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Case Report
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Isoniazid Induced Psychosis in a Patient of Pulmonary Tuberculosis - A Case Report

Shreshth Khanna*

Department of Pharmacology, Maulana Azad Medical College, India

Abstract

Isoniazid is one of the most commonly implicated anti-tubercular medicines in substance induced psychosis. We report a case of isoniazid induced psychosis in a 31 years old patient pulmonary tuberculosis patient.

Keywords: Tuberculosis; Isoniazid; Psychosis; Substance induced psychosis; Brief psychiatric rating scale

Introduction

ISONIAZID (Isonicotinic Acid Hydrazide), also called INH is a first-line drug in the treatment of tuberculosis. INH has been in use for the treatment of tuberculosis for many decades. It is one of the first line drugs used in patients of tuberculosis [1].

South-East Asian region bears the maximum burden of tuberculosis with more than 44% burden of tuberculosis incidence. India has the maximum prevalence of tuberculosis in the world [2].

Psychosis is a mental disorder which causes people to perceive or interpret things differently from those who are around them [3]. Substance-induced psychosis, also known as drug-induced psychotic disorder, is any psychotic episode that is related to the abuse of an intoxicant [4]. There remains a paucity of evidence of the cases of isoniazid-related psychiatric illnesses. We report a similar case of suspected isoniazid-induced psychosis.

Case Presentation

A 31-year-old male educated up to high school, shopkeeper by profession, belonging to middle socio-economic strata in urban area with no prior psychiatric history was brought by his wife to the psychiatry outpatient department with the complains of incoherent speech, garbled sentences, paranoid ideation regarding his family (plotting against him and conspiring to steal his belongings), auditory hallucinations and shouting at people who were not around since the last 2 days. These symptoms were associated with intermittent insomnia and a desire to stay in isolation and darkness.

The Brief Psychiatric Rating Scale (BPRS) is one of the commonly used scales to establish about the possible presence and severity of various psychiatric symptoms [5]. The BPRS (Brief Psychiatric Rating Score) was 47 in this patient as evaluated by the psychiatrist on 5th day.

The symptoms started about 4 weeks after he was put on isoniazid 300 mg/day, rifampicin 600 mg/day, ethambutol 800 mg/day and pyrazinamide 1500 mg/day, for pulmonary tuberculosis and pyridoxine (vitamin B6) 20 mg/day for prophylaxis against neuropathy by the prescribing physician. There was no history of recent ingestion of any psychoactive substances. He had a family history of social anxiety disorder and bulimia nervosa.

The physical examination was unremarkable and the vital signs were stable and testing including a complete blood count, chest X-ray and urine toxicology screening. A thyroid function test initially showed a marginally low Thyroid-Stimulating Hormone (TSH) with normal triiodothyronine and thyroxine. A computed tomography scan of the head showed no abnormality. Due to absence of any other imminent cause of this behavior an initial diagnosis of drug induced psychosis due to isoniazid was taken into consideration.

Thereafter, all the anti-tubercular therapy was stopped by the prescribing physician. Although, he responded minimally after the isoniazid was stopped, the paranoid ideation persisted. The patient was put on tablet olanzapine 10 mg/day, tablet lorazepam 2 mg/day. Rifampicin, pyrazinamide and ethambutol were subsequently reintroduced, one by one to monitor a possible relapse of

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Correspondence:
Shreshth Khanna, Department of Pharmacology, Maulana Azad Medical College, Bahadur Shah Zafar Marg, India, Tel: 7042801204; E-mail: shreshthkhanna@gmail.com

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symptoms. Isoniazid was not reintroduced as it was the most likely offending drug taken into consideration for the symptoms and was subsequently replaced with levofloxacin 750 mg/day by the treating physician to complete the anti-tubercular treatment regimen as per the guidelines. Subsequently, the patient became asymptomatic after taking olanzapine for a period of 15 days.

He stopped taking olanzapine 7 weeks after his visit to the treating physician, but agreed for a follow up in the clinic. He remained asymptomatic in the subsequent follow-up visits to the hospital.

