ACUTE GENERALIZED EXANTHEMATOUS PUSTULOSIS

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Summary

25 years old Filipino male patient referred from accident and emergency with generalized skin lesions of one week duration. The lesions started on the face and flexures then spread to become generalized. Patient gave a history of upper respiratory tract infection and he was on paracetamol tablet. Three days after starting paracetamol tablets the lesion appeared and fever peaked. Investigations were done and the diagnosis was acute generalized exanthematous pustulosis. The patient received systemic corticosteroids, systemic antihistamine and topical antibiotic for short course with satisfactory response. The Patient showed resolution of the condition and disappearance of the lesions on the second week with post inflammatory hyperpigmentation. There was no recurrence of the disease during the following six weeks of follow up and his laboratory parameters were back to normal.

Introduction

Acute generalized exanthematous pustulosis (AGEP) is a rare disease that has been classified as pustular psoriasis Von Zumbusch type for years. In 1968 Baker and Ryan were the first to assume that AGEP represents its own entity[1]. Macmillan, in 1973, described a similar case, he called it drug induced generalized pustular rash[2]. Acute generalized exanthematous pustulosis (AGEP) is an uncommon, acute, febrile eruption characterized by numerous nonfollicular pinhead sterile pustules on an erythematous background, mainly beginning in the skinfolds and/or on the face, associated with peripheral blood leukocytosis with an elevated neutrophil count[3,4,5,6]. The onset of the disease is acute; resolution of pustules occurs spontaneously within fewer than 15 days [2]. Fever, elevated leukocyte counts and appearance of multiple pustules tend to be associated with an acute bacterial infection, but AGEP is not due to bacterial pathogens as the content of the pustules is sterile. In few cases the etiology of AGEP appears to be a viral infection (enterovirus or parvovirus B19) or reaction to mercury, but most cases of AGEP (90%) have been described in association with the intake of drugs[2,6]. The time mediating between the drug administration and the skin eruption is normally less than two days, and the lesions last from one to two weeks, followed by a superficial desquamation [5,7].

Case report

25 years old Filipino male patient referred from accident and emergency with generalized skin lesions of one week duration. The lesions started on the face and flexures then spread to become generalized. Patient gave history of upper respiratory tract infection and he was given paracetamol tablet for three days followed by the appearance of the lesion associated with fever. The patient had no past or family history of psoriasis. On examination patient was febrile, not pale. Vital signs were normal. Dermatologic examination showed generalized small non follicular pustular eruptions on erythematous base with crusted lesions on the trunk, upper and lower extremities and scalp. Purpuric lesions were also seen on the upper and lower extremities (Figs 1 a-f). The buccal mucosa showed single erosive lesion. Swab was taken for gram stain, culture and sensitivity. Blood test (complete blood count, erythrocyte sedimentation rate, liver and kidney function tests and serum Immunoglobulin level) were done. Skin Biopsy was taken as well. The Patient showed resolution of the condition and disappearance of the lesions on the second week with post inflammatory hyperpigmentation on the trunk and extremities (Figs 2 a-b) and normal skin on other sites (Figs 2 c-d)

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Figs. 1 (a-e) - Showing the distribution of lesions
Figs. 2 (a-d) 2 weeks after treatment showing postinflammatory hyperpigmentation on the trunk & extermities

