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Case Report

Lichenoid eruption due to antitubercular drugs: a case report

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ABSTRACT

Adverse drug reactions can be predictable or unpredictable. Regardless, they must be communicated to patients to improve the quality of healthcare. According to the World Health Organization (WHO), in the year 2020, tuberculosis was the thirteenth leading cause of death worldwide. For the clinician who commonly encounters tuberculosis, the effectiveness of antitubercular drugs such as rifampicin, isoniazid, pyrazinamide and ethambutol are complicated by the severity of adverse reactions. This requires the physicians to weigh both the benefits and the risks of using these medications and to choose appropriate management strategies. Here, we report a case of lichenoid drug eruption related to antitubercular drugs in an elderly gentleman diagnosed to have extrapulmonary tuberculosis. The skin disorder presented with thickness and hyperpigmentation of the skin. The exact offending drug could not be conclusively identified but therapy was continued under the cover of a topical steroid and an antihistamine agent. The medical reporting of such cases is essential to identify one of several cutaneous adverse reactions seen with antitubercular drugs. Furthermore, it aids in alerting health care professionals and the public of the potential undesirable effects of these drugs.

Keywords: Antitubercular drugs, Cutaneous adverse reactions, Lichenoid drug eruption, Extrapulmonary tuberculosis

INTRODUCTION

Lichenoid drug reaction is uncommon in general medical practice. Its incidence among patients taking first line antitubercular therapy is roughly 10%.[1] Clinically, these lesions resemble lichen planus but with subtle differences. In Lichenoid drug reaction, the latency period ranges from months to years; the average being 2-4 months depending on the nature of the drug, dosage and duration of the therapy. Unlike lichen planus which usually involves flexural surfaces, Lichenoid drug eruption is characterized by extensive symmetric flat topped violaceous plaques involving the trunk and extremities.[2] Lichenoid drug eruption does not commonly involve the mucosa which signifies a more serious condition and hence, requires removal of the offending agent.[3] History of photosensitivity can be present in Lichenoid drug eruption because skin exposed to ultraviolet radiation causes photochemical reaction, and thus the body recognizes the drug or its metabolites as non-self-antigen.[4] It is imperative as well to rule out autoimmune disease as these conditions can mimic adverse drug reaction.[5] Absolute eosinophil counts (AEC) greater than 1500 per mm^3 is considered moderately high and is frequently seen with Lichenoid drug eruption. It is common to have the AEC count high in drug allergies and it usually disappears when the causative drugs are stopped.[6] In the present study the absolute eosinophil count was normal. Thus, it is vital not only to rely on investigations but also on clinical skills.

Some of the common offending drugs are captopril, enalapril, chloroquine, methyl dopa and D-penicillamine. Common antitubercular drugs that cause lichenoid drug eruptions are isoniazid and rifampicin.[7]

CASE REPORT

History

Mr. X, a 63-year-old gentleman, retired schoolteacher, diagnosed with extrapulmonary tuberculosis for the past 3 months, taking antitubercular drug regimen (isoniazid, rifampicin, and ethambutol) presented with generalized pruritic scaly lesions for 20 days; the severity of the pruritis progressively increased during this time period. He also noticed that exposure to sunlight aggravated the symptoms. He had no previous history of allergies, autoimmune disease, other comorbidities or similar episodes. He was not on any over the counter medications or herbal therapy.

General examination

The general condition of the patient was fair. The patient was conscious, oriented to time, place and person. All his vital signs were normal. Pallor was observed. Lymphadenopathy was present in the cervical and inguinal regions with no icterus, clubbing, cyanosis and edema.

Systemic examination

No significant abnormalities were detected.

Local examination

Scalp and face

Multiple well-defined discrete hyperpigmented purplish plaques were seen over the scalp, periorbital region and the forehead.

Trunk

Symmetrical multiple well-defined erythematous or violaceous papules, were seen on the trunk and extremities.

Upper limbs and lower limbs

Diffuse bilateral scaling and fissuring of the skin involving the extensor aspect of the limbs were seen. There was no involvement of the flexure aspect of the extremities.

Nail changes and mucosa

There were no changes detected in the nail, the mucosa and genital areas.

Investigations

All routine blood investigations were done (Table 1). The complete blood count revealed mild anemia. Skin biopsy results showed florid lichenoid response and focal hyperkeratosis; eosinophils and plasma cells were found in the dermal infiltrate.

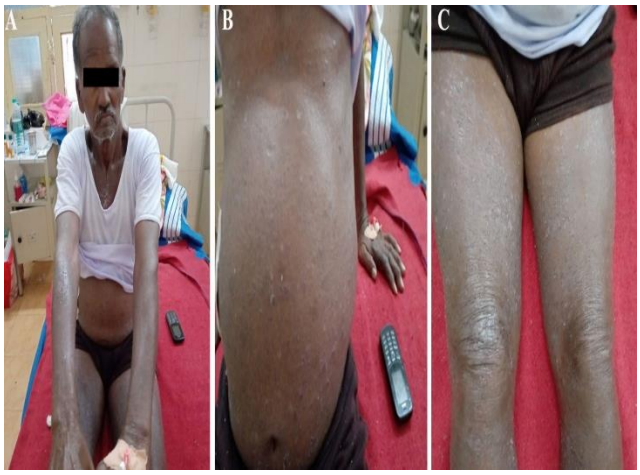

Figure 1: Anatomical sites for lichenoid drug reaction.

Table 1: Routine blood investigations.

