Nifedipine-induced acute generalized exanthematous pustulosis in a case of acute glomerulonephritis

Sir,

Acute generalized exanthematous pustulosis (AGEP) is a disease characterized by the rapid occurrence of many sterile nonfollicular pustules usually arising on an edematous erythema, often accompanied by leucocytosis and fever.[1] Drugs are attributed as the most important cause of AGEP, although, rarely, it can be due to infections or idiopathic.[2] Herein, we report a case of AGEP induced by nifedeipine in a patient of acute glomerulonephritis.

A 27-year-old male patient diagnosed as a case of acute glomerulonephritis on furosemide and enalapril for last 3 months was admitted to the medical unit of our institute with severe hypertension and was prescribed nifedipine for control of the hypertension. On the third day of treatment with nifedipine, he developed fever, which was followed by a generalized skin rash consisting of numerous discrete 2-3 mm pustules over an erythematous skin affecting the upper extremity, chest, abdomen and thighs [Figure 1]. The patient's past medical history was negative for any similar eruptions, psoriasis or any drug allergies. On bacteriological and mycological examination of the pustules, no organisms could be isolated. Tzanck test was negative for any acantholytic cells or multinucleated giant cells. A skin biopsy showed spongiosis with dense subcorneal neutrophilic infiltrate and edematous papillary dermis with perivascular mixed mononuclear cell infiltrate. Based on the clinical features, negative microbiological study and histopathological findings, a diagnosis of AGEP was made and the suspected drug nifedipine was withdrawn and the patient prescribed oral cetrizine and paracetamol. After 2 days of stopping nifedipine, the patient became afebrile and there were no further new eruptions. At the end of 1 week, all the skin lesions were healing with desquamation.

Cutaneous drug reactions occur at a frequency of 1-8% and can be higher for certain classes of drugs.[3] AGEP is a severe cutaneous adverse reaction and has a typical clinical evolution pattern, in that the eruptions occur 24 h-3 weeks (average, 5 days) after administration of the offending drug and quickly resolve on discontinuation of the drug in a 1-2 week time period.[1,2,4,5] A recent multinational case control study, Euro SCAR, has found the highest risk of AGEP due to drugs like antibiotics (macrolides-pristinomycin, aminopenicillin, quinolone, sulfonamide), anticonvulsants, hydroxychloroquine, terbinafine and diltiazem.[1] Other drugs reported to be associated are glucocortcoids, oxicam, nonsteriodal anti inflammatory drugs (NSAIDs), fluconazole, chlorpromazine, mesalazine, allopurinol, enalapril, furosemide, nystatin and hydroxyzine.[1-12] The Euro SCAR study did not find any association of AGEP with psoriasis or infective causes, although earlier studies have shown a higher incidence of AGEP in psoriasis and even some have considered it as an entity no different from pustular psoriasis.[1,6] However, the clinical evolution pattern of AGEP is different as compared with pustular psoriasis. AGEP is mediated by T-cells, which produce high levels of CXL8 (interleukin-8) and granulocyte monocyte CSF.[2] CXCL-8 is also produced by keratinocytes in the lesion of AGEP.[2] AGEP can be confused with other pustular cutaneous dermatoses like pustular psoriasis, drug hypersensitivity syndrome with pustules, subcorneal pustular dermatosis, pustular vasculitis, bacterial, viral and fungal infections and, in severe cases, from toxic epidermal necrolysis. The temporal relationship of the development of the eruption with the intake of the suspected drug and its prompt subsidence on withdrawal of the drug along with the histopathological findings and negative microbiological study helps to arrive at a diagnosis. Among the calcium channel blockers, diltiazem has a very high risk of developing the eruption.[1,13,14] Cross reactivity with other calcium channel blockers like nifedipine and verapamil has been demonstrated by patch testing.[13] A knowledge of the possible groups of drugs responsible for the reactions is essential for the clinicians as prompt withdrawal of the offending drug helps resolution of the eruption, which otherwise can be occasionally fatal. Some patients may require the use of systemic corticosteroids.[15] Because AGEP is a T-cell-mediated reaction, it is suppressed by steroids like any other T-cell-mediated reaction; nevertheless, it should be kept in mind that steroids can themselves be a cause of AGEP.[1,9]

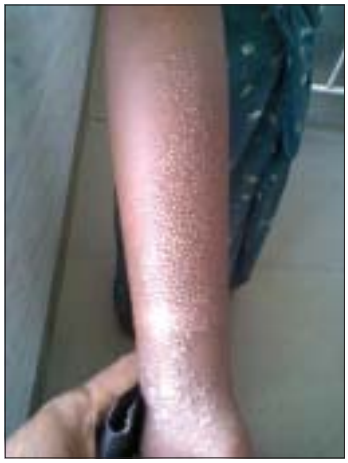

Figure 1: Numerous monomorphous pustules over the forearm

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