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ISONIAZID INDUCED EXFOLIATIVE DERMATITIS IN A PATIENT WITH LEFT RENAL AGENESIS

Medicine

Dr. Himanshu Sharma Junior Resident, Department of Respiratory Medicine, MMIMSR, Mullana, Ambala, Haryana.

Dr. Jai Kishan Professor & Head, Department of Respiratory Medicine, MMIMSR, Mullana, Ambala, Haryana.

Dr. Sukhjinder Pal Singh* Junior Resident, Department of Respiratory Medicine, MMIMSR, Mullana, Ambala, Haryana. *Corresponding Author

ABSTRACT

Cutaneous drug reactions with anti-TB drugs can occur any time after institution of drugs. Due to the use of fixed drug combination tablets under DOTS in RNTCP, it becomes difficult to identify the culprit drug. It also makes reintroduction of drugs a lengthy and difficult process. Here we present a case of isoniazid induced severe exfoliative dermatitis occurring after 55 days of starting category I antitubercular treatment in a patient of pulmonary tuberculosis with left renal agenesis. To the best of our knowledge very few cases of isoniazid induced exfoliative dermatitis have been reported.

KEYWORDS

isoniazid, exfoliative dermatitis, cutaneous drug reaction

Introduction: -

India is home to about 1/4th of all global TB cases. Mortality rate due to TB in India is approximately twice than that of the global mortality rate according to WHO Global TB Report.[1] TB treatment in India is done under RNTCP in which directly observed treatment with fixed dose combination daily regimen is given. First line drugs used for tuberculosis are Isoniazid(H), Rifampicin(R), Ethambutol(Z), Pyrazinamide(E) in new cases and in addition to these, streptomycin(S) in re-treatment cases.

All these drugs are known to cause adverse drug reactions like hepatotoxicity, skin lesions, neuropathy, nephrotoxicity and ototoxicity. Skin related ADRs are common and are seen in approximately 6% patients of TB which are started on Anti TB drugs. Skin reaction can be caused by any one or combination of ATT drugs.[2]

TB and its co-morbid conditions like HIV, immune-suppressant conditions can also have cutaneous and mucosal manifestations in which cases it becomes difficult to differentiate between lesions that are drug induced or disease induced.

Skin lesion can range from mild self- limiting reaction to severe forms like Steven Johnson Syndrome. Skin lesion can be a pruritic rash, maculopapular lesion, urticarial eruptions, lichenoid lesion or severe forms like exfoliative dermatitis and Steven Johnson syndrome. Exfoliative dermatitis also known as erythroderma, is a form of cutaneous hypersensitivity reaction that occurs after 6-8 weeks of starting therapy. The tendency of the drug to cause erythroderma is most by pyrazinamide followed by streptomycin, ethambutol, rifampicin and isoniazid with rates for pyrazinamide being 2.4%.[2]Here we present a case of a patient who was started on Category I ATT and developed severe exfoliative dermatitis after about 8 weeks.

Case report –

A male patient 80 years old presented to us with complaints of severe skin reaction with itching and dryness of skin over whole body since last 5 days. Patient was a known case of pulmonary tuberculosis sputum for AFB positive and was started on HRZE regimen under category I DOTS 55 days ago. Patient was taking medication regularly and was showing clinical and radiological signs of improvement. 5 days before presenting to us, patient started developing redness and swelling over face and arms, legs and trunk. On presentation, he had scaly eruptions with desquamation of skin over legs, arms, forearms, palms of hands, soles, scalp and trunk with hyper-pigmented patches over extensor surfaces of forearms, shins and over maxillary region of face (Figure 1)(Figure 3)(Figure 5). There was no mucosal involvement.

Investigations showed raised Absolute Eosinophil Count (726/cu mm), B. urea (90mg/dl), S. creatinine (1.33mg/dl). Sputum for AFB was negative. HIV was also negative. Diagnosis of ATT induced exfoliative dermatitis was considered as patient had no previous history of drug allergy or skin condition and was taking no drug other than fixed dose combination ATT drugs. On ultrasound abdomen, there was an incidental finding of left renal agenesis with right renal parenchymal changes.

ATT was stopped immediately and oral anti histaminic were started after which rash and swelling subsided and itching improved over next 10 days. It was planned to reintroduce ATT in a sequence of isoniazid, rifampicin, ethambutol and pyrazinamide. On re-introduction of isoniazid patient again developed itching and rash. Re-challenge with rifampicin, ethambutol and pyrazinamide was uneventful. So, isoniazid was stopped and modified regimen with rifampicin, ethambutol and pyrazinamide was started and the patient is kept on regular follow up and doing well. Improvement following stoppage of drugs is shown in figures [compare Figure 1(one) vs 2(two), 3(three) vs 4(four) and 5(five) vs 6(six)].

Figure 1

Figure 2

Figure 3

Figure 4

Figure 5

Figure 6

Skin lesions on arms and legs (Figure 1,3,5) and pictures showing improvement after stopping isoniazid (Figure 2,4,6)

Discussion: -

Cutaneous adverse drug reactions (CADR) to ATT drugs is well known and are seen in around 5.7% cases. CADR is defined as skin reactions secondary to systemic administration of drugs (oral/ subcutaneous/ intravenous/ intramuscular/ inhalation). The allergic reactions can be immediate hypersensitivity reaction, delayed hypersensitivity reaction, due to cumulative effects of drugs, adjuvant effect as in case of rifampicin and clofazimine or due to release of tuberculoproteins. The adverse drug reaction can also occur to other drugs being used concomitantly or with nutritional supplements or vitamins. Drug reaction may also occur due to accumulation of drugs which can be because of renal impairment which resulted in drug levels being higher, thus resulting in adverse drug reaction. Which in our case may be the cause of adverse drug reaction due to renal agenesis.

Exfoliative dermatitis/erythroderma is a generalized inflammatory disorder of the skin manifesting with erythema and scaling affecting >90% of the skin surface.[3] Approximately 10% of the cases are the result of drug reactions.[4] It is generally managed by antihistaminic drugs and emollients. Steroids can be given to accelerate the process of shedding of skin. It has been well established that anti-TB drugs are among the commonest drug that cause cutaneous drug reactions.[5]

Adverse drug reactions can lead to alteration and interruption in treatment resulting in increased risk of treatment failure, drug resistance, relapses and increase the risk of complications. Fixed drug combination tablets are used to treat TB in India. Due to combination of different drugs in one tablet it becomes difficult to establish the agent causing the reaction. Re-introduction of the drugs which has to be done one by one makes it a lengthy process. Alteration of regimen results in use of a less effective regimen, increases the duration of treatment and decreases patient compliance.

Anti-tubercular drugs usually cause minor side effects but severe skin reactions can also occur as in our case and should be kept on mind when a patient on ATT presents with skin lesions of any severity.

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