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ISONIAZID INDUCED PANCREATITIS: A CASE REPORT

Pharmacology

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ABSTRACT

Isoniazid (INH) is one of the first line drugs for category I antitubercular therapy (ATT). The most notable adverse effect due to INH is hepatitis. Acute pancreatitis is rarely caused by medications with an estimated incidence of 0.1-2%. Isoniazid is a rare cause of acute pancreatitis. We here report a case of patient diagnosed with tubercular meningoencephalitis was started ATT consisting of RIMACTAZID (Rifampicin + Isoniazid), Pyrazinamide, Ethambutol and Streptomycin along with prednisolone and within a week the patient developed pain abdomen with diarrhoea. Investigations showed abnormal pancreatic function and imaging suggested acute pancreatitis. ATT were temporarily stopped and 10 days later pancreatic enzymes returned to normal values. Suspected Adverse Drug Reaction was reported. The causality of isoniazid was found to be 'probable' by the WHO-UMC causality scale and causal relationships of other drugs were evaluated and found to be 'possible'.

KEYWORDS

Anti tubercular therapy, Acute pancreatitis, Isoniazid.

INTRODUCTION

There are many etiological risk factors for acute pancreatitis, including a history of alcohol abuse, gallstones, endoscopic retrograde cholangiopancreatography and manometry, trauma or surgical procedures near the pancreas, certain medications, hyperlipidaemia, infection and chronic hypercalcemia.[1,2]

Among antitubercular therapy (ATT) isoniazid (INH) is the first line drug along with rifampicin, pyrazinamide, ethambutol and streptomycin. It is bactericidal and acts by inhibiting synthesis of mycolic acid and is metabolized by hepatic N-acetyltransferase.[3] INH has infrequent major adverse effects, including hepatitis, peripheral neuropathy, hypersensitivity reactions (fever, skin eruptions or hematologic alterations) along with lupus-like syndrome that is reversible on discontinuation of INH.[3,4] The most notable adverse effect is hepatitis. The estimated rate of clinical hepatitis in patients given INH alone is approximately 0.6%.[5] Acute pancreatitis is rarely caused by medications with an estimated incidence of 0.1-2%.[6] Isoniazid is a rare cause of acute pancreatitis.[7] Here we are reporting a case of acute pancreatitis in a young girl who developed it after few days of her ATT.

CASE REPORT

A 15 years old female presented with fever on and off for one year, abnormal body movement one day ago and altered consciousness for one day to outpatient and was admitted. On examination general condition was serious, sedated, poorly nourished, moderate pallor, per abdomen soft and liver 2cm below right costal margin was found. She was diagnosed with tubercular meningoencephalitis, status epilepticus and shock She was managed with intravenous (iv) fluids,

oxcarbazepine, ceftriaxone, vasopressors and supportive care. MRI brain showed right frontal tuberculoma and MRI spine revealed prevertebral and paravertebral collection. Ortho consult was taken for taken for vertebral collection and Ash brace was applied. On day 2 of hospitalization category I anti tubercular therapy (ATT) consisting of consisting of RIMACTAZID (Rifampicin+Isoniazid), pyrazinamide, ethambutol and streptomycin along with prednisolone, were started. Four days later she complained of pain abdomen with diarrhoea and six days later her condition deteriorated with drop in oxygen saturation.

Ultrasonography abdomen showed bulky pancreas with coarse echotexture. Two days later the ultrasonography findings indicated a pancreas that appeared heterogenous in echotexture, mildly bulky with hypoechoic areas which suggested acute pancreatitis (Figure 1). Pancreatic function test was done for confirmation. Serum amylase 1167 U/L (N 20-96 U/L) and serum lipase 3047 U/L (N 13-60 U/L) were significantly increased. Meanwhile, in view of persistent fever, antibiotic was changed to meropenem. CT abdomen was further done which revealed bulky body and tail of pancreas with areas of necrosis with peri pancreatic stranding. Other laboratory test results were included SGOT 34U/L, SGPT 27U/L, albumin 1.8mg/dl, platelets 37000/cumm and Hb 7.1gm%.

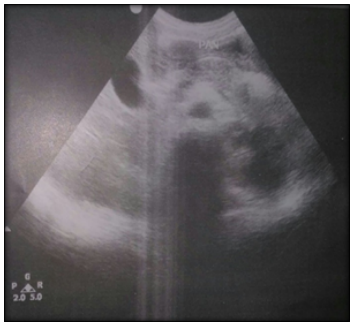

Figure 1. Ultrasonographical findings in isoniazid induced pancreatitis

A possibility of drug induced pancreatitis was considered and ATT was suspended and antiepileptic were changed from carbamazepine to phenytoin and phenobarbitone. She was given fresh frozen plasma transfusion in view of hypoalbuminemia and deranged bleeding profile. Two days later her abdominal pain was reduced and 7 days later her serum amylase and lipase normalised to 53mg/dl and 37mg/dl respectively. As her sensorium and general condition were improving her parents request she was discharged.

The adverse drug reaction (ADR) was reported to ADR monitoring center by filling suspected adverse drug reaction reporting form version 1.2. The causality assessment was done and was found to be probable by WHO-UMC causality scale. The causal relationships of other drugs in the regimen with the reaction were evaluated and found to be possible.

DISCUSSION

As reported in the literature acute pancreatitis induced by INH is a rare complication, that usually occur within 3-4 weeks of start of therapy and reversed by withdrawal of the medicine. However with drug re-challenge the symptoms can recur[4,9] In this case she developed symptoms within a week of start of ATT and her pancreatic enzymes returned to normal after 10 days post-withdrawal of isoniazid. Though both INH and rifampicin are associated with acute pancreatitis,[10] but it is very rare to have acute pancreatitis due to rifampicin. Similar case of isoniazid induced acute pancreatitis has been reported earlier.[12]

It is very important to identify INH induced pancreatitis as the development of this condition might be erroneously recognized either

as an effect of the underlying illness or to some other medications.[4]

Since drug induced acute pancreatitis is potentially reversible and mandates permanent avoidance of isoniazid so the correct and early recognition of the reaction with prompt drug withdrawal is necessary.[8,9] INH-induced acute pancreatitis recognition becomes more vital, due to possible confounding effect of rifampicin and other drugs which are part of first line regimen of ATT.

The exact mechanism for development of acute pancreatitis remains unclear. A dose-dependent manner on the first encounter or a possibility of a hypersensitivity syndrome against INH after a re-challenge has been suggested.[4,9,11] Using therapeutic range and screening of known risk factors (liver or renal disease) can play important role in preventing INH toxicity. Importantly, INH induced

hepatitis and pancreatitis can be completely recovered if the drug is withdrawn early.[10] A high index of suspicion and early withdrawal of isoniazid is the key to avoiding hazardous consequences.

CONCLUSION

We believe that it is important to report this unusual adverse event in which Isoniazid was found to have 'probable' causality in this case of acute pancreatitis.

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