Blood investigations	Values
Hb (gms/dl)	10.7
MCV (fl)	94.3
WBC total count (cumm)	$8,200\times10^3$
Neutrophil (%)	37.0
Lymphocytes (%)	41.1
Monocytes (%)	18.8
Eosinophils (%)	10.5
Platelets (lakhs/cumm)	1.77
RBS (mg/dl)	144
LFTs	Within normal limits

Management

Antitubercular regimen (based on the body weight) was continued for a total duration of 6 months.

Mometasone 0.1% cream was prescribed twice a day for 2 weeks.

T. bilastine 20 mg was prescribed once daily for 10 days.

Self-care tips were advised such as avoiding skin products containing harsh ingredients like perfumes and to abstain from scratching the area to prevent infection.

Follow-up

After 2 weeks the symptoms improved and did not reappear with continuation of ATT and the patient was further recommended to apply emollients as needed. The patient was counselled about the need to adhere to the ATT drug regimen and he was assured that the skin manifestation would gradually resolve upon cessation of the drugs.

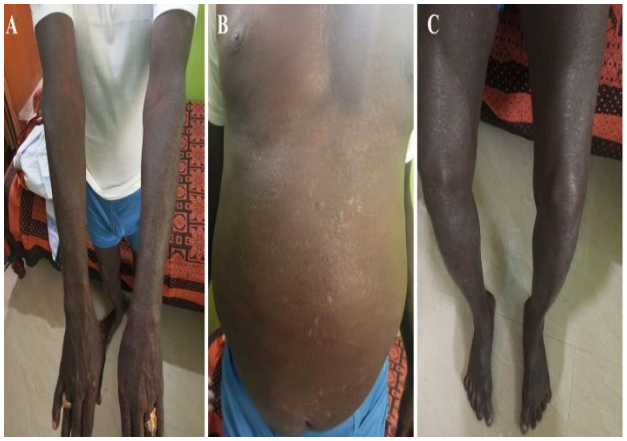

Figure 2: After treatment.

DISCUSSION

The spectrum of tuberculosis associated cutaneous adverse drug reactions is wide.[8] The lack of acute biochemical markers and gradual onset of lichenoid drug eruption make it difficult to establish a temporal relationship and assign causality.[9] It is postulated that the mechanism of lichenoid tissue reaction is the expansion of the T cells which recognize the drug as foreign. T cells produce a delayed immune response or hypersensitivity type 4 reaction to the administered drug; key mediators in this reaction are INF-α, which further causes the activation of IFN-γ and CXCR3 ligands. As a result, there is accumulation of cytotoxic TH1 cells and dendritic cells in the lesion that stimulates the inflammatory cascade. It is characterized by symmetric eruption of flat topped, erythematous or violaceous papules resembling lichen planus on the trunk and the extensor aspect of the extremities.[7]

In our study, the gold standard histopathological biopsy specimen report was consistent with lichenoid drug eruption. The findings found in biopsy in favor of drug induced etiology was epidermal parakeratosis, transdermal necrotic keratinocytes and the presence of eosinophils.[10]

The first line therapy used for Lichenoid drug eruptions is high potency topical steroids although there are no randomized clinical trials supporting their use. More data is available supporting the use of acitretin, systemic steroids and other immunosuppressants.[8]

Most of the patients remember the interval between initiation of the agent and the initial appearance of the cutaneous drug reaction. A latent period with at least two to twelve months has been reported between start of treatment and the onset of lichenoid drug eruption.[11] The latency period depends on class of drugs, the dosage formulation and the individual reaction.[2]

As skin manifestations from adverse drug reactions are confusing, therefore a practical approach is warranted. The clinician must recognize an eruption as drug induced, manage the drug reaction in active stage, manage the complications, identify host factors including genetic predilection and prevent the recurrence of the cutaneous adverse drug reaction. One such clinical approach that assembles the aforementioned aspects is designated by the 5 A's.

The clinical approach to evaluating an adverse drug reaction involves the 5 A's: appreciation, assessment, analysis, assistance and aftermath. The first step is appreciation which involves understanding that the unwanted effect may be from the therapeutic treatment. In this case, the observed cutaneous skin reactions were due to the antitubercular drugs. The second step includes assessment of the noxious effect of the drugs used, the disease being treated and the characteristics of the patient being treated. The third aspect is analysis of the data gathered; this is designed to determine if the adverse drug reaction is related to the offending agent. The next step is assistance. Usually in mild cases the treatment is supportive and symptomatic. In the present scenario specialists were consulted to assist in the management of the patients. The final step is the aftermath which comprises the care following treatment. This involves clear communication to the patient and family members as to the role of the drug in causing the adverse reaction.[12]

Strict vigilance after treatment is mandatory as complications such as exfoliative dermatitis, relapse and resistance to tuberculosis can occur.[2]

Recording and reporting of cutaneous adverse drug reactions has been weak in the chain of measures to ensure future drug safety. This neglect may be serious later on as re-exposure can have detrimental effects. As in this case, adverse drug reactions may often be delayed and have a long latency period. Health care professionals, patients, pharmacologists and regulatory authorities should be proactive to detect, document and to spread knowledge and ensure safety of the public. Various methods to assess causality of cutaneous adverse reactions are Naranjo probability scale and Uppsala monitoring center scale.[13]

CONCLUSION

On confirmation of the diagnosis, the practical dilemmas are managing tuberculosis associated cutaneous adverse drug reactions. The quandary is whether to stop the current treatment for tuberculosis or for the therapy to be continued. By implementing the evaluation steps of adverse drug reactions, the dermatologist decided to continue treatment and manage the side effects, as stopping the regimen would lead to complications such as relapse, resistance and further transmission of tuberculosis in the community.

Furthermore, pharmacovigilance reporting and assessment is needed to harbor the knowledge of the unwanted effects and to raise awareness of medications. In this case**,** follow-up of the patient revealed that he had improved clinically.

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