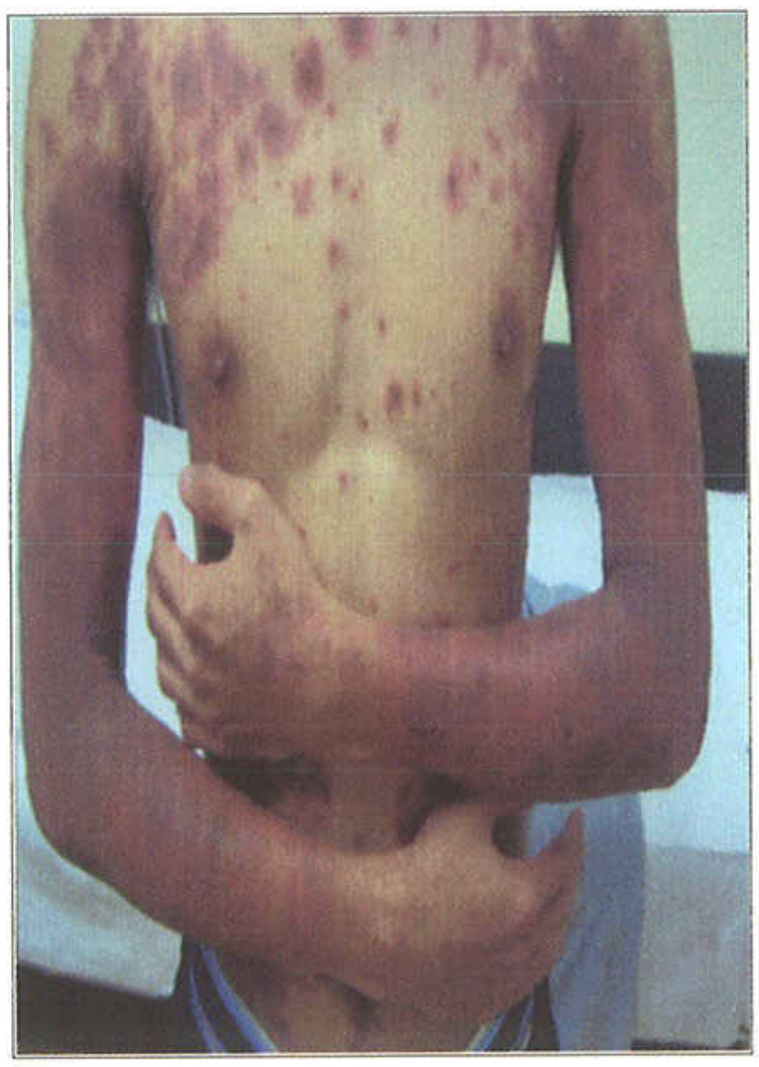

Fig. 1-a (before)

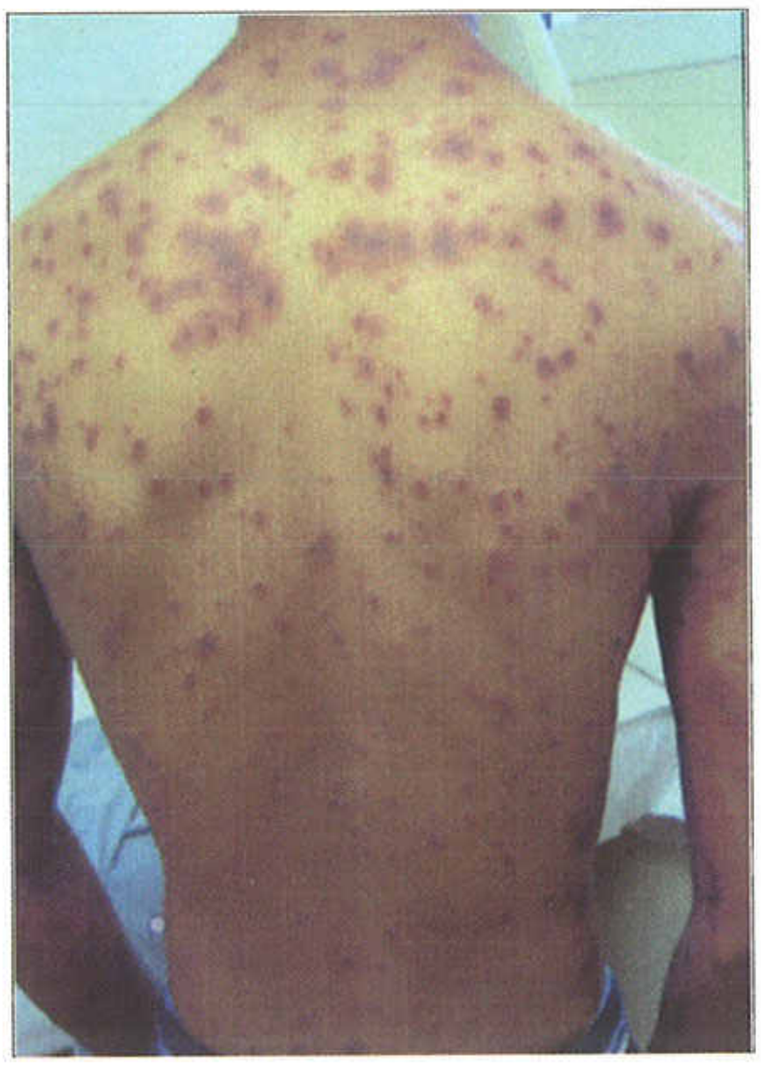

Fig. 1-b (before)

