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Case Report

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Isoniazid-Induced Psychosis & Peripheral Neuropathy in a Middle-Aged Male with Pulmonary Tuberculosis: A Rare Case Report

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HIGHLIGHTS

- Rare INH complication
- INH-induced psychosis
- Peripheral neuropathy observed
- Elevated suicide risk
- Effective multidisciplinary care

Key Words:
Isoniazid
Psychosis
Peripheral neuropathy
Tuberculosis
Pyridoxine deficiency
Antitubercular therapy
Neuropsychiatric adverse effects

ABSTRACT

Introduction: Isoniazid (INH) is a first-line antitubercular drug widely used in the treatment of tuberculosis. Although generally safe and effective, it may rarely cause neuropsychiatric adverse effects, including psychosis and peripheral neuropathy. The concurrent occurrence of both complications in a single patient is uncommon and may result in substantial psychological distress and functional impairment if not identified promptly. **Aim & Objective:** To highlight the rare occurrence of isoniazid-induced psychosis and peripheral neuropathy in the same patient and emphasize the importance of early recognition and multidisciplinary management of these adverse drug reactions. **Case Presentation:** A 53-year-old male receiving antitubercular therapy for pulmonary tuberculosis developed paranoid delusions, auditory hallucinations, agitation, and somatic preoccupation within two months of treatment initiation. Following completion of therapy, psychotic symptoms resolved spontaneously. Subsequently, he experienced persistent tingling, numbness, burning sensations in the limbs, sleep disturbances, and marked impairment in daily functioning. Due to severe psychological distress and persistent neuropathic symptoms, he attempted suicide on three occasions. Neurological examination revealed sensory deficits involving fine touch sensation. Routine laboratory investigations were largely normal except for vitamin D insufficiency, while MRI brain showed insignificant chronic small-vessel ischemic changes. **Result:** Based on the temporal association with antitubercular therapy, a diagnosis of isoniazid-induced psychosis (in remission) with peripheral neuropathy was made. Treatment with pyridoxine, vitamin B12, GABAergic agents, selective serotonin reuptake inhibitors, benzodiazepines, vitamin D supplementation, and transcutaneous electrical nerve stimulation (TENS) resulted in significant clinical improvement within one month. **Conclusion:** Early recognition and comprehensive management of isoniazid-related neuropsychiatric complications are essential to reduce morbidity, improve quality of life, and optimize treatment outcomes in patients receiving antitubercular therapy.

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INTRODUCTION

Tuberculosis (TB) remains a major global health challenge, with isoniazid (INH) forming the cornerstone of first-line antitubercular therapy because of its potent early bactericidal activity. Despite its efficacy and widespread use, INH is associated with several adverse effects involving the hepatic, neurological, & psychiatric systems. Among these, neuropsychiatric complications such as psychosis and peripheral neuropathy are uncommon but clinically important because they may significantly impair quality of life, reduce treatment adherence, and increase morbidity [1].

Isoniazid-induced psychosis is a rare adverse drug reaction that has been described in both adults and children receiving antitubercular therapy. Clinical manifestations include paranoid ideation, hallucinations, agitation, obsessive compulsive symptoms, mood disturbances, and suicidal behavior. Baytunca et al. reported a case of schizoobsessive disorder associated with INH therapy in a child, emphasizing the diverse psychiatric presentations associated with the drug [2]. Similarly, suicidal psychosis secondary to isoniazid has been documented by Iannaccone et al. [3]. Additional reports by Witkowski et al., Alao and Yolles, and Pallone et al. further support the association between INH therapy and acute psychotic symptoms in individuals without prior psychiatric illness [4-6]. Peripheral neuropathy is a more frequently recognized neurological complication of INH therapy and typically presents with paresthesia, tingling, numbness, burning sensation, and distal sensory deficits. The condition is primarily attributed to pyridoxine depletion caused by interference of INH with vitamin B6 metabolism.

