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Case Report

Ethambutol induced subacute cutaneous lupus erythematosus in an elderly female with co-morbidities

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ABSTRACT

Papulosquamous lesions in an elderly female with multiple co-morbidities often pose diagnostic challenge. We present an interesting case of anti-tubercular treatment (ATT) induced sub-acute cutaneous lupus erythematosus. The patient presented with papulosquamous lesions in generalised distribution, which showed interface dermatitis on histopathology. The serology for anti-nuclear antibodies, anti-Ro and anti-La was positive. The rash resolved spontaneously after stopping all the suspected drugs. Oral provocation was performed with first line anti-tubercular drugs and ethambutol was found to be the culprit drug, which was later confirmed by reappearance of skin rash by inadvertent ingestion of one dose of ethambutol by the patient.

Keywords: Ethambutol, Subacute cutaneous lupus erythematosus, Drug induced, DI-SCLE, Anti-tubercular treatment

INTRODUCTION

Papulo-squamous skin lesions in elderly females with multiple co-morbidities often pose diagnostic challenge.[1] We describe an interesting case of similar eruption.

CASE REPORT

A 58-year-old female, known case of pulmonary tuberculosis, chronic kidney disease, generalized anxiety disorder and rheumatoid arthritis, presented with moderately itchy, erythematous scaly plaques over trunk and extremities for 3 weeks. She complained of repeated episodes of chills, but no other systemic complains. The eruption was progressive and associated with significant pruritus and oozying. The patient was uncomfortable and bedridden.

Clinical examination revealed large confluent erythematous scaly plaques over extensor aspect of upper and lower extremities, upper chest, abdomen, back and buttocks, with sparing of face, scalp, palms and soles, mucosal sites and nails. The scales were coarse, dirty-grey in color, semi-adherent and not associated with foul smell. There were multiple superficial linear erosions over pressure bearing sites such as buttocks and back. There was no facial or pedal edema, lymphadenopathy or organomegaly. Vital parameters were unremarkable.

She had moderate anemia (hemoglobin- 9.3 g/dl) and deranged kidney function (urea- 83 mg/dl; normal range 15-39 mg/dl, creatinine- 3.16 mg/dl; <1 mg/dl). Other hematological parameters and liver function tests were unremarkable. Serology for anti-nuclear antibody, anti-Ro and anti-La was positive. Serology for HIV and Venereal Disease Research Laboratory test were negative. Skin biopsy from back showed epidermal atrophy, hydropic degeneration of basal keratinocytes with multiple necrotic keratinocytes, lymphocytic exocytosis with upper dermal edema and sub-epidermal and perivascular lymphocytic

infiltration. However, lesional direct immunofluorescence was negative for IgG and C3.

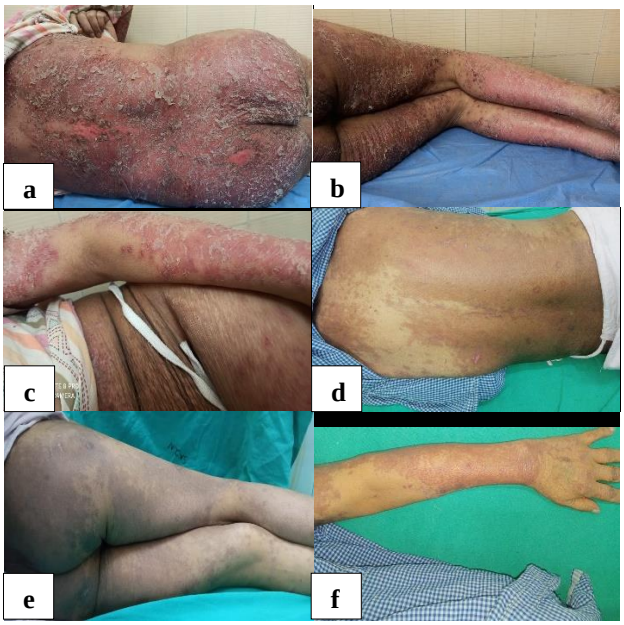

Figure 1 (a-c): Shows multiple large confluent erythematous plaques associated with coarse, dirty grey, semi-adherent scaling over trunk and upper and lower extremities and multiple superficial linear erosions over buttocks and back; and (d-f): shows almost complete resolution of skin lesions with residual post-inflammatory hyperpigmentation.

