Isoniazid Induced Hepatitis and Psychosis in a Single Patient – Case report

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ABSTRACT

A 22-year-old female who was a known case of tubercular meningitis on anti-tubercular therapy, presented to the emergency room with complaints of recurrent vomiting, markedly reduced appetite, yellowish discoloration of eyes, abnormal behaviour and delusion of reference. There was no prior history of psychiatric illness or hepatitis like illness. Her liver enzymes were elevated more than 3 times of reference value and mental status examination revealed features of acute psychosis. Hepatitis resolved completely after isoniazid was discontinued and psychosis resolved fully only after treatment with amisulpride was begun. The patient was later rechallenged with isoniazid successfully and remained symptom-free 3 months after discharge from the hospital. This is an unusual presentation where both hepatitis and psychosis due to isoniazid occurred together simultaneously.

Keywords: Isoniazid hepatitis, Isoniazid psychosis

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INTRODUCTION

Isoniazid (INH) is one of the primary drugs used in the treatment of mycobacterium tuberculosis infection and is included in all drug regimens used for the treatment of tuberculosis. The commonly known side effects of INH are peripheral neuropathy and hepatitis. Rarely, rash, psychosis, seizures, and even death have been reported on conventional doses of this drug[1,2] . We report a case in which both isoniazid induced hepatitis and psychosis were present together.

CASE REPORT

A 22 year old Asian female was admitted on 22nd of December 2013 with complaints of

recurrent vomiting, markedly reduced appetite ,epigastric discomfort and yellowish discoloration of eyes of 1 week duration. The patient also had history of abnormal behaviour over the same time in the form of irrelevant talking, violent behaviour and incongruent acts. The patient was a known case of tubercular meningitis since 24 weeks and was on continuation phase of anti-tubercular treatment, taking isoniazid 300mg and rifampcin 450mg along with pyridoxine. She had no previous history of alcohol intake, discoloration of eyes or psychiatric illness nor any such family history. General physical examination revealed jaundice which deepened over the initial days of hospitalization. She was afebrile. Liver span was normal and there were no clinical features of chronic liver disease. Mental status examination revealed features of acute psychosis using DSM IV criteria with delusions, hallucinations, suspiciousness, and agitation.

Investigations revealed a normal haemogram, coagulogram and kidney function test. Liver function test showed features of hepatitis with AST 118 mg/dl , ALT 87mg/dl , bilrubin of 4.4 mg/dl (unconjugated 3.3mg/dl), ALP 73 mg/dl, serum protein 6.8 mg/dl and albumin 4.0 mg/dl. Liver function test was repeated 1 day later which showed a worsening trend with bilrubin of 7.3 mg/dl, AST 183 mg/dl and ALT 90 mg/dl .Hepatitis serology panel (A,B,C& E) was negative. ANA was negative. Iron profile & Wilsons profile was also normal. Coagulogram was normal. Sonography showed periportal cuffing only with normal ducts and liver size. Non-contrast computed tomography(NCCT) head was normal.

In hospital, on day 2nd , isoniazid was stopped and ofloxacin was added to rifampcin .LFT monitoring was done on daily basis. Vomiting and epigastric discomfort settled on 2nd day of stopping isoniazid but patient persisted with psychosis and amisulpride was added on advice of a psychiatrist. The psychotic symptoms resolved 3 days after adding the antipsychotic and apetite improved after 1 week of hospital stay.

Liver enzymes (ALT and AST) recovered to normal levels 3 days after stopping isoniazid and bilrubin levels became normal after two weeks.

The patient was rechallenged with low dose of isoniazid(50 mg) while continuing amisulpride, rifampcin and ofloxacin with regular monitoring of liver function . The patient tolerated the drug well and dose was titrated to 300mg/d over period of 3 weeks . Amisulpride was later stopped and patient is doing well after 3 months of follow up.