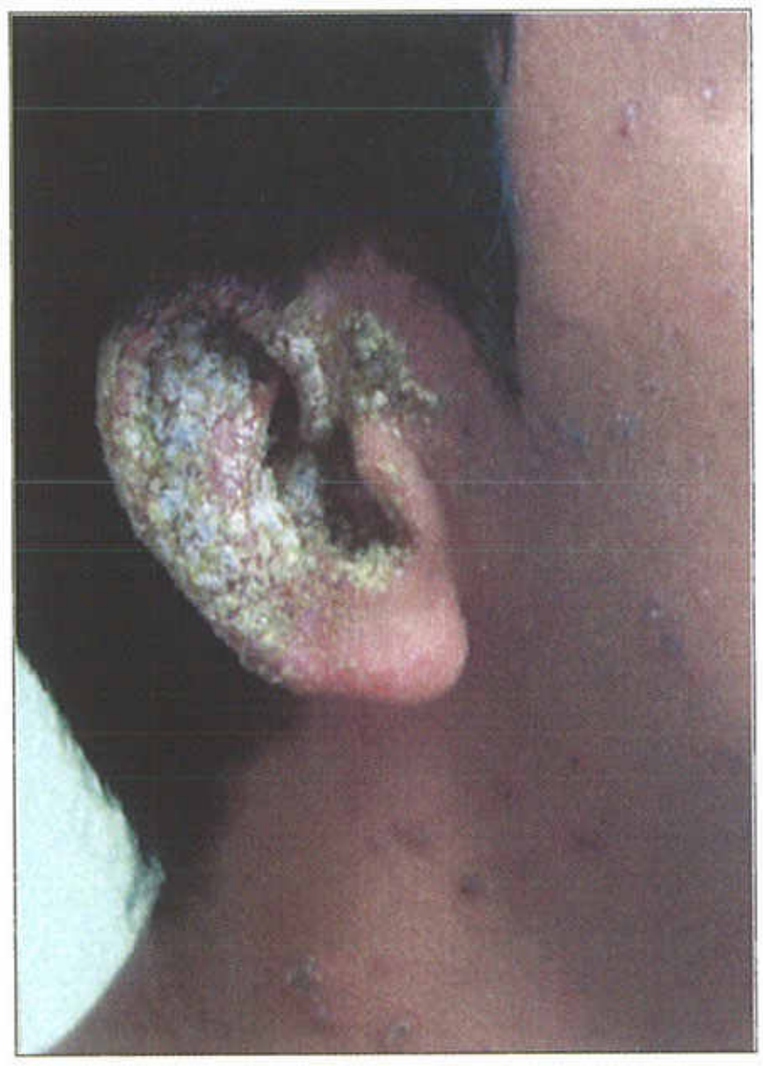

Fig. 1-c (before)

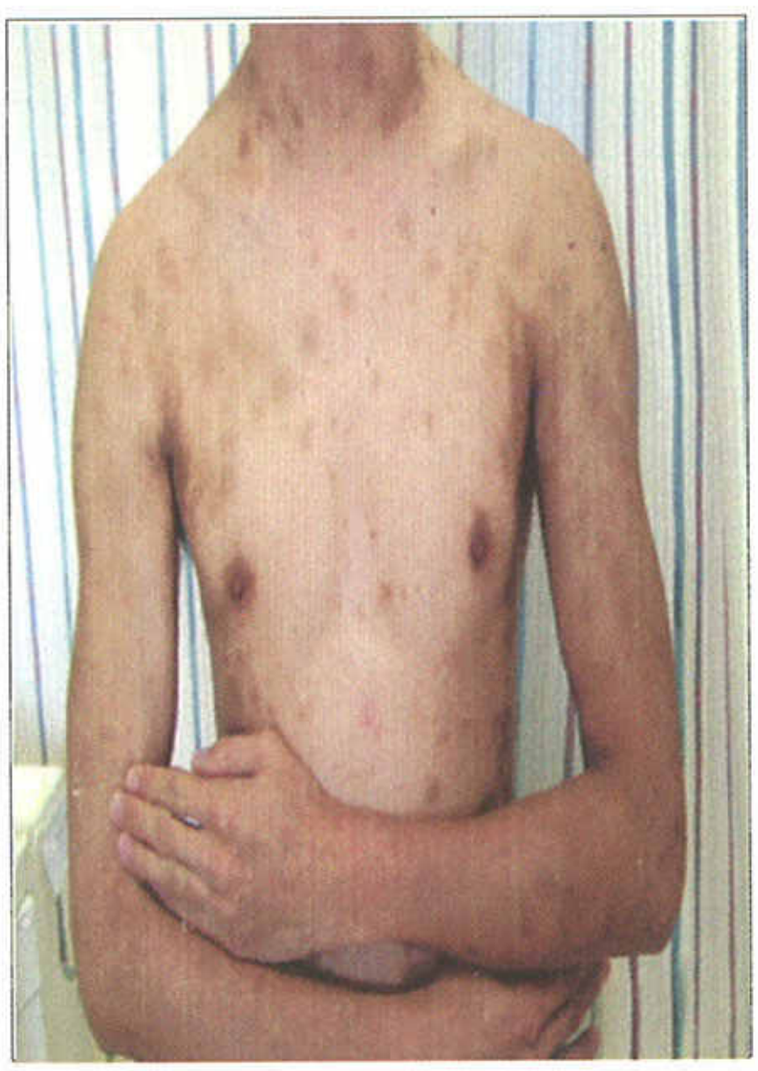

Fig. 1-b (after)

