Cycloserine induced psychosis with hepatic dysfunction

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ABSTRACT

With the increase in the cases of multidrug resistance tuberculosis, second line anti-tubercular drugs like the cycloserine are being prescribed frequently. Isoniazid and ethambutol are reported to cause psychosis like state; however, few reports of cycloserine induced psychosis are available. To the best of our knowledge, this is the first case of cycloserine induced psychosis with hepatic dysfunction.

KEY WORDS: Anti-tubercular treatment, cycloserine, multidrug resistant tuberculosis, psychosis

Introduction

Cycloserine (D-4-amino-3-isoxazolidine) is a broad spectrum antibiotic produced by streptomyces-orchidaceus and is commonly used as a second line anti-tubercular treatment (ATT) in multidrug tuberculosis (MDR-TB). ATT induced psychosis is reported with drugs like isoniazid (INH) and ethambutol (EB). Few reports of cycloserine induced psychiatric disorders like delusions and hallucinations, mania and associated seizures are available.

With the emergence of MDR-TB and extensively drug-resistant TB, second line drugs like the cycloserine are used more frequently. We report a case of cycloserine induced psychosis with hepatic dysfunction.

Case Report

A 45-year-old male patient weighing 60 kg, with sputum positive pulmonary Koch’s was put on directly observed treatment (DOTs) Category-I as per revised national TB control programme guidelines on May 2012. On completion of extensive phase of the treatment patient remained acid fast bacilli (AFB) positive. Patient was labeled as Category-I failure and was prescribed Category-II treatment. Patient did not respond to this regimen too. Sputum culture for AFB and drug sensitivity showed the patient to be resistant to INH, rifampicin, streptomycin and EB. At this point of time, liver functions and all basic biochemical parameters were within normal limits. Hence, it was decided to change the treatment to DOTs Category-IV in December 2012, which included injection. Kanamycin 0.5 g intramuscular once daily 6 days a week, tablet levofloxacin 500 once daily, tablet ethionamide 500 mg once daily, tablet cycloserine 500 mg once daily, tablet pyrazinamide 1250 mg in daily divided doses and tablet pyridoxine 100 mg once daily.

In July 2014, the patient manifested with change in his behavior with aggression, violence with wife and other family members, anxiety, restlessness, irrelevant talking, insomnia, recent loss of interest in work, family, clothes and food; for which psychiatric consultation was sought.

The Hamilton score was 18 and brief psychotic rating score was 33 on 3rd day. There were no signs of neurological deficiency. Cycloserine was suspected as the possible offending agent for the adverse event. Thus, DOTs Category-IV regimen was de-challenged on July 2014. The patient was hospitalized and prescribed antipsychotic drugs like injection lorazepam 2 mg at bed time and as and when required, injection haloperidol 5 mg intramuscular twice daily, injection promethazine 50 mg intramuscular once daily, tablet olanzapine 10 mg twice daily, tablet nitrizepam 10 mg twice daily, tablet thiamine 100 mg 3 times a day. After brief de-challenge of 3 days and co-prescribed anti-psychotic medicine, most of the symptoms subsided and the patient improved within 4 days. Keeping this in view, cycloserine containing regimen was again started after 4 days. On 3rd day of taking cycloserine patient again exhibited similar change in behavior. DOTs Category-IV regimen was stopped and the patient was put on the tablet. Levofloxacin 500 once daily, tablet macrozide 750 mg once daily and tablet...
pyridoxine 100 mg once daily. Antipsychotic drugs were continued.

The patient had no history of smoking, alcohol or drug abuse. There was no associated pathology or history of concurrent drug intake. He had no family history of mental disorders. Only recent disinterest in work, family, food, clothes was reported by attendants to present adverse event. No history of anxiety or any conflict with family friends or at work place was reported. Clinical examination revealed that patient was well oriented to time, place and person, having normal pulse rate, icterus positive with, no palpable lymphadenopathy; blood pressure was 128/88 mmHg, chest examination showed bilateral decreased air entry with wheeze, cardiovascular examination was normal, abdomen and central nervous system (CNS) examination were also normal.