The causality assessment of the adverse drug reaction came out to be possible for this case using the Naranjo Causality Assessment Scale [6]. The case was reported to the ADR monitoring center under the Pharmacovigilance Program of India (PvPI).

Discussion

Tuberculosis remains a major health problem in India. The incidence and prevalence of the disease has decreased compared to the previous decades, still it accounts for maximum DALYs lost among the various communicable diseases. Some of the factors that may contribute to an increase in the number of TB cases include HIV infection; social problems such as poverty, homelessness and drug abuse [7].

In this case the patient was diagnosed as a case of pulmonary tuberculosis and initially treated with a regimen of four first line drugs isoniazid, rifampicin, pyrazinamide and ethambutol. The BPRS is a rating scale which is used by clinicians and researchers to measure psychiatric symptoms such as depression, anxiety, hallucinations and unusual behavior. The scales first published in 1962 is one most widely used scales to measure psychotic symptoms [8]. An expanded version of the test was created in 1993 by Ventura et al. [5].

The presence and severity of various psychiatric symptoms are rated on a Likert scale ranging from 1 (not present) to 7 (extremely severe). The total possible scores vary from 0 to 126 with higher scores indicating more severe psychopathology [9].

The association of administration of anti-tubercular therapy and the onset of psychotic symptoms in the absence of any previous psychiatric history provided a strong support for a diagnosis of drug-induced psychosis. Isoniazid is implicated in many cases of psychosis, hence it was first considered to be responsible for the psychotic episode.

Besides psychosis, isoniazid has been implicated in a number of other neuropsychiatric conditions including paranoia, obsessive-compulsive disorder, depression and mania, others including peripheral neuropathy, sleep disturbances, headache and blurring of vision have been seen [10].

In this case the onset of the psychotic symptoms that developed 4 weeks after initiation of the anti-tubercular therapy and partial resolution was seen after 7 days of isoniazid discontinuation and completely resolved 15 days after treatment with olanzapine. The symptoms onset and resolution were in contrast to a case of drug induced psychosis with a previously unremarkable personal and familial psychiatric history that presented with psychotic symptoms within 12 days of initiation and resolved completely within 2 days of discontinuation of therapy. The patient remained asymptomatic without medication at a 1-year follow-up [11].

In another case of isoniazid-associated psychosis the person had a previously positive psychiatric history. A change in the mental status of this patient was observed within a week of initiation of isoniazid therapy. Psychotic symptoms continued for 5 days after isoniazid was stopped, eventually the patient was completely asymptomatic within a week [12].

The drug induced psychotic symptoms usually range from a few days to 2 months after treatment onset with isoniazid [13].

Although the exact cause remains obscure, there are a few suggested mechanisms for isoniazid-associated psychosis.

These mechanisms implicate an over- or underproduction of the monoamine neurotransmitters serotonin, dopamine and norepinephrine.

One of the mechanism involves isoniazid acting as a Monoamine-Oxidase Inhibitor (MAO-I), thus preventing the degradation of catecholamine's, serotonin and ultimately leading to raised concentration of these neurotransmitters at the synapse [14].

Another mechanism suggests that pyridoxine deficiency ultimately leading to a reduction in the concentration of the neurotransmitters. Isoniazid combines with pyridoxal (a form of vitamin B6) to form a complex that inhibits the action of pyridoxal kinase. The action of pyridoxal kinase is to convert pyridoxal to pyridoxal phosphate, which is an important coenzyme in the metabolism of amino acids, including tyrosine and tryptophan (precursors of catecholamines). The result is a decrease in the metabolism of amino acids to dopamine, norepinephrine, and serotonin [15].

Patients with pyridoxine deficiency excrete a number of metabolites of tryptophan in the urine (e.g., Xanthurenic acid), after a loading dose of tryptophan is given. This test could also be used to assess pyridoxine deficiency status in addition to obtaining a blood concentration. However, pyridoxine deficiency is unlikely in our patient, as she was taking a pyridoxine supplement. Although the actual mechanism remains to be elucidated, the clinicians should be wary of the possibility of isoniazid induced psychosis [15].

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