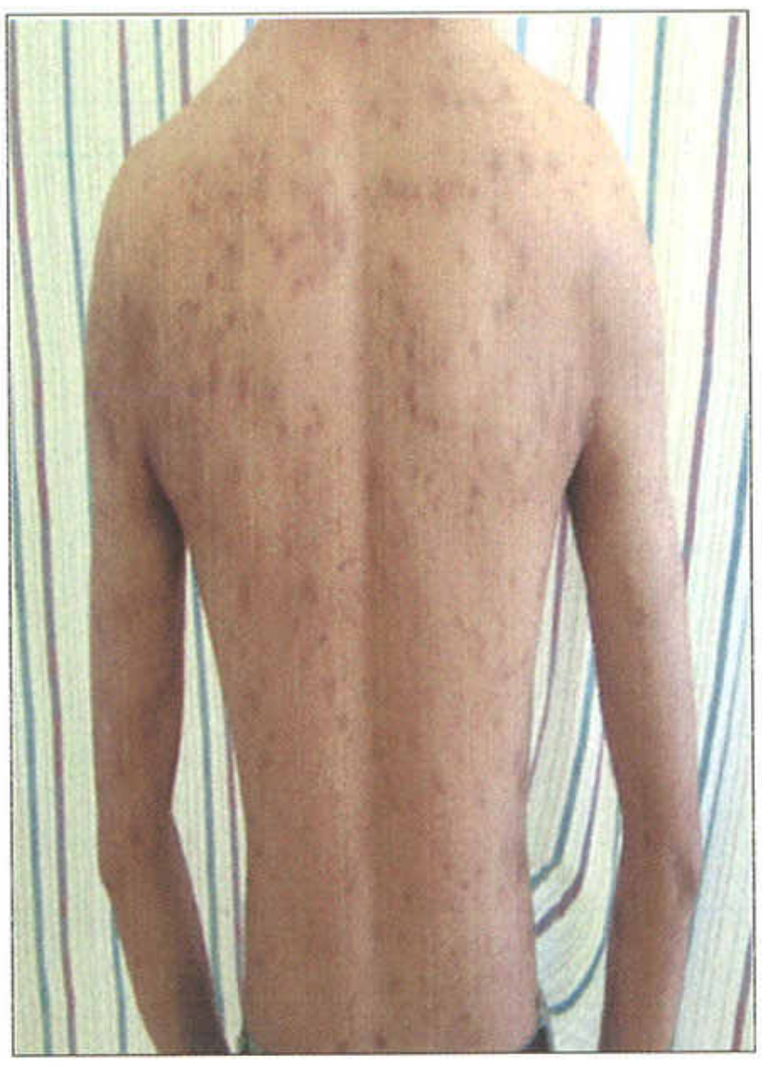

Fig. 2-b (after)