Mandel highlighted the protective role of pyridoxine supplementation in preventing INH-induced neuropathy [7]. Furthermore, studies have shown that individuals with "slow acetylator" status involving N-acetyltransferase-2 (NAT2) polymorphisms are at greater risk of developing neurotoxicity [8]. Goel et al. demonstrated electrophysiological evidence of more severe neuropathy among slow acetylators compared with rapid acetylators receiving INH therapy [9]. More recently, Stettner et al. suggested that pharmacogenomic risk stratification may help identify patients susceptible to INH-induced polyneuropathy [10].

The exact pathophysiological mechanism underlying INH-induced neuropsychiatric manifestations is not completely understood. However, INH is known to interfere with pyridoxine metabolism, leading to reduced synthesis of gamma-aminobutyric acid (GABA) and alterations in serotonin and catecholamine pathways. These neurotransmitter disturbances have been implicated in the development of both psychosis and neuropathy [5,11]. Overview of isoniazid-induced psychosis and peripheral neuropathy **(Figure 1)**.

Although isolated reports of INH-induced psychosis and peripheral neuropathy are available in the literature, the simultaneous occurrence of both complications in the same patient is exceedingly rare. We report a case of a middle-aged male with pulmonary tuberculosis who developed psychosis followed by persistent peripheral neuropathy during antitubercular therapy, highlighting the importance of early recognition and multidisciplinary management of neuropsychiatric adverse effects associated with isoniazid.

