

## A RARE CASE OF ISONIAZID INDUCED ERYTHRODERMA

Deshna Lad<sup>1</sup>, Malay Chaudhari<sup>2</sup>, Ashish Jagati<sup>3</sup>, Supriya Malhotra<sup>\*,†,4</sup>, Pankaj Patel<sup>5</sup>

<sup>1</sup>Department of Pharmacology, Smt. NHL Medical College, Ahmedabad, Gujarat, India

<sup>2</sup>Department of Dermatology, Smt. NHL Medical College, Ahmedabad, Gujarat, India

<sup>3</sup>Department of Dermatology, Smt. NHL Medical College, Ahmedabad, Gujarat, India

<sup>4</sup>Department of Pharmacology, Smt. NHL Medical College, Ahmedabad, Gujarat, India

<sup>5</sup>Dean, Smt. NHL Medical College, Ahmedabad, Gujarat, India

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### ABSTRACT

Tuberculosis (TB) has existed for millennia and remains a major global health problem. It causes ill-health in millions of people each year and in 2015 was one of the top 10 causes of death worldwide, ranking above HIV/AIDS as one of the leading causes of death from an infectious disease. Erythroderma, or generalized exfoliative dermatitis is an uncommon but serious skin disorder which results in generalized scaling eruption of the skin. It is usually drug induced, idiopathic, or secondary to underlying cutaneous or systemic diseases. Theoretically, any drug may cause exfoliative dermatitis. Isoniazid is established the first-line antitubercular drug and an essential component of all antitubercular regimens. Erythroderma caused by isoniazid is an uncommon but serious adverse drug reaction. We report here a case of a 54-year-old male patient who presented with generalized redness and exfoliation of skin with itching after 6 weeks of antitubercular treatment (ATT). ATT was stopped immediately, and antihistaminics and steroids were started. The patient improved over a period of 2 weeks. On sequential rechallenge, she developed similar lesions all over the body with isoniazid, hence confirming the diagnosis of isoniazid-induced erythroderma.

**Key words:** Adverse drug reaction–Erythroderma–or generalized exfoliative dermatitis–Isoniazid–Tuberculosis

### 1 INTRODUCTION

Tuberculosis (TB), a common infectious disease in the developing countries is caused by a bacterium called *Mycobacterium tuberculosis*. The bacteria usually attack the lungs, but TB bacteria can attack any part of the body such as the kidney, spine, and brain. Antitubercular therapy with the first line drugs is very effective. [1] A major adverse reaction to one of the first line antituberculous drugs, which results in discontinuation of that drug, has several implications and complicate the antiTB treatment. [2] Cutaneous adverse drug reactions (CADR) is one of the commonly observed side effects. [3, 4] CADR is defined as skin reactions secondary to sys-

temic administration of drugs (oral/subcutaneous/ intravenous/intramuscular/inhalation). It has been well established that anti-TB drug are among the commonest drug that cause cutaneous drug reactions. [4] Most common adverse effects of isoniazid are peripheral neuritis and hepatitis, which are more common in alcoholics and older patients, but CADR are rare with incidence of <0.001% to maximum of 3/1000 patients treated. [5]

Erythroderma or exfoliative dermatitis is an inflammatory disorder in which erythema and scaling occur in a generalized distribution involving more than 90% of the body surface. [6] It can be fatal, even when properly managed, primarily because of its metabolic burden and complications. Hence it is mandatory to establish its etiopathology in order to facilitate precise management. This disorder may be the morphologic presentation of a variety of cutaneous and systemic diseases, and a thorough workup is essential.

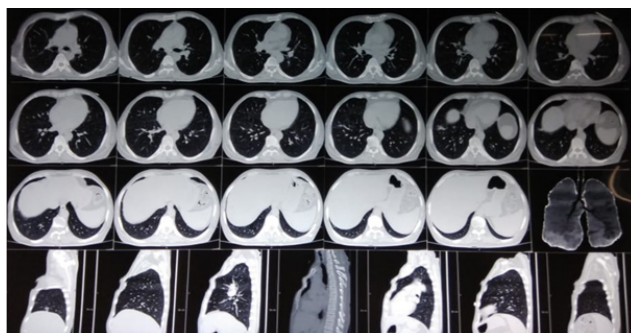
\* Corresponding author.

