

Clozapine induced acute pancreatitis - A case report

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Abstract

Antipsychotic medication is an important reason for drug-induced pancreatitis especially when two or more antipsychotics are used in combination along with other medications. Two percent of acute pancreatitis are drug induced.

Here we report a case of acute pancreatitis subsequent to clozapine treatment at therapeutic doses in 24-year-old male patient with schizophrenia. “Patients in this review were not otherwise unusual except on treatment of anti-psychotic medication. There were no remarkable trends in respect to patient age, sex, alcoholic history during acute pancreatitis presentations. Anti-psychotic associated Acute pancreatitis requires a good clinical evaluation, accurate blood levels and decision to support the diagnosis and to differentiate it from actual cause of pancreatitis.

Keywords: clozapine, acute pancreatitis, schizophrenia

Introduction

Clozapine is an atypical antipsychotic drug which belongs to the chemical class of dibenzodiazepines. Its main action is to block the dopamine receptors in the limbic system. It is a valued drug in the treatment of refractory schizophrenia which was futile to respond with previous neuroleptic therapy. It rallies both positive and negative symptoms. The efficacy and side effect profile of clozapine are unique. Indeed, clozapine has been used to treat tardive dyskinesia and other movement disorders. The well-known adverse effects of clozapine are granulocytopenia, tiredness and hypersalivation, acute pancreatitis was one of the rare complications of this drug.

The mechanism by which clozapine could produce acute pancreatitis remained unclear. Nevertheless, we advocate a careful biological follow-up (measuring periodically the concentrations of amylase, lipase and triglycerides)

during the treatment by clozapine. In this present paper, we report a case of acute pancreatitis ensuing to clozapine treatment at therapeutic doses in 24-year-old male patient with schizophrenia. Diagnosis of pancreatitis was suggested by clinical examination and abnormal laboratory values of pancreatic enzymes and confirmed by C-T scan and ultrasonography. The causal incrimination of clozapine in this case seems likely as all other possible causes of pancreatitis were excluded, as acute pancreatitis developed shortly after the introduction of the drug and as the pancreatic enzymes normalized after clozapine was stopped. No rechallenge to confirm the causal relationship was endeavoured.

Case report

The 24-year-old male patient visited emergency department of government general hospital, Vijayawada with the complaints of acute abdominal pain, vomiting which was aggravated after taking food and haematuria for 4 days. His vitals are normal. On physical examination, a slight abdominal tenderness was observed. Blood investigation revealed progressive increase in the serum levels of amylase and lipase. CT abdomen was performed which showed distended gall bladder and acute pancreatitis with peripancreatic inflammatory changes with minimal ascites and left pleural effusion.

Further history revealed that he was under depression due to his father's death which progressed to schizophrenic disorder. Thereafter he was treated for acute exacerbation of the psychosis, during the acute episode he had negative symptoms of schizophrenia like anhedonia, apathy, avolition, laughing to self, delusions, hallucinations.

He denied alcohol use and was not taking other substances associated with medication-induced

pancreatitis and there is no past history of similar symptoms. Primarily he was treated with trihexyphenidyl and injection flupentixol, risperidone but his symptoms were not subsided.

He was eventually started with clozapine on outpatient basis at the dose of 50mg and maintained with daily doses of clozapine of 300 mg for 6 months. After 3 weeks, he presented with the above symptoms. There was a progressive increase in the serum levels of amylase 560 U/L and lipase, also mild elevation of liver enzymes and his lipid profile was normal. He was in the intensive care unit and medicine ward for 15 days. He made a full recovery.

The pancreatic enzymes normalized quickly within a few days after discontinuation of the treatment.

Figure 1:



CECT OF ABDOMEN

Figure showing bulky pancreas with fluid collections and surrounding inflammatory changes s/o acute pancreatitis

Discussion

Although atypical antipsychotic-induced pancreatitis has been reported, the pathophysiological mechanism of these adverse events remains unclear. Most anti-psychotic-induced pancreatitis occurs within 6 months after administration, however our case developed pancreatitis

more than 6 months after the start of clozapine treatment. A thorough evaluation for pancreatitis was done in this patient but there is no evidence suggestive of an association between clozapine treatment and acute pancreatitis was found. Hence more study is required to further evaluate the effects of atypical antipsychotics on pancreatic function and pancreatitis. In addition to close monitoring for development of obesity and impaired glucose metabolism, it is prudent to exercise caution in treating patients at high risk for pancreatitis with these medications.

This includes patients with elevated triglycerides, a prior history of pancreatitis, alcohol abuse, metabolic abnormalities and medications that increase the risk of pancreatitis. Patients who have tolerated the medication in the short term should not be viewed as being free from risk of pancreatitis.

Furthermore, when patients present with pancreatitis and biliary disease of unclear aetiology, careful evaluation and a high index of suspicion are necessary to determine if medications such as clozapine may be contributing to the aetiology of pancreatitis.

It is assumed that the phenomenon of subclinical, asymptomatic pancreatitis during increasing dosage of clozapine occurs more often than previously supposed. The monitoring of serum amylase levels during slow increase in clozapine is recommended; if leucocytosis or eosinophilia is present, the possibility of even a subclinical and asymptomatic pancreatitis should be considered.

Conclusion

The incidence of drug induced pancreatitis is increasing globally, especially in patients taking antipsychotics like clozapine, risperidone. Here in this case, we don't have any other associated factor which contributes to acute

pancreatitis except drug history of clozapine. So, awareness needs to be raised in clinicians regarding this association in order to correctly identify aetiology of pancreatitis and discontinue clozapine when suspected as a causative factor. Further studies should be undertaken to identify mechanisms, dose duration responses to these drugs.

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