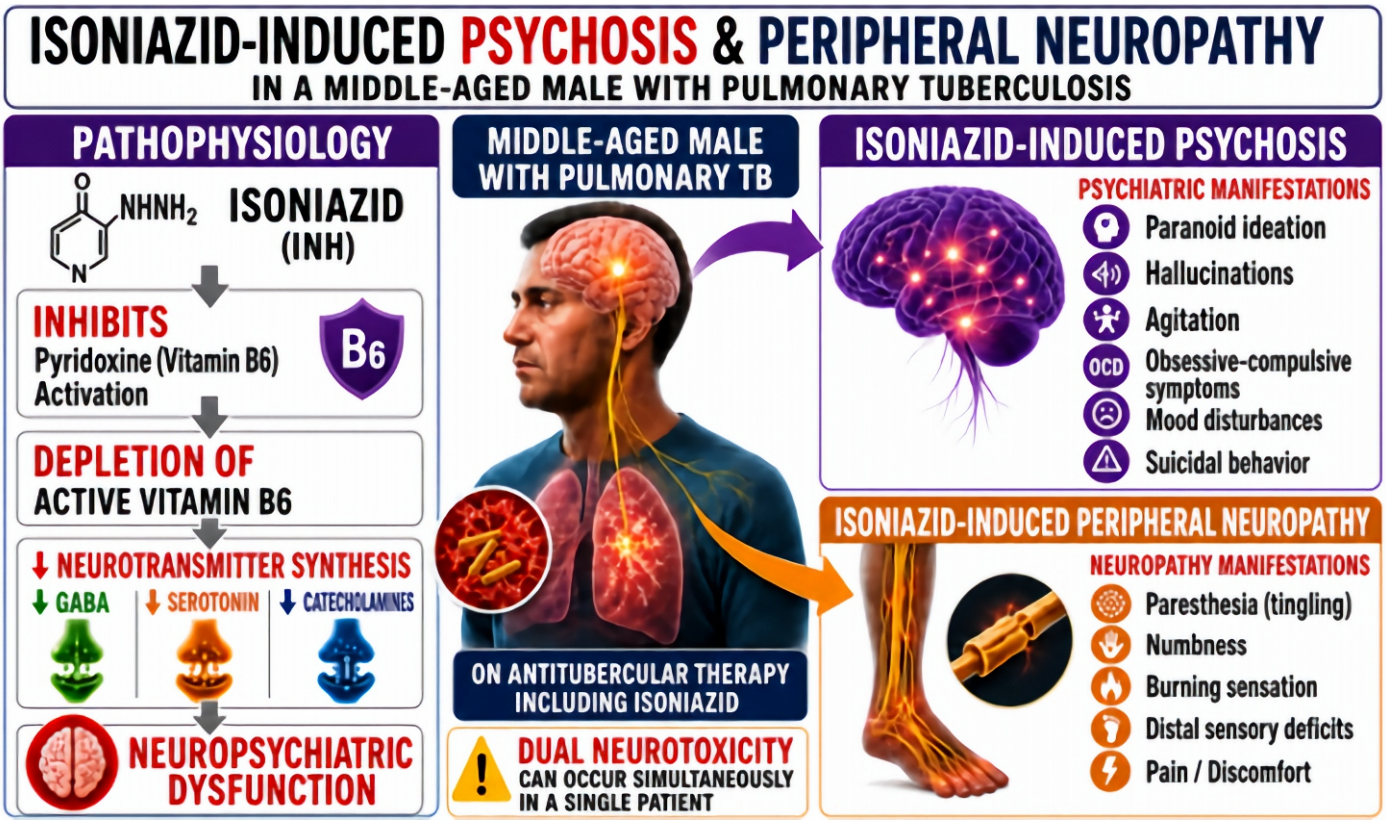

Figure 1: Pathophysiology and clinical spectrum of isoniazid-induced psychosis and peripheral neuropathy in pulmonary tuberculosis.

CASE PRESENTATION

A 53-year-old married male with no history of substance use, psychiatric illness, or family history of psychiatric disorders was diagnosed with pulmonary tuberculosis eight months prior and was initiated on antitubercular therapy (ATT), which he received for six months. During the initial two months of treatment, the patient developed behavioral disturbances characterized by suspicion that his neighbors were practicing black magic against him and causing body aches and tingling sensations. He subsequently developed agitation, paranoid delusions, auditory hallucinations, and marked somatic preoccupation.

The psychotic symptoms resolved spontaneously following completion of the ATT regimen, suggesting a possible association with isoniazid exposure. However, the patient continued to experience persistent body aches, tingling numbness, and excessive preoccupation with these symptoms. Over time, his symptoms progressively worsened, with the addition of severe burning sensations in the limbs, resulting in significant sleep disturbance and impairment in day-to-day functioning. Due to unbearable symptoms persisting for nearly 4–6 months, the patient attempted suicide on three occasions and was eventually admitted to a tertiary care hospital for further evaluation and management. Clinical Course and Symptom Progression **(Table 1)**.

Investigations & Diagnosis

The patient reported multiple prior consultations at different hospitals for his persistent body pains and neuropathic symptoms. He had undergone several blood investigations and had received irregular treatment with multivitamins, analgesics, and nutritional supplements without significant symptomatic improvement.

General physical examination revealed stable vital signs and no abnormal physical findings. Detailed systemic and neurological examinations were performed.

Neurological examination demonstrated sensory deficits involving fine touch sensation, while other domains of central nervous system examination were normal. Laboratory investigations, including complete blood count (CBC), liver function tests (LFT), renal function tests (RFT), random blood sugar (RBS), and serum vitamin B12 levels, were within normal limits. However, serum vitamin D levels were found to be insufficient. Magnetic resonance imaging (MRI) of the brain showed insignificant chronic small vessel ischemic changes.

Mental status examination revealed marked preoccupation with body pain and burning sensations. The patient also reported diurnal variation in pain symptoms, significantly affecting sleep and occupational functioning. No active psychotic symptoms or depressive cognitions were elicited during evaluation. Based on the temporal association with antitubercular therapy, spontaneous remission of psychotic symptoms after treatment completion, and persistent neuropathic symptoms, a diagnosis of isoniazid-induced psychosis (attained remission) with isoniazid-induced peripheral neuropathy was considered. Clinical Investigations, Management, and Outcome **(Table 2)**.

Management & Outcome

The patient was managed with adequate doses of vitamin B6 (pyridoxine), vitamin B12, and GABAergic supplements for neuropathic symptoms. In addition, selective serotonin reuptake inhibitors (SSRIs) along with short-term benzodiazepines were prescribed to address persistent anxiety and sleep disturbances. Vitamin D supplementation was also initiated for the correction of deficiency.

For management of neuropathic pain, the patient underwent multiple sessions of transcutaneous electrical nerve stimulation (TENS). Over the course of one month, the patient reported significant improvement in neuropathic symptoms, reduction in pain severity, improved sleep, and better overall functioning.

