



**A CASE REPORT ON ISONIAZID INDUCED CUTANEOUS REACTION**

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**ABSTRACT**

Cutaneous reaction is a known complication of isoniazid drug therapy, although infrequent. Isoniazid is the first line drug for the treatment of tuberculosis. Tuberculosis is a common communicable public health problem. First line treatment for tuberculosis includes Isoniazid, Rifampicin, Ethambutol and Pyrazinamide. A 57 years old male patient developed cutaneous reaction by first line antitubercular therapy (ATT). In present case, the patient is a known case of Hypertension on regular medications and recently diagnosed with Pulmonary Tuberculosis and started ATT. After 3 weeks, he was presented with cutaneous reactions. Pulmonologist stopped ATT and added Antihistamines. After a week his condition was improved. After the rechallenge test with isoniazid he developed rashes again. Patient was recovered after withdrawn of the tablet Isoniazid. Cutaneous reaction in a patient on ATT can be one of the complication of tablet isoniazid. Physicians, Clinical Pharmacists & other health care providers should be aware of the adverse reactions of drugs. We need to monitor the possible reactions at regular intervals during therapy. As a health care provider, we need to prevent and minimize drug induced reactions through proper patient education & counselling.

**KEYWORDS:** Pulmonary tuberculosis, Antitubercular therapy, Isoniazid, Cutaneous reaction.

**INTRODUCTION**

Tuberculosis is a common communicable disease, caused by the bacteria *Mycobacterium tuberculosis*, an acid fast bacilli, which commonly affects the lungs. It can also affects other parts of the body like kidney, spine, bone.<sup>[1]</sup> The incidence rate of tuberculosis, as per WHO tuberculosis statistics is 28% cases, India was among the eight countries accounting for more than two-third (68.3%) of the total TB patients count.<sup>[2]</sup> Clinical manifestation of it includes cough, fatigue, fever, night sweats, chest pain, dyspnea, and hemoptysis in case of lung involvement.<sup>[3]</sup> First-line agents for treatment of TB disease consist of isoniazid, rifampicin, pyrazinamide, and ethambutol.<sup>[4]</sup> Among the first-line anti-tubercular agents, isoniazid is the drug of choice for use in preventive therapy and the primary drug for use in combination therapy for active tuberculosis.<sup>[5]</sup> In adults, the dose of isoniazid is 5 mg/kg up to 300 mg daily as a single dose daily, or 15 mg/kg up to 900 mg per day in 2-3 divided doses per week is recommended. In pediatrics, the dose is 10 to 15 mg per kg up to 300 mg daily as a single dose; or 20 to 40 mg per kg up to 900 mg per day in 2-3 divided doses per week is recommended. Peripheral neuropathy is also a commonly associated adverse event of isoniazid therapy, some patients also report a rash or pruritus or cutaneous reaction with incidence of 19%.<sup>[6]</sup>

**CASE REPORT**

A 57 years old male with a known case of hypertension since 5 years, on regular treatment, had a habit of chronic smoking. He was presented to the hospital with chief complaints of productive cough yellowish in color, fever, body pains, lack of appetite, wheezing, and dyspnea for 20 days. He was advised with chest x-ray, sputum for CBNAAT. His chest x-ray was interpreted with consolidatory changes, nodules in superior segments of lower lobes of bilateral lungs and posterior segment of right lung lower lobe (fig.1). His sputum CBNAAT was interpreted positive for mycobacterium tuberculosis pathogen. Based on the investigations, he was diagnosed as Hypertension with Pulmonary Tuberculosis. He was started with 1st line anti-tubercular therapy (ATT). After 3 weeks of ATT therapy, he was presented to the hospital with complaints of severe rashes and itching all over the dorsal side of the trunk, for the last 2 weeks (fig.2). Immediately, ATT was stopped and started on antihistamines.



Figure 1: Chest X-ray.



Figure 2: Cutaneous reaction on dorsal side of the trunk.

## DISCUSSION

Toxidemia, commonly known as Cutaneous Adverse Drug reactions (CADR), are skin reactions occur from systemic drug administration which ranges from mild erythematous skin lesions like reactions to more severe reactions like Lyell's syndrome.<sup>[7]</sup>

It includes maculopapular skin reactions; urticaria and angioedema; and the spectrum of skin lesions including fixed drug eruptions, erythema multiforme, Stevens-Johnson syndrome, DRESS (drug reaction with eosinophilia and systemic symptoms; also called drug hypersensitivity syndrome), and toxic epidermal necrolysis. Together these reactions account for the majority of all drug-induced skin manifestations. It may be caused either due to immunological conditions (i.e., drug allergy) or non-immunologic conditions (i.e., drug intolerance). Drug allergies are estimated to account for <10% of all adverse drug reactions, with drug intolerance accounting for the other 90%.<sup>[8]</sup>

In the present case, the patient presented with rashes and itching for 2 weeks, all over the dorsal side of the trunk within 3 weeks of ATT therapy. ATT was stopped, and improvement was seen after starting on antihistamines for a week. However, the patient developed rashes again after rechallenge test with isoniazid and improved after stopping it leading to the diagnosis of isoniazid-induced cutaneous reaction. Then, he started with Rifampicin

600mg, Pyrazinamide 100mg, Ethambutol 800mg, Levofloxacin 750mg for 2 months of intensive phase followed by Rifampicin 600mg, Ethambutol 800mg, Levofloxacin 750mg for the continuous phase.

The underlying pathogenesis of this hypersensitivity, whether immune-mediated and/or toxic in nature, is unclear. Predisposing factors for hypersensitivity reactions to ATT include HIV infection, polypharmacy, advanced age, autoimmune disease, and renal or liver impairment. In a large tertiary care center study on CADR with antitubercular drugs, pyrazinamide was the most common offending drug (2.38%), followed by streptomycin (1.45%), ethambutol (1.44%), rifampicin (1.23%), and isoniazid (0.98%).<sup>[1]</sup> In contrast to the findings of the above-mentioned study, pyrazinamide, ethambutol, and rifampicin were well-tolerated by our patient; however, she developed reaction to isoniazid.<sup>[9]</sup> There are less case reports of cutaneous reaction induced by isoniazid alone reported so far.

## CONCLUSION

Cutaneous reaction is a rare but potentially fatal drug reaction with isoniazid. Immediate withdrawal of offending medication along with supportive measures carries good prognosis. Hence, cautious use of isoniazid can aid in early detection and management of this ADR.

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