† Email: [supriyadmahotra@gmail.com](mailto:supriyadmahotra@gmail.com)

A detailed outline of the patient's history to elicit possible triggering events, including infections, drug ingestion, topical application of medications, sun/ultraviolet exposure and other factors, should be determined. Management of the skin disorder continues to be a challenge due to its multiple etiologies. The prognosis of erythroderma is determined by its underlying cause. [7] Cutaneous adverse drug reactions (CADR) with antitubercular treatment (ATT) can make further management of TB challenging. There may be considerable morbidity, even mortality, particularly with severe cutaneous adverse drug reaction (CADR). [8, 9] Here we report a rare case of Miliary tuberculosis developing Erythroderma to Isoniazid.

## 2 CASE REPORT

A 54-year-old Indian man was diagnosed as a case of Miliary TB when he was evaluated for fever and cough with expectoration. High-resolution computed tomography of chest showed extensive miliary opacities in both lung fields. [Figure 1]

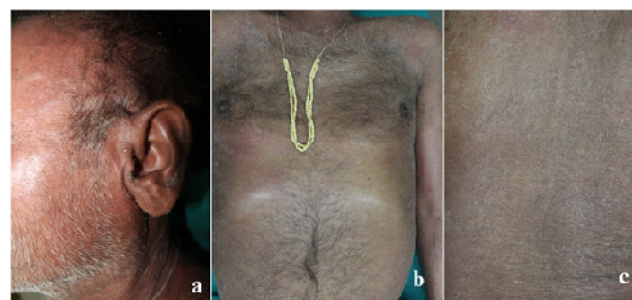


**Figure 1.** High-resolution computed tomography of chest showing extensive miliary opacities in both lung fields

He was started on the first-line antitubercular drugs as per Directly Observed Treatment Short Course regimen for TB. After 6 weeks of ATT, he reported to dermatology department of our hospital, for complaints of acute onset erythema along with severe itching all over the body for the last 7-8 days. Dermatological examination revealed diffuse generalized erythema with coarse, large dry scaling all over the body. [Figure 2 a, b, c] Erythema and scaling were more pronounced over trunk and legs. Whitish plaques present over bilateral buccal mucosa.

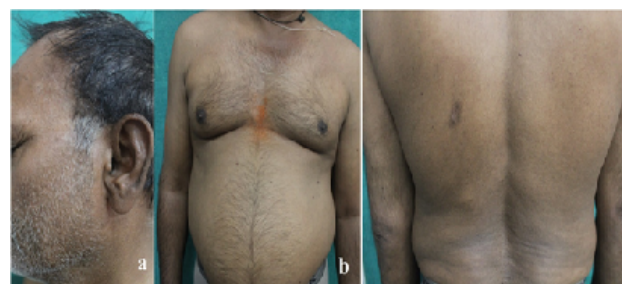
On investigations; patient's LFT was altered suggestive of AKT induced Hepatitis. No significant lymphadenopathy or hepatosplenomegaly was observed.

There was no history of any other drug intake, or history of jaundice, chest pain, palpitation, and dyspnea on exertion. There was no preexisting dermatosis or prior exposure to chemical precipitants of dermatitis or any other medical problem. Family history was negative for similar conditions or skin disorders. General physical examination was unremarkable while systemic examination revealed edema feet. HIV-ELISA was nonreactive.



**Figure 2.** Erythema with coarse, large dry scaling over : a) Face b) Chest c) Back

ATT was stopped immediately. Oral antihistaminics and oral steroids were started along with supportive therapy and topical emollients. The patient improved over a period of 1–2 weeks with decreased erythema and a significant reduction in scaling. [Figure 3 a, b, c]



**Figure 3.** Corresponding clinical photograph after withdrawal of isoniazid : a) Face b)Chest c) Back

On rechallenge after 2 weeks of stopping ATT, individual drugs were reintroduced in a sequential manner starting with Isoniazid, followed by Rifampicin, pyrazinamide then Ethambutol at last at an interval of 1 week between the drugs. Prior to isoniazid rechallenge, he did not develop any signs of CADR but on introducing isoniazid, he rapidly developed similar erythematous lesions with intense itching within 48 h. Isoniazid was withdrawn and diagnosis of “isoniazid induced erythroderma” was made. At present, the patient was given symptomatic treatment with topical emollients, oral steroids and oral antihistamines. The lesions subsided in 1 week, and the patient was prescribed alternative regimen of ATT excluding isoniazid. The causality assessment was “certain” on WHO-UMC causality assessment scale.