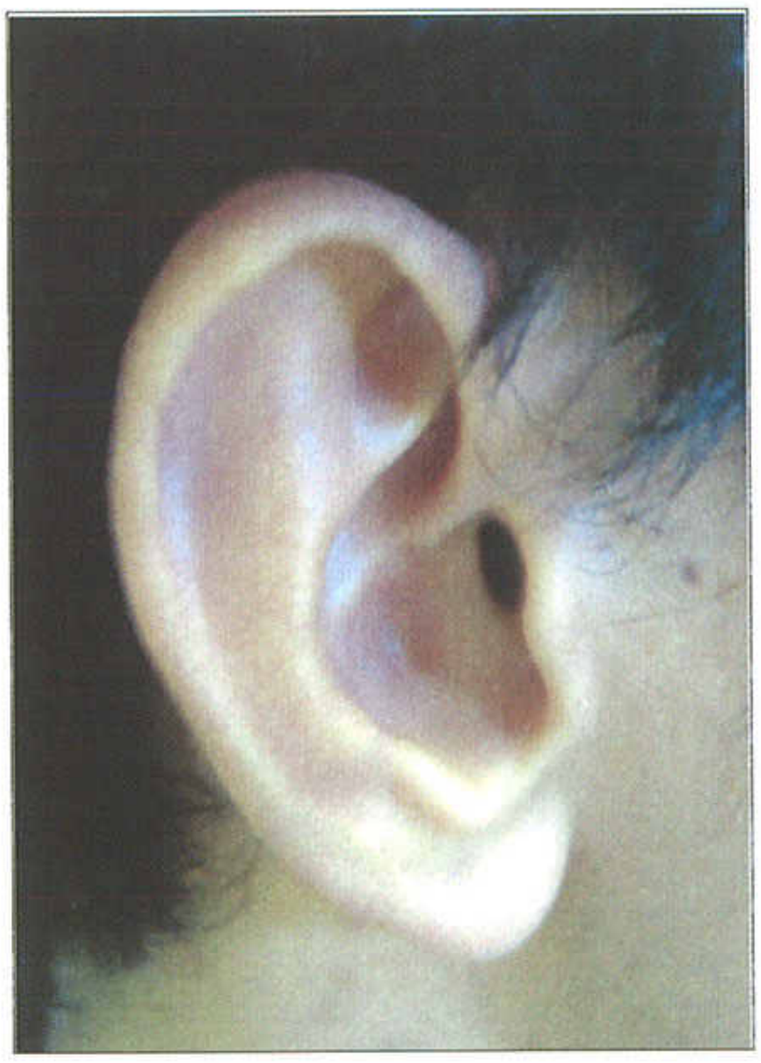

Fig. 2-c (after)

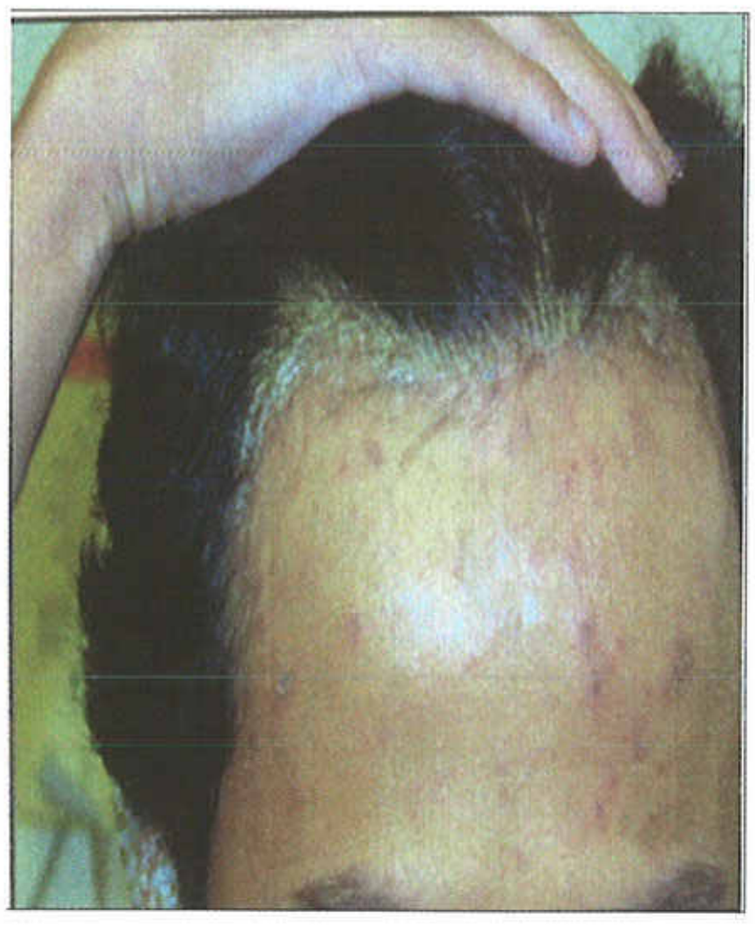

Fig. 2-d (before)