She was taking anti-tubercular treatment (ATT) consisting of isoniazid, rifampicin and ethambutol for 2 months and hydroxychloroquine and propranolol for 1 year.

Based on the clinical presentation, temporal association with ATT, a diagnosis of ATT induced subacute cutaneous lupus erythematosus (SCLE) was considered. Isoniazid, rifampicin and ethambutol were stopped. She was treated with betamethasone valerate cream (0.05%), white soft paraffin-based cream and oral antihistamines. There was significant improvement within 1 week of discontinuing the medication and all lesions resolved completely in 3 weeks with residual post-inflammatory hyper-pigmentation.

After resolution of skin lesions oral provocation was done uneventfully with pyrazinamide, isoniazid and rifampicin respectively (started with one-fourth dose followed by half dose and then full dose). Hence, ethambutol was considered the culprit drug. She was started on isoniazid, rifampicin, pyrazinamide and levofloxacin for tuberculosis. There was no recurrence of rash after starting of the new regimen. Two months later the patient presented with similar rash. It was found that she had been inadvertently prescribed ethambutol by another practitioner. There was recurrence of rash within 24 hours of taking one dose of ethambutol, hence confirming our suspicion. This episode was managed with short course of oral prednisolone. The patient did not complain of any skin lesions when she was followed up after 6 months.

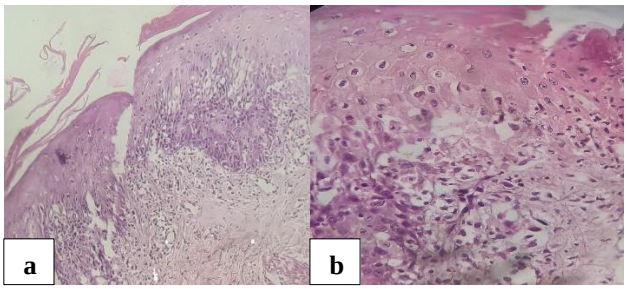

Figure 2 (a and b): Hematoxyllin and eosin stained biopsy from back showed epidermal atrophy, hydropic degeneration of basal keratinocytes with multiple necrotic keratinocytes, lymphocytic exocytosis with upper dermal edema and sub-epidermal and perivascular lymphocytic infiltration at 100x and 400x magnification.

DISCUSSION

Sudden appearance of generalised papulo-squamous lesions in an elderly female prompts multiple differentials including psoriasis vulgaris, endogenous dermatitis, contact dermatitis, connective tissue diseases, pityriasis rubra pilaris, drug rash among others.[1] As in the present case, temporal correlation between starting of the drug and onset of the skin rash is a helpful indicator to consider the diagnosis of drug rash. ATT have been reported to be associated with several types of drug rash.[2-5] The association between ATT and SCLE is reported less frequently.[6]

The gold standard test to establish drug causality is oral provocation test. The sequence of drug challenge is debatable.[2] In the present case pyrazinamide had not been prescribed before the onset of skin rash. Among the other three first-line drugs the patient was provoked with isoniazid followed by rifampicin based on the lesser incidence of drug reaction compared to ethambutol. Moreover, the drug causality was confirmed two months later when the rash reappeared after inadvertent ingestion of single dose of ethambutol.

Drug induced SCLE (DI-SCLE) is under-recognised and under-reported. The mean time of onset of skin lesions ranges between 2 weeks to upto 3 years.[6] Marzano et al reported DI-SCLE as 12% of their cohort of SCLE over 10 years. Widespread involvement including lower extremities was reported more in DI-SCLE compared to idiopathic SCLE, while concurrent systemic features were more common in the latter. ANA positivity was seen in all patients associated with the presence of anti-Ro and Anti-la antibodies in all but one patient. These antibodies disappeared after clinical resolution of the disease and none of the patients evolved into systemic lupus erythematosus after 4 years.[7] Our patient had classic presentation of SCLE after intake of ATT. Serology for

anti-nuclear antibody, anti-Ro and anti-La was positive and histopathological features were concurrent with the diagnosis.

CONCLUSION

Conclusively, drug reaction is an important possibility in generalised psoriasiform eruption in a middle-aged female on multiple drugs, especially ATT. It is important to perform Histopathological analysis and screen for anti-nuclear antibodies as DI-SCLE can present as generalized psoriasiform eruption.

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