## 3 DISCUSSION

Cutaneous adverse drug reactions (CADR) are one of the commonly observed major adverse effects of anti-tubercular therapy reported in 5 % of tubercular patients. [10] CADR associated with anti-tubercular treatment include morbilliform rash, erythema multiforme syndrome, urticaria, lichenoid eruption and other more serious ones like SJ syndrome and exfoliative dermatitis.

Erythroderma is an intense generalized redness of the skin, first described by Von Hebra in 1868. It is an inflammatory disorder and an extreme state of dysmetabolism characterized by extensive erythema and scaling all over the body classically involving more than 90% of the body surface. It is of great concern because of significant risk of morbidity and mortality owing to dysmetabolism and its complications, in addition to the risks inherent to the underlying disease and its therapy. [11] Majority of cutaneous hypersensitivity reactions occurred within 2 months after the initial dose. In our case, patient develop erythroderma by the end of 6 weeks of treatment. He developed reaction to isoniazid. He tolerated ofloxacin and azithromycin. The underlying pathogenesis of this hypersensitivity, whether immune-mediated and/or toxic in nature, is unclear. [12] Human immunodeficiency virus (HIV) infection, polypharmacy, advanced age, autoimmune disorders, and pre-existing renal or liver impairment were common pre-disposing conditions for development of CADR(Hypersensitivity) to anti-tubercular treatment. Workup of our patient relieve no risk factors except use of anti-tubercular drugs. [13] Drug-induced erythroderma has the best prognosis among all the causes of erythroderma often resolving in 2–6 weeks. [14] In a large territory care centre study on CADR with anti-tubercular drugs pyrazinamide was the commonest offending drug (2.38%), followed by Streptomycin (1.45%), Ethambutol (1.44%), Rifampicin (1.23%) and Isoniazid (0.98%). [15]

In the present case, the patient presented with erythema and scaling involving more than 90% of the body surface area along with itching within weeks of ATT. ATT was stopped, and a significant improvement was noted within 1-2 week. However, the patient developed exfoliative dermatitis again after rechallenge test with isoniazid and improved after stopping it leading to the diagnosis of isoniazid-induced erythroderma. Prompt resolution of the lesions after withdrawal of the ATT and start of oral antihistaminics further supported the diagnosis. The patient was now prescribed rifampicin 600 mg, pyrazinamide 1000 mg, ethambutol 1200 mg, and levofloxacin 750 mg for a period of 2 months in intensive phase followed by continuation phase for 4 months.

There are many case reports of exfoliative dermatitis with other antitubercular drugs; but, to the best of our knowledge, only 4 cases of erythroderma induced by isoniazid alone is reported so far. [15–17]

#### 4 CONCLUSION

Erythroderma as a rare but potentially fatal drug reaction with isoniazid. Immediate withdrawal of offending drug along with supportive measures carries good prognosis. Hence, cautious use of isoniazid can help in early identification and management of this ADR. The single most important factor to prevent adverse patient outcome is education of the patient about the symptoms of cutaneous reactions, and prompt recognition and discontinuation of the drugs by the health care providers.

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#### **AUTHOR BIOGRAPHY**

**Deshna Lad** Department of Pharmacology, Smt. NHL Medical College, Ahmedabad, Gujarat, India

**Malay Chaudhari** Department of Dermatology, Smt. NHL Medical College, Ahmedabad, Gujarat, India

**Ashish Jagati** Department of Dermatology, Smt. NHL Medical College, Ahmedabad, Gujarat, India

**Supriya Malhotra** Department of Pharmacology, Smt. NHL Medical College, Ahmedabad, Gujarat, India

**Pankaj Patel** Dean, Smt. NHL Medical College, Ahmedabad, Gujarat, India