine induced pancreatitis. Obviously, reexposure of a patient to a drug with the risk of a potentially fatal complication can be ethically justified only if the suspicious drug is essential for treatment of a significant disease. Therefore in the absence of re-challenge, we believe it is probable that paroxetine was a causative agent in our case of acute pancreatitis.

The association between selective serotonin reuptake inhibitors (SSRI) and acute pancreatitis is recognized by World Health Organization (WHO).[10] Compared with the frequent use of SSRIs, the number of reports in the literature of pancreatitis appears to be generally low.[10] Paroxetine, a SSRI, has a low side-effect profile, even at high doses, and is a popular choice in depression therapy worldwide. According to an analysis performed on the data in the WHO database of adverse drug reactions at the end of the second quarter of 2002, there were 53 reports of pancreatitis related to paroxetine.[10] According to information provided by the manufacturers, acute pancreatitis is a rare event associated with paroxetine.[11]

According to WHO an adverse reaction is "A response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function". Serious Adverse Event or Reaction "any untoward medical occurrence that at any dose" results in death, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is life-threatening.[12] Given these definitions our case re-

port of a probable paroxetine induced acute mild pancreatitis is a serious adverse event.

No pharmacologically plausible link exists between paroxetine and pancreatitis. This implies that the pancreatitis is facilitated by traits of the patient and not by (known) pharmacological traits of the drug. Such patient-related adverse drug reactions are called type B reactions and characterized by the lack of a dose-effect relationship, very low incidence but usually severe in nature. It is a constant reminder to the physician that the existence of a possible adverse drug reaction should be part of every differential diagnosis. Physicians should be informed about this type B adverse drug reaction, since unintended re-exposure may have a dramatic sequel.[13]

CONCLUSION

In summary, we present a clinical case of acute mild pancreatitis most likely related to paroxetine use. Taking the potential severity of this disease and the widespread use of paroxetine into account, the association should always be kept in mind when investigating possible causes for acute pancreatitis. If paroxetine is suspected as the causative agent then it should be discontinued and re-challenge should be avoided.

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