Scholars Journal of Medical Case Reports
Abbreviated Key Title: Sch J Med Case Rep
ISSN 2347-9507 (Print) | ISSN 2347-6559 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Psychiatry

Induced Psychosis in a Patient Treated for Pulmonary Tuberculosis

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DOI: https://doi.org/10.36347/sjmcr.2025.v13i09.027 | **Received:** 02.07.2025 | **Accepted:** 07.09.2025 | **Published:** 13.09.2025

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Abstract | **Case Report**

Isoniazid is a cornerstone drug in tuberculosis treatment due to its high efficacy but is associated with rare neuropsychiatric side effects, including psychosis. The exact mechanisms are not fully understood but may involve inhibition of monoamine oxidase, oxidative stress affecting NMDA receptors, and disruption of vitamin B6 metabolism, leading to neurotransmitter imbalances. Psychosis onset varies from days to weeks after treatment initiation. We report a case of a 40-year-old patient who developed psychotic symptoms eight weeks after starting isoniazid-based treatment for pulmonary tuberculosis.

Keywords: Psychosis, pulmonary tuberculosis, Induced psychosis, isoniazide, éthambutol.

INTRODUCTION

Isoniazid (isonicotinic acid hydrazide) is a first-line medication in the treatment of tuberculosis (TB). It has been used to treat tuberculosis for several decades and remains one of the most effective and specific drugs against TB [1].

It has been one of the treatments used for both active tuberculosis and latent TB infection for many years [2]. Isoniazid is associated with a variety of adverse reactions affecting the central and peripheral nervous systems, such as insomnia, headaches, muscle twitching, optic neuropathy, peripheral neurotoxicity, psychosis, and agitation [3]. It can cause psychiatric side effects, including symptoms such as delusions, hallucinations, abnormal behavior, disorganized thoughts, and euphoria [4,5]. Pulmonary tuberculosis is a major health problem in Morocco, and isoniazid is one of the key first-line drugs used in its treatment. Several case reports have found that most cases of psychosis associated with antitubercular agents were caused by isoniazid, whereas psychosis induced by ethambutol (EMB) is rare. We present here the case of a patient who developed psychosis after 8 weeks of starting antitubercular treatment.

CASE PRESENTATION

A 40-year-old male patient, married and father of three children, working as a mechanic, with no personal or family history of psychiatric disorders or substance use, was diagnosed with pulmonary tuberculosis approximately two months prior. He was brought to the psychiatric emergency unit by his wife and sister due to a sudden behavioral change characterized by irritability, insomnia, soliloquy, and persecutory delusions, claiming that the police were going to take revenge on him. His wife also reported that he was experiencing auditory hallucinations, which he frequently mentioned, stating that he received commands often accompanied by psychomotor agitation.

These symptoms appeared around eight weeks after the start of his antitubercular treatment with ERIP 4, which included isoniazid (INH) 300 mg/day, rifampicin 600 mg/day, ethambutol 800 mg/day, and pyrazinamide 1600 mg/day.

Psychiatric evaluation revealed a motorically stable patient of slight build. Contact was difficult; he was highly distressed by the auditory hallucinations, which he described during the interview, repeatedly stating that “they are going to kill my children.” Physical examination was unremarkable. He underwent a blood workup including electrolytes, complete blood count, thyroid function tests, lipid profile, and syphilis serology—all of which were within normal limits. A brain CT scan also revealed no abnormalities.

Following consultation with the prescribing physician, the antitubercular treatment was discontinued. The patient was started on Amisulpride 400 mg/day. The

intensity of his symptoms diminished after stopping the medication, and within 15 days, all psychotic symptoms had completely resolved. He was referred back to his primary physician for treatment adjustment.

In the absence of any other obvious cause for the behavioral changes, a preliminary diagnosis of drug-induced psychosis—most likely due to isoniazid—was considered, as such side effects, though rare, have been previously described in the literature following use of this medication.

