Correspondence

Ethambutol-Induced Toxic Epidermal Necrolysis

Sir,

Adverse drug reaction (ADR) is an important cause of morbidity, hospital admission, increased health expenditure and even death. Cutaneous ADRs account for majority of ADRs in hospitalized patients and can range from mild exanthemas to Stevens-Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN).¹ We hereby report a young female who developed TEN due to commonly prescribed anti-tubercular drug, ethambutol and was treated successfully with steroid and antibiotics.

A 25 year old, young married female who was diagnosed to have tubercular lymphadenitis, was started on four drug anti-tubercular treatment (RHZE). On 8th day of ATT, she developed generalised papulosquamous rashes involving both thighs, legs, trunk, face and oral cavity. She was admitted outside and was put on antibiotics along with steroids. Patient improved slightly, was discharged after 5 days but ATT was continued. Four to five days later patient again developed generalised body rashes with greater intensity for which she was referred to us. On examination she was febrile, vitals were stable, had erythematous patches over both malar prominences with haemorrhagic crusts present over the lips and anterior nares (Fig. 1), multiple areas of erosions all over the body with thick adherent yellow crusts, some showing whitish scales, hyperpigmentation and thick dystrophic nails (Figs. 2 and 3). Nikolsky sign was positive. Rest of the examination was normal. Patient was diagnosed as a case of toxic epidermal necrolysis however no concrete evidence of tuberculosis was found, either on clinical examination or on investigations. Investigations revealed neutrophilic leukocytosis and cultures were sterile. Antitubercular drugs were discontinued and she was put on intravenous methyl prednisolone (125mg x 6 hourly), antibiotics, silver sulfadiazine cream for local application, anaesthetic gel for mouth ulcers and IV fluids. The skin lesions of patient improved gradually. After about a month of treatment, antitubercular drugs isoniazid, rifampicin, pyrazinamide and ethambutol were restarted individually and sequentially, starting from low doses and escalating gradually at a regular interval of 3 days to find out the offending agent. On reinstituting the ethambutol her skin lesions flared up. She was discharged on 45th day and is doing well on follow-up and no need to add the ATT was felt.

TEN is a rare life threatening disorder characterised by extensive necrolysis and detachment of full thickness epidermis, generally induced by drugs. Separation of the dermo-epidermal junction gives skin the typical “wet dressing” appearance². ADRs are important because they occur frequently; require discontinuation of medication to prevent serious morbidity and even death. The extent of epidermal sloughing may vary and forms a basis for the classification of an individual case as SJS or TEN. SJS includes cases with less than 10% epidermal detachment, mucosal lesions, and widespread purpuric lesions; SJS / TEN overlap when the epidermal detachment is between 10 and 30%; mucosal lesions, widespread purpuric lesions, and TEN when the epidermal detachment is more than 30%, and mucosal lesions and widespread purpuric lesions are present³. The pathophysiological mechanism of SJS and TEN have not been fully elucidated. The aetiological factors of SJS and TEN are

Fig. 1: Clinical photograph showing erythematous patches over both malar prominences with haemorrhagic crusts present over the lips and anterior nares.

Fig. 2 and 3: Clinical photographs showing multiple areas of erosions over the hands and feet with thick adherent yellow crusts, some showing whitish scales, hyperpigmentation along with thick dystrophic nails.
diverse; drugs being the cause in more than 80% cases of TEN and about 40-50% cases of SJS. The common drugs implicated include NSAIDS, anti-convulsant and certain antibiotics. In countries like India, where tuberculosis is rampant, anti-tubercular drugs have been shown to be one of the leading cause. In anti-tubercular drugs, thiacetazone, streptomycin, PAS, pyrazinamide and isoniazid are the main drugs responsible for TEN however ethambutol is uncommonly reported. Mucous membranes are affected in nearly all cases. ADRs are life-threatening due to multisystem involvement and mortality ranges from 25 - 70%.

Supportive management still remains the mainstay of treatment of TEN. This involves skilled clinical assessment with early identification of the culprit drug and immediate withdrawal, close fluid and electrolyte monitoring, nutritional support, meticulous wound and eye care and antimicrobial therapy. Specific therapy for these conditions is yet not available, however corticosteroids and immunoglobulin have been used with some beneficial effect. Younger age, early medical aid, lesser area of involvement, absence of co-morbidity and early use of corticosteroids portend a favourable prognosis.

We thus present this case to sensitize the physicians about such severe drug reactions which are usually caused by commonly prescribed drugs. This report also highlights the importance of early recognition, prompt withdrawal of the offending drug and appropriate treatment to prevent significant morbidity and mortality.

**SC Chaudhary**, V Atam**, Abhinav Gupta***, Rajesh Arya****, Dheeraj Soni****

*Assistant Professor, **Professor, ***Resident, ****Senior Resident, Department of Medicine, C.S.M. Medical University, UP, Lucknow

Received: 27.09.2010; Revised: 31.12.2010; Accepted: 31.12.2010

References