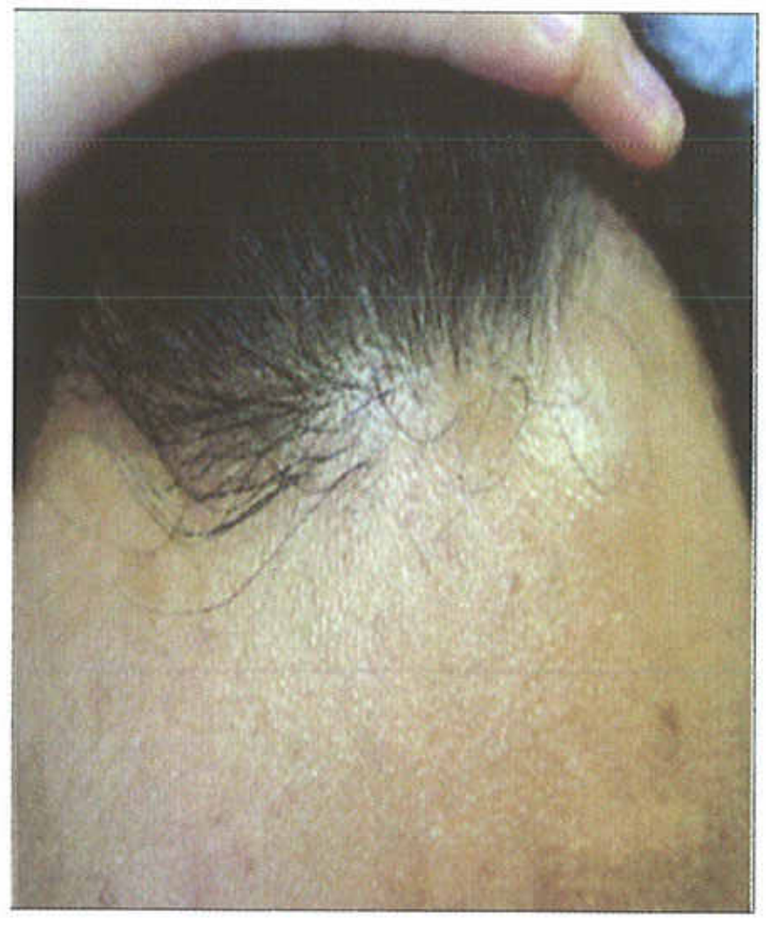

Fig. 2-d (after)