Table 1: Timeline of Clinical Course and Symptom Progression

Timeline	Clinical Events
8 months before presentation	Diagnosed with pulmonary tuberculosis and started on antitubercular therapy (ATT)
First 2 months of ATT	Developed paranoid ideas, auditory hallucinations, agitation, and somatic preoccupation
After completion of ATT	Psychotic symptoms resolved spontaneously
Following 4 –6 months	Persistent tingling, numbness, body aches, burning sensation of limbs, sleep disturbance
Progressive course	Multiple consultations and irregular symptomatic treatment without improvement
Prior to admission	Three suicidal attempts due to severe neuropathic symptoms
At tertiary care admission	Evaluated for persistent neuropathy and psychiatric symptoms
After treatment	Significant symptomatic improvement within one month

Table 2. Investigations, Management, and Outcome

Domain	Findings / Interventions
General physical examination	Stable vitals; no significant abnormality
Neurological examination	Sensory deficits involving fine touch; other CNS findings are normal
Laboratory investigations	CBC, LFT, RFT, RBS, and serum Vitamin B12 within normal limits
Additional findings	Serum Vitamin D insufficiency
Neuroimaging	MRI brain showed insignificant chronic small vessel ischemic changes
Mental status examination	Significant somatic preoccupation, anxiety, and sleep disturbance; no active psychosis or depressive cognition
Final diagnosis	Isoniazid -induced psychosis (attained remission) with isoniazid - induced peripheral neuropathy
Pharmacological management	Vitamin B6, Vitamin B12, GABAergic supplements, SSRIs, short - term benzodiazepines, and Vitamin D supplementation
Non-pharmacological management	Multiple sessions of transcutaneous electrical nerve stimulation (TENS)
Outcome	Significant improvement in neuropathic symptoms and sleep within one month

RESULT

The patient developed psychotic symptoms, including paranoid delusions, auditory hallucinations, agitation, and somatic preoccupation, within two months of initiating antitubercular therapy. These symptoms resolved spontaneously following completion of treatment, supporting a diagnosis of isoniazid-induced psychosis. However, persistent peripheral neuropathy manifested as tingling, numbness, burning sensations, sleep disturbances, and significant impairment in daily functioning. Neurological examination revealed sensory deficits involving fine touch sensation, while laboratory investigations were unremarkable except for vitamin D insufficiency. Following treatment with pyridoxine, vitamin B12 supplementation, GABAergic agents, selective serotonin reuptake inhibitors, benzodiazepines, vitamin D supplementation, and transcutaneous electrical nerve stimulation (TENS), the patient demonstrated marked improvement in neuropathic symptoms, psychological well-being, sleep quality, and functional status within one month of therapy.

DISCUSSION

Neuropsychiatric adverse effects associated with isoniazid (INH) are uncommon but clinically significant complications of antitubercular therapy. Reported manifestations include psychosis, obsessive-compulsive symptoms, mania, peripheral neuropathy, and other neurologic disturbances. Baytunca et al. described a pediatric case presenting with schizo-obsessive symptoms following INH exposure, while Iannaccone et al. reported suicidal psychosis associated with isoniazid therapy [2,3]. Similar presentations of acute psychosis induced by INH have also been documented by Witkowski et al., Pallone et al., and Alao and Yolles [4–6]. In addition to psychiatric manifestations, several studies have established the association between INH therapy and peripheral neuropathy, particularly among individuals with predisposing metabolic or genetic risk factors [7–10]. However, the simultaneous occurrence of psychosis and persistent peripheral neuropathy in the same patient remains rarely reported in the literature.