The patient was subsequently treated with rifampicin, pyrazinamide, ethambutol, and ofloxacin, and did not experience any further psychotic symptoms.

DISCUSSION

In our case, the patient was diagnosed with primary pulmonary tuberculosis and was initially started on antitubercular treatment (isoniazid, rifampicin, ethambutol, pyrazinamide).

The temporal association between the initiation of antitubercular therapy and the onset of psychotic symptoms, in the absence of any psychiatric history, strongly suggested a diagnosis of drug-induced psychosis.

The majority of psychosis cases reported in the literature related to antitubercular agents have been attributed to isoniazid or cycloserine.

A wide range of psychiatric disorders has been associated with isoniazid use, including behavioral and mood disturbances, memory problems, psychosis, obsessive-compulsive neurosis, and mania [6].

Suicidal ideation, hallucinations, and paranoid delusions have also been reported following administration of the drug.

The onset of psychosis can occur within a few days to several months after starting treatment, with the early weeks being the most commonly reported period in the literature, making it a diagnosis of exclusion [7].

In our case, the patient developed psychotic symptoms eight weeks after the initiation of antitubercular treatment. The symptoms subsided following the discontinuation of the antitubercular therapy and the initiation of treatment with Amisulpride, and completely disappeared after 15 days.

The presentation of our patient and the remission of symptoms were similar to that of a 21-year-old woman [6] with no notable psychiatric history, who experienced acute-onset paranoid delusions, agitation, and insomnia within four days of starting INH at 300 mg. Her symptoms completely resolved within 21 days of initiating olanzapine.

Similarly, another patient [8] developed isoniazid-induced psychosis four weeks after starting antitubercular treatment. After discontinuing the medication, the symptoms diminished, although auditory hallucinations and paranoid ideation persisted. The patient was started on olanzapine 10 mg/day and lorazepam 2 mg/day by a psychiatrist, and became asymptomatic after 15 days of treatment.

Another case involved a 28-year-old patient with pulmonary tuberculosis and no psychiatric history, who developed psychotic symptoms four days after starting standard four-drug antitubercular therapy. Isoniazid was initially identified as the probable culprit, and all antitubercular drugs were discontinued, resulting in the disappearance of the psychotic symptoms.

Antitubercular treatment was then reintroduced with ethambutol, rifampicin, and pyrazinamide, but symptoms reappeared after five days. Ethambutol was suspected this time, and its discontinuation led to remission of the psychotic symptoms.

In this case, both isoniazid and ethambutol were found to be responsible for the patient's psychotic behavior and had to be discontinued. The patient was then treated with rifampicin, pyrazinamide, and ofloxacin [9].

The main side effect of ethambutol is retrobulbar neuritis. Central nervous system toxicity is not widely reported, and the resulting psychosis is extremely rare. The exact mechanism of ethambutol-induced psychosis remains unclear. The symptomatology of ethambutol-induced psychosis is nearly identical to that of isoniazid-induced psychosis [10].

The mechanism underlying isoniazid-induced psychiatric disorders is not clearly understood, but it is known that the drug interferes with several metabolic processes essential to neuronal function.

Cases of psychosis may be due to isoniazid's inhibition of monoamine oxidase (MAO), which prevents the breakdown of catecholamines and serotonin.

Another possible explanation is a reduction in N-methyl-D-aspartate (NMDA) receptors due to the oxidative effects of isoniazid.

A further mechanism involves the disruption of vitamin B6 metabolism, as isoniazid interacts with its active form, pyridoxal phosphate, leading to excessive excretion. This disturbs the synthesis of serotonin, catecholamines, and gamma-aminobutyric acid (GABA). This pyridoxine depletion mechanism is also responsible for peripheral neuropathy [7,11].

Other factors that may predispose individuals to the development of psychotic illness include diabetes mellitus, hepatic insufficiency, a history of previous psychotic episodes, and advanced age [12].

