CASE REPORT

Acute Generalized Exanthematous Pustulosis (AGEP) due to Dapsone in a patient with leprosy

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Introduction

Acute Generalized Exanthematous Pustulosis (AGEP) is a dermatosis characterised by an acute episode of appearance of sub-corneal sterile pustules over erythematous-edematous skin. AGEP is often associated with systemic symptoms such as high grade fever and is usually considered to be an adverse drug reaction, although a viral etiology is sometimes implicated. Here we report a case of AGEP following the intake of dapsone in a patient with leprosy.

Case Report

A 22 year-old male presented with a single slightly raised hypopigmented and hypoesthetic skin lesion on his left knee to the Department of Dermatology, Gandhi Medical College, Hyderabad, India, and was diagnosed clinically as having Borderline Tuberculoid (BT) leprosy. No major nerve trunk was involved. He did not give any past history of skin disorders including psoriasis. A skin biopsy showed histopathological features consistent with BT leprosy. The patient was started on dapsone (100 mg daily) and rifampicin (600 mg monthly) as specified for the WHO MDT PB regimen. However, on the 9th day after starting therapy, the patient developed a generalised macular erythematous eruption all over the body, on which within the next 2 days, very superficial groups of tiny pustules developed, predominantly on the trunk and limbs. These pustules were more marked on the back and sides of the trunk. The patient was afebrile and denied taking any other drugs except MDT PB. A full blood count was normal except for moderate leucocytosis. Liver function tests were within normal limits. The patient was diagnosed as having AGEP based on clinical findings. A skin biopsy was taken from affected skin on the trunk, and it showed classical...
features of AGEP, which are subcorneal vesicles containing dense neutrophil infiltrate, and inflammatory changes and mild vasculitis in the papillary dermis (Figures 1 and 2). The MDT had been stopped when the skin eruption appeared and the patient was put on 20 mg of prednisolone daily, and supportive therapy. Prednisolone was tapered over the next 2 weeks. The generalised exanthematous pustulosis while subsiding presented as generalised exfoliation and entire eruption regressed within the next 2 weeks. When drug therapy was reintroduced after 4 weeks, rifampicin was given first. It did not bring back the eruption. By exclusion, dapsone was considered the offending drug although re-challenge was not done. Dapsone was substituted with clofazimine in the regimen. Both clofazimine and rifampicin were well tolerated.

Discussion

AGEP, as the name suggests is characterised by the appearance of generalised exanthematous macular eruption accompanied by non-follicular subcorneal sterile pustules all over the skin and is predominantly a drug induced dermatosis. Until the early 1990s AGEP was considered a variant of pustular psoriasis. However, it was later recognised as a distinct drug eruption and in effect, some cases previously reported as ‘drug-induced pustular psoriasis’ were actually AGEP.1,2

The onset of AGEP is always acute, accompanied by an episode of fever, which regresses in a few days. Resolution of the pustules occurs spontaneously within 4–10 days after discontinuing the suspected drug. AGEP appears to be a drug-induced, T lymphocyte cell-mediated disease, wherein the effector function of T cells leads to a neutrophil-rich

Figure 1. AGEP eruption in skin: Photomicrograph of skin showing sub-corneal vesicles containing a dense neutrophilic infiltrate and a few lymphohistiocytic cell collections in the dermis with mild vasculitis (H&E stain 100 X).
inflammation. T lymphocytes are involved in some neutrophilic inflammatory responses, and may orchestrate the immune reaction by high CXCL8 (formerly known as interleukin-8) chemokine production directly or indirectly via interleukin-17 production. AGEP may provide a useful model for characterising T cells with this particular function leading to a neutrophilic inflammation.

The main triggering drugs implicated in AGEP are antibiotics, mostly beta-lactams. Other medications, such as anti fungal drugs, non-steroid anti-inflammatory drugs, analgesics, anti-arrhythmic, anti-convulsant and antidepressant drugs are also reported to induce AGEP. Triggering agents may be administered orally or topically. A case of AGEP provoked by a patch test with acetaminophen has been described. Three cases of AGEP occurring 24 to 48 hours after a spider bite have been reported. AGEP is presently considered as an adverse drug reaction that can occur in any age group.

**Figure 2. AGEP eruption in skin: Photomicrograph of skin showing a dense neutrophilic infiltrate within the stratum corneum (H&E stain 400 X).**

Dapsone Hypersensitivity syndrome (DHS) is a well documented adverse drug eruption observed in patients of leprosy, with the reported incidence ranging from 1.3% to 3.6%. DHS typically presents with a triad of fever, erythema and inflammation of skin, and internal organ involvement especially of the lungs and liver. However, it is not associated with eruption of sub-corneal pustules, which is the hallmark of AGEP and its characteristic histopathology. DHS must be promptly identified, as untreated the disorder could be potentially fatal. In comparison, AGEP is a benign cutaneous adverse drug reaction, which resolves spontaneously on discontinuation of the offending drug with no significant systemic involvement.

We have not found any previous published reports of AGEP in patients with leprosy on treatment. This could be the first reported case of AGEP attributable to dapsone in a leprosy patient.
References