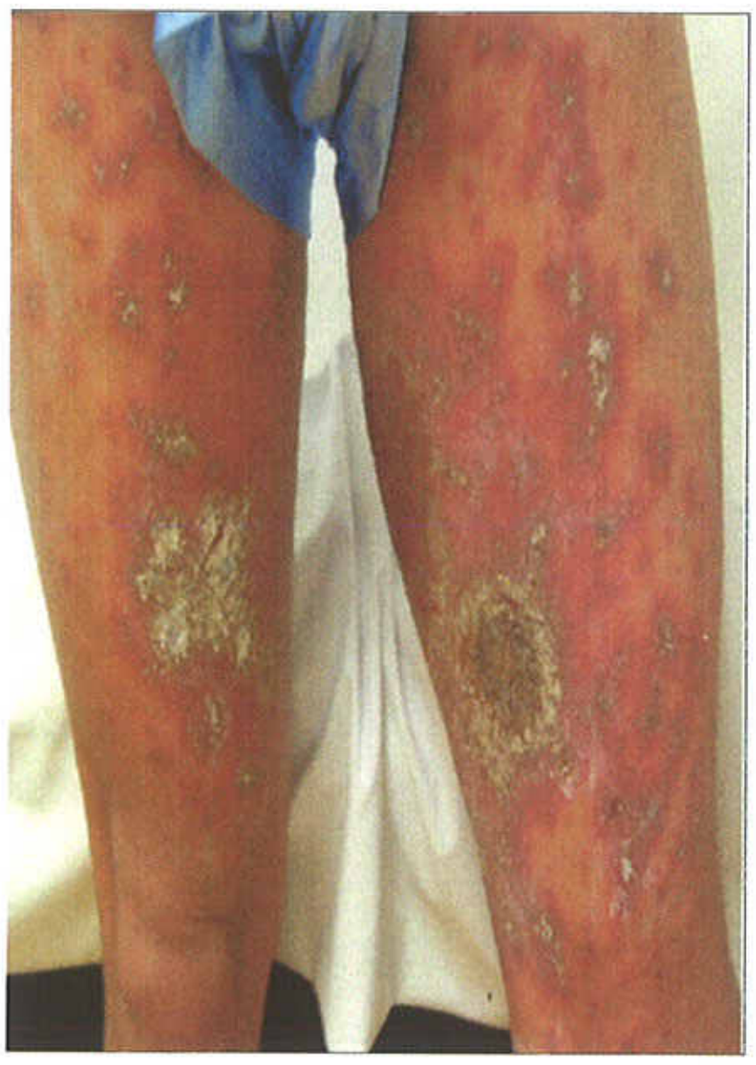

Fig. 1-e

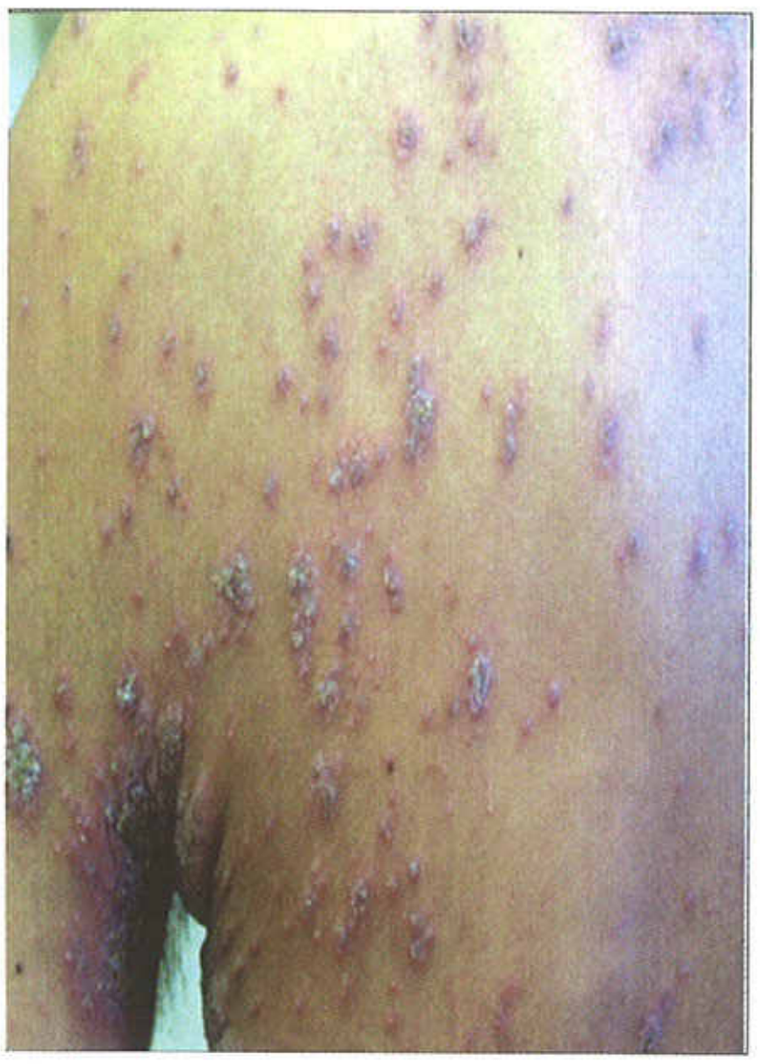

Fig. 1-f Showing close-up view of the lesions

Investigations

Complete blood count showed leuckocytosis with neutrophilia and eosinophilia and normal erythrocyte sedimentation rate. Blood chemistry showed a mild increase in aminotransferasis (GOT & SGPT) and normal kidney function. Gram stain showed gram positive cocci with scanty polymorphonuclear cells. Culture taken from several pustules was negative. Skin biopsy taken from a pustule on the left flank and stained by H&E showed the presence of subcorneal spongiform pustules, perivascular inflammatory infiltrate of neutrophil and eosinophil with focal areas of leukocytoclastic vasculits. (Figs 3 a-c)

Discussion

Diagnosis of drug-induced cutaneous eruption demands circumstantial evidence and the exclusion of other diagnostic possibilities. Although there are clinical and histological similarities between AGEP and generalized pustular psoriasis. AGEP is defined by rapid onset following the introduction of the drug and marked predominance of antibiotics as triggering agents (90% of the cases) [3]. Clinically, it is characterized by polymorphism of eruption, single episode, quick course of action, absence of arthritis and frequent administration of drugs [7,9]. However, in pustular psoriasis, the eruption is mono-