Regarding the management of patients with suspected isoniazid-induced psychosis, early discontinuation of the drug is the primary priority.

In some cases, it is necessary to initiate treatment with anxiolytics and antipsychotics to control acute symptoms, the duration of which varies according to different authors [12].

Regarding the role of pyridoxine (vitamin B6), stronger scientific evidence is needed before definitive recommendations can be made.

However, vitamin B6 supplementation is advised to prevent exacerbation of psychosis upon reintroduction of isoniazid, thereby allowing an effective antitubercular regimen to be maintained without compromising the use of isoniazid [13].

CONCLUSION

Antitubercular-induced psychosis is a rare but serious adverse event primarily associated with isoniazid. Liaison psychiatry and effective communication between specialists enable monitoring of psychiatric symptoms from the start of treatment, thus facilitating early interventions. It is crucial that psychiatrists assess the impact of medications on mental health and collaborate with treating physicians to adjust therapies accordingly.

RÉFÉRENCE

1. World Health Organization. Guidelines on the management of latent tuberculosis infection. Geneva, Switzerland: World Health Organization; 2020.
2. Murray JF, Schraufnagel DE, Hopewell PC (2015) Treatment of tuberculosis. A historical perspective. Ann Am Thorac Soc 12(12):1749–1759. https:// doi. org/ 10. 1513/ Annal sATS. 201509- 632PS
3. Bangert MK, Hasbun R (2019) Neurological and psychiatric adverse effects of antimicrobials. CNS Drugs 33(8):727–753. https:// doi. org/ 10. 1007/ s40263- 019- 00649-
4. Esposito S, Canevini MP, Principi N (2017) Complications associated with antibiotic administration: neurological adverse events and interference with antiepileptic drugs. Int J Antimicrob Agents 50(1):1–8. https:// doi. org/ 10. 1016/j. ijant imicag. 2017. 01. 027
5. Kass JS, Shandera WX (2010) Nervous system effects of antituberculosis therapy. CNS Drugs 24(8):655–667. https:// doi. org/ 10. 2165/ 11534 340- 00000 0000- 00000
6. Gomes J, Durães D, Sousa A, Afonso H. Isoniazid-induced acute psychosis in a patient with pleural tuberculosis. Case Rep Psychiatry. 2019 Feb 13;2019: 4272941
7. Arya S, Sukhija G, Singh H. Acute Psychosis after Recent Isoniazid Initiation. J ClinDiagn Res. 2015;9(6): VD01–2
8. Shreshth Khannaa Suchita Pantb Harsh Khannac, Isoniazid-Induced Psychosis in a Patient with Pulmonary Tuberculosis: A Case Report 2023 DOI: 10.1159/000530779
9. Prasad R 1,✉, Rajiv Garg 1, Sanjay Kumar Verma 1, Isoniazid- and ethambutol-induced psychosis, 2008 Oct-Dec;3(4):149–151. doi: 10.4103/1817-1737.43083
10. Hsu CW, Chu KA, Lu T, Lai RS, Lu JY. Ethambutol-induced psychosis: A case report. Zhonghua Yi Xue Za Zhi (Taipei) 1999; 10:724-7
11. Lagos M, Pineda C, Saavedra L, Cortez V, Ortiz D, Tamayo A, *et al.,* Tuberculosis ysalud mental: aspectos etiológicos, terapéuticos y evolutivos. Psicosom psiquiatr.2021;18:44–56.
12. Alfawaz S, Alattas N, Alhammadi M, Waqar S, Al Alola S. Acute psychosis secon-dary to isoniazid in pediatric pulmonary tuberculosis: A case report and literaturereview. Int J Pediatr Adolesc Med. 2020; 7:196–8
13. Yadav R, Kumar M, Kumar N, Chacham S. Pyridoxine in isoniazid induced psycho-sis. Sudan J Paediatr. 2022;22(2):190–2