

Isoniazid Psychosis

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Introduction

Isoniazid (INH) is the drug of choice in any combination of antituberculous therapy in Nepal. Although several of its side effects e.g. hepatitis are well recognized, the effect of the drug on the central nervous system is less often diagnosed. In this report, we describe two cases of INH psychosis to point out its not too uncommon occurrence in patients receiving antituberculous therapy.

CASE 1

Mr. P.S., a 42-year-old male, was admitted with the complaints of fever and altered sensorium for seven days. He had a doubtful history of cough with blood-streaked sputum. There was no history of treatment with antituberculous drugs in the past. On examination, the patient was drowsy with signs of meningeal irritation. No other abnormalities were detected. Chest X-ray revealed a right apical soft tissue infiltration. There was mild lymphocytosis and an ESR of 62mm. first hour CSF examination showed a high protein of 160mg%, normal sugar of 70mg% and 120 cells/mm which were predominantly lymphocytes. The diagnosis of tuberculous meningitis was made along with pulmonary T.B. The patient was started on rifampicin 450mg, INH 600mg, pyrazinamide 2g, ethambutol 1400mg and pyridoxin 10mg daily. His condition improved significantly over the next three days. However, five days after the start of therapy, he developed insomnia, aggressiveness and was not

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responding to verbal commands. A diagnosis of INH psychosis was made. INH was withdrawn immediately and the patient was put on intravenous fluids and pyridoxin was increased to 40mg daily. His mental status returned to normal within 24 hours.

CASE 2

Mrs. R.L., a 54-year-old housewife from Humla District, was admitted with the complaints of intermittent fever, cough with purulent sputum and weight loss for one year. On examination, she was found to be cachectic, pale, drowsy and had mild pitting oedema. Her vital signs were: pulse 122/min, blood pressure 85/50 and axillary temperature 37°C. There were crepitations all over the chest with no bronchial breathing. The abdomen was distended with tenderness and rigidity. There were no cardiovascular abnormalities. Complete hemogram showed a high ESR of 72mm in first hour and anemia of 8.3gm%. Renal and liver function tests were within normal limits. A chest X-ray showed miliary shadows over both lung fields. No AFB was found in the sputum on five different occasions. A diagnosis of miliary tuberculosis was made. She was started on rifampicin 450mg, INH 300mg, pyrazinamide 1.5g and ethambutol, 1000 mg. After five days, the patient became stuporose, refusing her food and medication. She was depressed, drowsy and irritable. A diagnosis of INH psychosis was made clinically. INH was stopped and she was put on parenteral fluids. Her condition improved and was completely well within two days. INH was restarted at 100 mg/day and gradually increased to 200 mg/day with no further complications.

Discussion

Isoniazid is the commonest drug used in the treatment of tuberculosis. It is bactericidal and affects actively multiplying bacilli. The drug has been associated with various adverse reactions, the incidence and severity of which are related to the dosage and duration of drug administration. With daily dosage of 5 mg/Kg/day, adverse reactions are noted in about 5% of cases. Adverse reactions are seen more commonly among slow acetylators, in malnourished individuals, diabetics, alcoholics and old people.

The side effects of INH include hepatitis, allergic reactions (fever, skin rashes), peripheral neuropathy, other neurological complications (encephalopathy, loss of memory, optic atrophy, convulsions, involuntary twitching, tremor, etc) and psychiatric problems.

INH induced psychiatric reactions present a spectrum of symptoms ranging from minimal or borderline reactions to toxic psychosis. Symptoms of behavioral toxicity include insomnia, nightmares, drowsiness, mild depression or excitement, anxiety, mild euphoria, irritability, increased sensitivity to noise, restlessness, transient loss of memory, separation of ideas and reality and loss of self control. In more severe forms, depression may progress to a delirious state and even paranoid psychosis. How INH causes psychosis is not known. It is seen both in rapid and slow acetylators. Unlike peripheral neuropathy these psychiatric complications are not prevented by the administration of pyridoxine, but withdrawal of drug reverses the complication.

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