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Case Report

Isoniazid induced acute generalised exanthematous pustulosis

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ABSTRACT

Tuberculosis (TB) poses major health problem in developing countries including India. According to WHO in 2010 survey, there were about 9.4 million active pulmonary TB Patients worldwide, out of that 2.3 million case were found in India. Isoniazid is known to be the least toxic among the first line antitubercular drugs. Hypersensitivity reactions due to Isoniazid may present in the form of fever and skin rash. We hereby report a case of acute generalised exanthematous pustulosis due to isoniazid in a patient on anti-tubercular treatment. We also established the causality, severity, and preventability of the suspected adverse drug reactions (ADRs).

Keywords: Acute generalised exanthematous pustulosis, Causality, Isoniazid

INTRODUCTION

Tuberculosis (TB) poses major health problem in developing countries including India. According to WHO in 2010 survey, there were about 9.4 million active pulmonary TB Patients worldwide, out of that 2.3 million case were found in India.[1]

Adverse drug events (ADE) during anti-tuberculosis treatment contributes to 7% of all drug related adverse events. Skin related adverse events are associated with all anti-tuberculosis drugs and it is common side effect in patient on anti-tuberculosis treatment (ATT).[1]

Isoniazide is known to be the least toxic among the first line anti-tuberculosis drugs. Major adverse drug reaction with isoniazid are neurological manifestations in the form of peripheral neuropathy, toxic psychosis and convulsions are common. While hypersensitivity reactions due to Isoniazid may present in the form of fever and skin rash.[2]

We hereby report a case of acute generalised exanthematous pustulosis due to isoniazid in a patient on anti-tubercular treatment. We also established the causality, severity, and preventability of the suspected adverse drug reactions (ADRs).

CASE REPORT

A 22-year-old female patient of urban area of Yavatmal district, belonging to a lower socio-economic family, visited a microscopy centre situated in SVNGMC Yavatmal with complaints of cough with expectoration and fever, loss of appetite, and weight for the past 1 month. The sputum was examined as per Revised National Tuberculosis Control Programme (RNTCP) by Zeihl-Neelson (ZN) staining for acid-fast bacillus (AFB) and was found to be positive. Chest radiograph showed bilateral upper zone infiltration. On the basis of microscopy, and radiography, the patient was diagnosed as a case of sputum positive new case of pulmonary tuberculosis. She was referred to the Directly Observed Treatment (DOT) centre of her area for the initiation of category I anti-tuberculosis therapy as per national RNTCP guidelines according to her weight (45kg). Category I anti-tuberculosis therapy includes isoniazid 600 mg (2 tablets), rifampicin 450 mg (1 capsule), pyrazinamide 1500 mg (2 tablets), and ethambutol 1200 mg (2 tablets).[3]

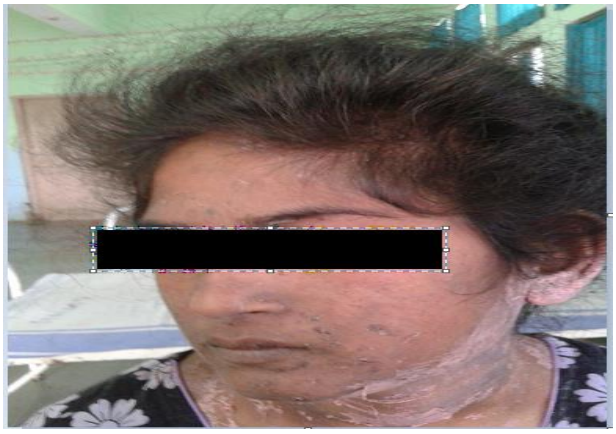

Figure 1: Pustular lesions (healed) on face and neck.

She tolerated the first dose of antituberculosis therapy. On the second day, the patient visited DOT centre with generalized exanthematous pustular rashes all over the body and more on both shoulders and upper and lower limbs and on the face predominantly. A diagnosis of antitubercular drug-induced exanthematous pustular rash was made by doctor on call in Department of skin and based on patient's history of occurrence of adverse drug reaction and time of administration of AKT, ethambutol is least suspected to cause this type of adverse reaction. Hence all anti-tubercular drugs were stopped except tab. Ethambutol. Rash resolved in 3 days. To identify culprit drug rechallenge was given with AKT as per standard protocol. Patient was explained about rechallange procedure and written inform consent taken. On the first day of rechallenge, she was given tab. Ethambutol along with tab. Pyrazinamide and rifampicin. All three drugs, ethambutol, pyrazinamide and rifampicin were well tolerated by patient. On the next day tab. Isoniazid was added and patient develops itching and pustular rash for which she was given symptomatic treatment. Isoniazid was discontinued after this reaction and rash subsided after 4 days. She was on regular follow-up with disappearance of rashes and signs and symptoms of tuberculosis.

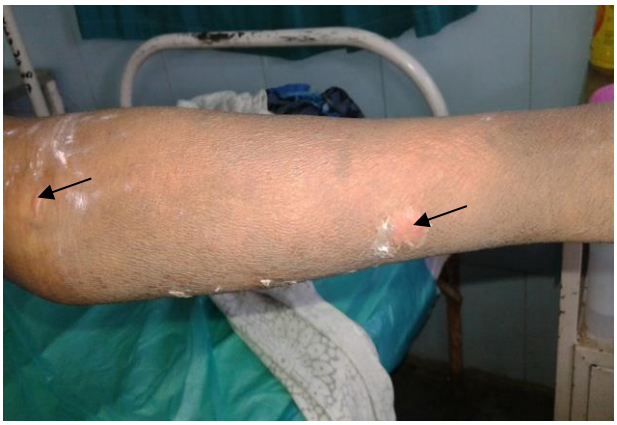

Figure 2: Arrow indicates pustular lesions on forearm.

Causality assessment was done using Naranjo algorithm and severity assessments as per the Hartwig scale.[4] Causality assessment revealed a probable association (Naranjo score 7) between the ADR and isoniazid. The severity was found to be moderate (Level 3). The preventability analysis revealed the ADR to be not preventable.

DISCUSSION

Cutaneous adverse drug reactions (CADR) are one of the most commonly observed major adverse effects of first line antitubercular therapy being reported in 5.7% of patient on ATT therapy. In CADR associated with the ATT includes erythema multiform, mobiliform rash, urticaria and more serious like Steven Johnson syndrome. Pyrazinamide is most common first line antitubercular drug responsible for CADR (2.38%) followed by steptomycine (1.45%), ethambutol (1.44%), rifampicin (1.23%) and isoniazide (0.98%).[5]

In our case, the patient developed the rash on the third day (after second dosing day of therapy) after initiating anti-tuberculosis therapy and disappeared after few days when the drug (isoniazid) was stopped. The rash again reappeared when isoniazid was restarted. The causal relationship between the drug and the ADR was found to be probable.

The management of such reactions needed withdrawal of the suspected drug and management of symptoms, if any. In this case, the suspected drug was stopped immediately following the ADR and antihistamines were added to manage associated itching due to drug reaction, to which patient responded well. The severity assessment revealed the ADR to be moderate (Level 3), suggesting that the

suspected drug should be withheld, discontinued, otherwise changed, and/or on antidote or other treatment is required. There was no increase in the length of stay. Since this patient did not have any past history of skin reaction due to isoniazid or any other drugs, therefore this reaction was unpreventable.

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