In the present case, the patient developed paranoid delusions, auditory hallucinations, agitation, and somatic preoccupation within the initial months of antitubercular therapy (ATT), followed by persistent tingling, numbness, and burning sensations involving the limbs. The temporal association between symptom onset and initiation of ATT, along with spontaneous remission of psychotic symptoms following completion of therapy, strongly suggested INH-induced psychosis. Persistent neuropathic symptoms despite cessation of therapy further indicated significant neurologic involvement secondary to isoniazid exposure. The exact mechanism underlying INH-induced neuropsychiatric toxicity is not completely understood. Isoniazid interferes with pyridoxine metabolism, resulting in depletion of biologically active vitamin B6. This subsequently reduces the synthesis of gamma-aminobutyric acid (GABA), an important inhibitory neurotransmitter in the central nervous system. In addition, INH alters serotonin and catecholamine metabolism, thereby contributing to psychotic manifestations [5,11]. Girling extensively discussed the neurotoxic adverse effects of anti-tubercular drugs and emphasized the role of neurotransmitter imbalance in the development of psychiatric complications [11]. Pyridoxine deficiency also contributes significantly to peripheral neuropathy by impairing neuronal metabolism and axonal function. Mandel first demonstrated the importance of pyridoxine supplementation in preventing and reducing INH-induced neuropathy [7]. Another important factor implicated in INH neurotoxicity is the acetylator status of the patient. Individuals with slow N-acetyltransferase-2 (NAT2) acetylator genotype accumulate higher concentrations of INH metabolites & are therefore more susceptible to neurologic adverse effects. Lamb & Mauermann highlighted the importance of pharmacogenomics & NAT2 polymorphisms in susceptibility to INH-associated neuropathy [8]. Similarly, Goel et al. demonstrated more severe electrophysiological abnormalities among slow acetylators compared to rapid acetylators receiving ATT [9]. Stettner et al. further suggested that genotyping based risk stratification may help identify patients at increased risk for INH-induced polyneuropathy [10].

Although genetic testing was not performed in the present case, the prolonged and severe neuropathic manifestations raise the possibility of an underlying slow acetylator phenotype. Most reported cases of INH-induced psychosis and neuropathy improve after discontinuation of the offending drug along with pyridoxine supplementation. In our patient, psychotic symptoms resolved spontaneously after completion of ATT, whereas neuropathic symptoms persisted for several months and caused severe psychological distress, leading to suicidal attempts. Management involved vitamin B6 and B12 supplementation, GABAergic agents, selective serotonin reuptake inhibitors (SSRIs), short-term benzodiazepines, & transcutaneous electrical nerve stimulation (TENS), following which the patient demonstrated significant clinical improvement within one month.

CONCLUSION

Although isoniazid-induced psychosis and peripheral neuropathy are infrequent complications of antitubercular therapy, they can result in substantial psychological and functional impairment if not recognized early. This case highlights the importance of close monitoring for psychiatric and neurologic adverse effects in patients receiving ATT, particularly those presenting with unusual behavioral symptoms or persistent neuropathic complaints. Early identification, prompt withdrawal or completion of the offending agent, pyridoxine supplementation, and multidisciplinary management can significantly reduce morbidity and improve patient outcomes.

CLINICAL SIGNIFICANCE

The clinical significance of this study lies in its potential to bridge the gap between research findings and practical healthcare applications. It emphasizes the importance of translating scientific observations into meaningful improvements in patient care, diagnosis, and treatment outcomes. By highlighting realworld relevance, the study contributes to evidence-based medical practice and supports informed clinical decision-making. Ultimately, the findings aim to enhance patient quality of life, optimize therapeutic strategies, and promote better disease management in clinical settings.

ABBREVIATIONS

INH: Isoniazid
TB: Tuberculosis
CNS: Central Nervous System
TENS: Transcutaneous Electrical Nerve Stimulation
GABA: Gamma-Aminobutyric Acid
SSRI: Selective Serotonin Reuptake Inhibitor

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AUTHOR CONTRIBUTIONS

All authors significantly contributed to the study conception and design, data acquisition, or data analysis and interpretation. They participated in drafting the manuscript or critically revising it for important intellectual content, consented to its submission to the current journal, provided final approval for the version to be published, and accepted responsibility for all aspects of the work. Additionally, all authors meet the authorship criteria outlined by the International Committee of Medical Journal Editors (ICMJE) guidelines.

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CONFLICT OF INTEREST

Authors declared that there is no conflict of interest.

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All data generated and analyzed are included within this research article. The datasets utilized and/or analyzed in this study can be obtained from the corresponding author upon a reasonable request.

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