A rare case of isoniazid-induced erythroderma

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Introduction

Tuberculosis (TB) is a common infectious disease in developing countries. Antitubercular therapy with the first line drugs is very effective and well-tolerated with only few major adverse reactions. Cutaneous adverse drug reactions (CADR) with antitubercular treatment (ATT) can make further management of TB challenging. Isoniazid is the first-line antitubercular drug par excellence and an essential component of all antitubercular regimens unless the patient is intolerant to it, or bacilli show resistance. 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.

Case Report

A 63-year-old Indian woman was diagnosed as a case of pulmonary TB when she was evaluated for fever and cough with expectoration. She was started on the first-line antitubercular drugs as per Directly Observed Treatment Short Course regimen for TB. After 8 weeks of ATT, she reported to dermatology department of our hospital, for complaints of acute onset erythema along with severe itching all over the body for the last 7–10 days.

Dermatological examination revealed generalized involvement of the body with extensive nonuniform dusky erythematosus scaly plaques involving the scalp, face, nape of the neck, trunk, arms, legs, palms, and soles [Figure 1]. Erythema and scaling were more pronounced over trunk and legs. Furthermore, the pruritic plaques were first noted on trunk and legs which increased in size and coalesced to involve the entire body in a few days. Scalp lesions formed red-yellow scales with hair loss [Figure 1]. On palms and soles, the exfoliative eruption led to severe sloughing of the epidermis. 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. Laboratory investigations were within normal limits. HIV-ELISA was nonreactive.

ATT was stopped immediately. Oral antihistaminics 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 2a].

Key Words: Adverse cutaneous drug reaction, erythroderma, isoniazid

ABSTRACT

Tuberculosis is a common infectious disease in developing countries. 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 63-year-old female patient who presented with generalized redness and scaling with itching after 8 weeks of antitubercular treatment (ATT). ATT was stopped immediately, and antihistaminics 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.
In contrast to the findings of the Figure 2:

...rifampicin, and isoniazid at last at an interval of 1 week between the drugs. Prior to isoniazid rechallenge, she did not develop any signs of CADR but on introducing isoniazid, she rapidly developed similar erythematous lesions with intense itching within 48 h [Figure 2b]. Isoniazid was withdrawn and diagnosis of “isoniazid induced erythroderma” was made. At present, the patient was given symptomatic treatment with topical emollients and oral antihistaminics. 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; whereas “probable” on Naranjo’s scale (Score 7) for isoniazid. The severity of ADR was found to be “moderate (level 3)” as per the modified Hartwig and Siegel Scale.

Discussion

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.[1]

Various causes of erythroderma in adults include pre-existing eczema, psoriasis, lymphoma, leukemia, and drugs such as phenylbutazone, hydantoin derivatives, carbamazepine, sulfonamides, penicillins, cimetidine, diltiazem, dapsone, allopurinol, gold salts, and lithium. Exposure to the causative drug may last for 2 weeks to several months before the reaction emerges. Drug-induced erythroderma has the best prognosis among all the causes of erythroderma often resolving in 2–6 weeks.[2]

In the present case, the patient presented with erythema and scaling involving more than 90% of the body surface area along with itching within 8 weeks of ATT. ATT was stopped, and a significant improvement was noted within 1 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 450 mg, pyrazinamide 1500 mg, ethambutol 1000 mg, and levofloxacin 750 mg for a period of 2 months in intensive phase followed by levofloxacin 750 mg, rifampicin 450 mg for a period of 4 months in continuation 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.[3] 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%).[1] 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. There are many case reports of exfoliative dermatitis with other antitubercular drugs; but, to the best of our knowledge, only 3 cases of erythroderma induced by isoniazid alone is reported so far.[3-5]

Higher incidence of TB and CADR in HIV-infected persons poses a challenge for clinicians, particularly in high HIV-prevalence settings. It is important to recognize the CADRs to ATT so that severe and potentially life-threatening adverse reaction can be identified and managed early. It is equally important to continue ATT in minor CADRs so that patients suffering from TB can be cured and rendered noninfectious as early as possible from uninterrupted ATT along with prevention of development of drug resistance.

To conclude, 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.

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Conflicts of Interest

There are no conflicts of interest.

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