DISCUSSION

Anti-tubercular drugs are widely used drugs in clinical practice due to high prevalence of mycobacterial infections especially in developing countries . Isoniazid is one of the main drugs in the armamentarium of anti- tubercular therapy.

Adverse drug reactions are known to occur with most of the anti-tubercular drugs and among the first line drugs Isoniazid has been the most commonly implicated drug in causing adverse reactions. The chance of adverse reaction is enhanced when the drug is to be taken for extended period of time as is done in tubercular meningitis where duration of regimen may range from 12 to 24 months.

Our extensive review of literature did not reveal a similar case with hepatitis and psychosis occurring together simultaneously in a single patient.

INH hepatotoxicity can manifest in the form of symptomatic hepatitis with derangement of liver function tests or it may present only as isolated elevation of liver enzymes. The management is guided by symptomology and degree of elevation of liver enzymes . The drug is stopped if patient has only isolated rise of enzymes more than 5 times normal or is symptomatic with enzymes more than 3 times. The patient can later be rechallenged with the drug once LFT has normalized and most patients tolerate the rechallenge successfully [3].

Psychosis is among the rare adverse effects of isoniazid. Psychiatric manifestations due to INH have been reported to occur more commonly in people with unstable personality but can occur in otherwise normal people as well. The psychosis can occur within few days to many months after initiating the drug.INH psychosis shows a great variability in its clinical presentation. As early as 1957, merely 5 years after INH came into general use for tuberculosis, 5 cases of psychiatric disturbances in patients taking INH were described [4]. Of these, 2 actually exhibited psychotic symptoms, one with paranoid delusions and the other with gender identity delusions.Both experienced

improvement within a few months of discontinuation of INH.[4]

Agarwal, in 1974, reported symptoms of restlessness, irritability, emotional instability, agitation, apprehension, and fluctuation in behavior after isoniazid therapy[5] . Bedi, in 1994, reported a case of INH-induced psychosis in a 74-year old who developed restlessness, irritability, aimless activity, and incongruous actions 10 days after start-ing isoniazid therapy.[6] In 1996, Tiwari reported a case of INH-induced psychosis presenting with disturbed sleep, restlessness, and abnormal behavior[7]. Iannacone in 2002 reported a case of suicidal psychosis due to iso-niazid.[8]. Shazia et. al. reported a case of isoniazid psychosis and seizures who responded to antipsychotics and benzodiazepines.[9]

In a case series of 37 patients with INH-associated psychiatric symptoms, a prodromal phase consisting of head-aches, dizziness, inability to concentrate, and irritability was also described. some patients suffered from delirium with psychotic features, whereas others exhibited predominantly neurotic symptoms. One subset of eight patients exhibited more classically schizophreniform delusions, in whom symptoms resolved within 3 to 6 weeks after treatment with neuroleptics and vitamins despite continuation of INH.[10] A 31-year-old woman developed paranoid delusions after 8 weeks of taking INH and pyridoxine for a positive tuberculin skin test. Just like our case her symptoms abated only minimally after INH was discontinued. She responded to 6 weeks of therapy with an antipsychotic medication and was symptom-free 11 months later[11].

Psychosis due to isoniazid responds either to cessation of drug intake or to antipsychotics or combining both the methods together depending upon the severity.In mild cases only an antipsychotic may be added whereas in severe psychosis isoniazid needs to be discontinued. Patient can be rechallenged with the drug successfully under cover of antipsychotics once psychotic symptoms have settled as was done in our case.

CONCLUSION

Clinicians should be aware of the broad range of adverse effect of isoniazid and that multiple adverse reactions can occur in a single patient. Isoniazid psychosis should be kept in differential diagnosis especially in patients of tubercular meningitis in whom psychotic behaviour may also be disease

related or due to concomitant use of corticosteroids. Mild cases can be managed using antipsychotics without cessation of the drug. Patients in whom the drug is stopped due to uncontrolled psychotic symptoms can be rechallenged successfully with isoniazid under cover of antipsychotics.

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