Laboratory investigations showed: Sputum AFB positive, hemoglobin 8.2 g/dL, total leukocyte count- 18000 cu3 mm, differential leukocyte count polymorphs - 78: eosinophils - 2 monocytes - 2; lymphocytes - 18 blood sugar fasting - 80 mg/dL, thyroid profile-normal, erythrocyte sedimentation rate - 42 mm/h, serum urea - 23 mg/dL, serum creatinine - 0.5 mg/dL, HIV - 1 and II-nonreactive, serum bilirubin - 5.4 mg/dL, alanine transferase - 192 mg/dL, alkaline phosphatase - 202 mg/dL, Vitamin B6 levels were normal, serum electrolytes were within normal limits. X-ray (PA view) showed bilateral decreased air entry with wheeze, cardiovascular examination was normal, abdomen and central nervous system (CNS) examination were also normal.

Discussion

The temporal relationship, the fact that brief de-challenge ameliorated the symptoms and re-challenge of cycloserine further aggravated the psychosis suggests that cyclosine was the suspected drug for the adverse drug event. Furthermore, the appearance of psychiatric manifestations could not be explained by any concurrent disease, drug or chemical. Adverse drug reaction (ADR) was probable as assessed by WHO uppsala monitoring the center causality scale and Naranjo’s score (score = 8).[6,7]

Severity of the reaction as assessed using Hartwig ADR severity assessment scale[8] classified the said ADR as potentially serious. Preventability assessment was done by using Schumock and Thornton scale[9] which classified the ADRs as preventable. The ADR was not studied for dose dependent response and in view of its uncertain mechanism it is difficult to comment on the type of ADR.

Sharma et al.[3] reported psychosis, delusions and hallucinations with cycloserine. While, mania was the main presentation reported by Bakhla et al.[4] and seizure with psychosis in the case reported by Fujita et al.[5] Unlike above cases our patient was aggressive, violent, restlessness, anxious and presented with insomnia and had severe hepatic dysfunction.

The exact mechanism of such ADR is uncertain. However, possible modulation of N-methyl-D-aspartate receptor (NMDAR) antagonists and partial agonist at NMDAR associated glycine site by the drug as proposed by Bakhla et al.[4] may be the possible mechanism, in this case. The current case further supports this hypothesis since aggression and insomnia suggests a CNS stimulant action of the drug although no seizures were observed in our patient.

Another interesting possibility remains that deranged liver function in our case may have contributed to the decreased metabolism of the drug and hence the response. However, this remains the constraint as drug levels could not be assessed.

The current case report highlights that the psychiatric evaluation should be done preferably before and after prescribing cycloserine containing MDR regimens so that such potentially serious reactions can be prevented before any permanent damage is done.

References

1. Prasad R, Garg R, Verma SK. Isoniazid- and ethambutol-induced psychosis. Ann Thorac Med 2008;3:149-51.
2. Behera C, Krishna K, Singh HR. Antitubercular drug-induced violent suicide of a hospitalised patient. BMJ Case Rep 2014;2014;bcr2013201469. doi: 10.1136/ bcr-2013-201469.
3. Sharma B, Handa R, Nagpal K, Prakash S, Gupta PK, Agrawal R. Cycloserine-induced psychosis in a young female with drug-resistant tuberculosis. Gen Hosp Psychiatry 2014;36:451.e3-4.
4. Bakhla AK, Gore PS, Srivastava SL. Cycloserine induced mania. Ind Psychiatry J 2013;22:69-70.
5. Fujita J, Sunada K, Hayashi H, Hayashihara K, Saito T. A case of multi-drug resistant tuberculosis showing psychiatric adverse effect by cycloserine. Kekkaku 2008;83:21-5.
6. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther 1981;30:239-45.
7. Edwards IR, Aronson JK. Adverse drug reactions: Definitions, diagnosis, and management. Lancet 2000;356:1255-9.
8. Hartwig SC, Siegel J, Schneider P.J. Preventability and severity assessment in reporting adverse drug reactions. Am J Hosp Pharm 1992:49:2229-32.
9. Schumock GT, Thornton JP. Focusing on the preventability of adverse drug reactions. Hosp Pharm 1992;27:538.

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