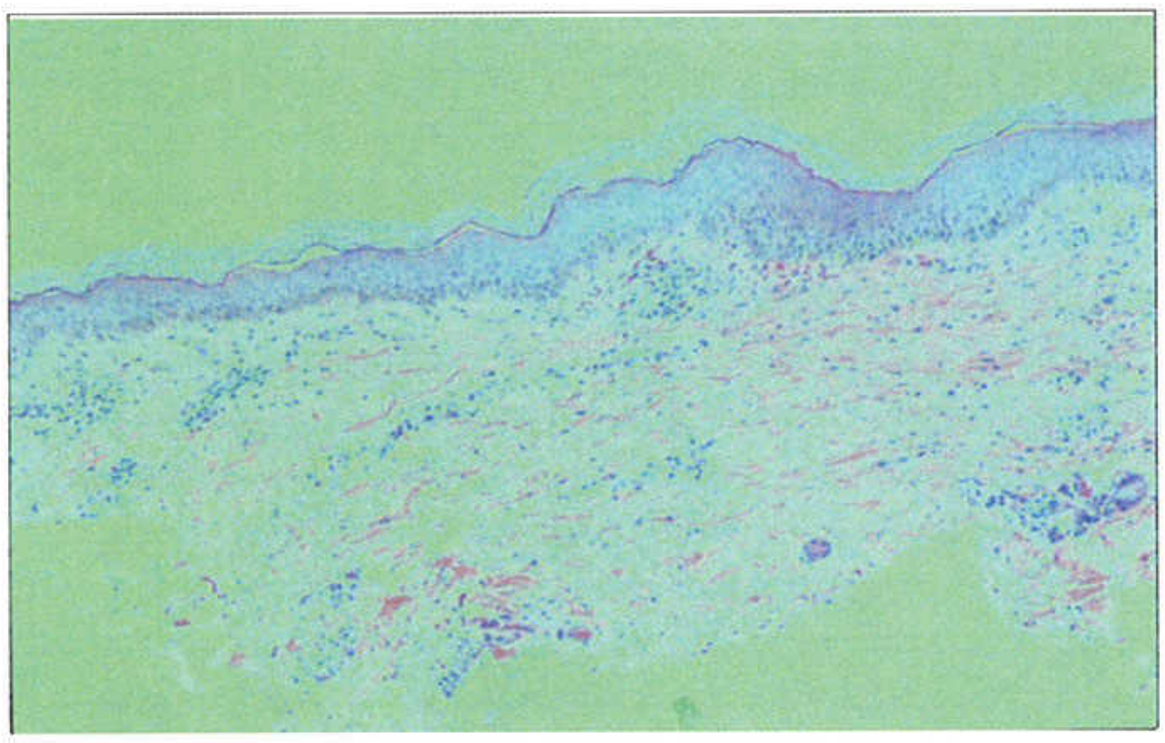

Fig. 3-a Low power stained by H&E (x10)

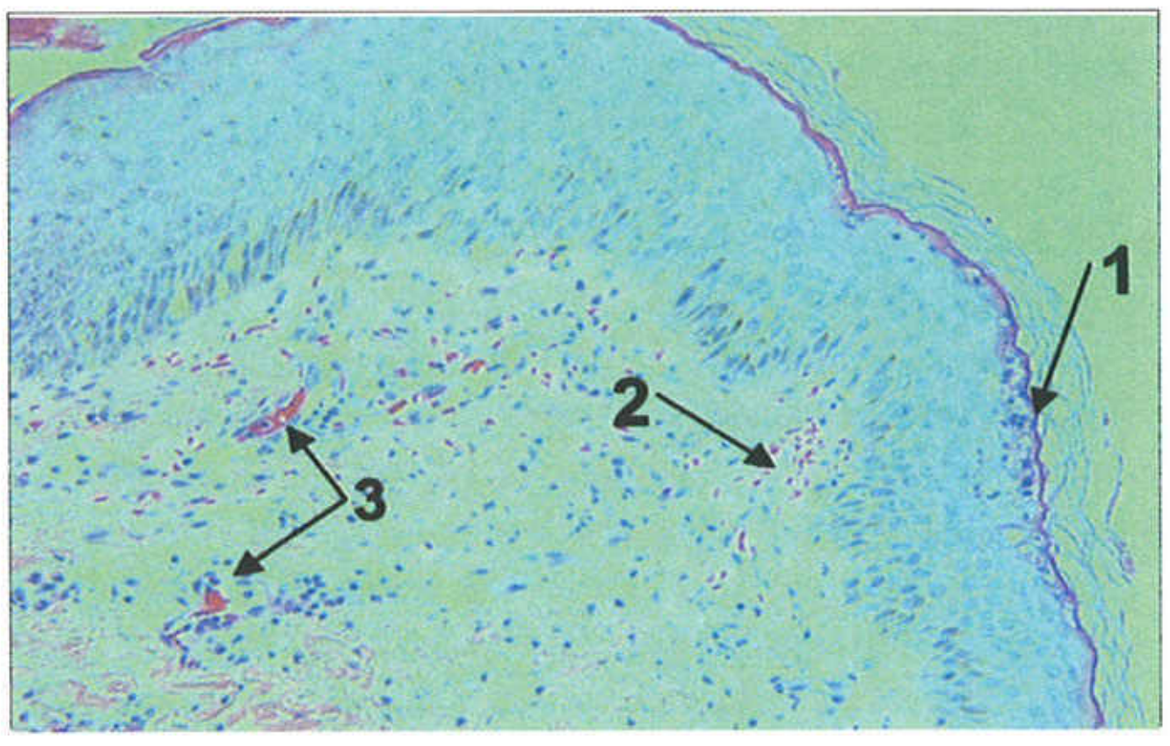

Fig. 3-b showing:
1. Subcorneal spongiform pustule.
2. Extravasated RBCs
3. Elemennt of leukoclastic vasculitis (x20)

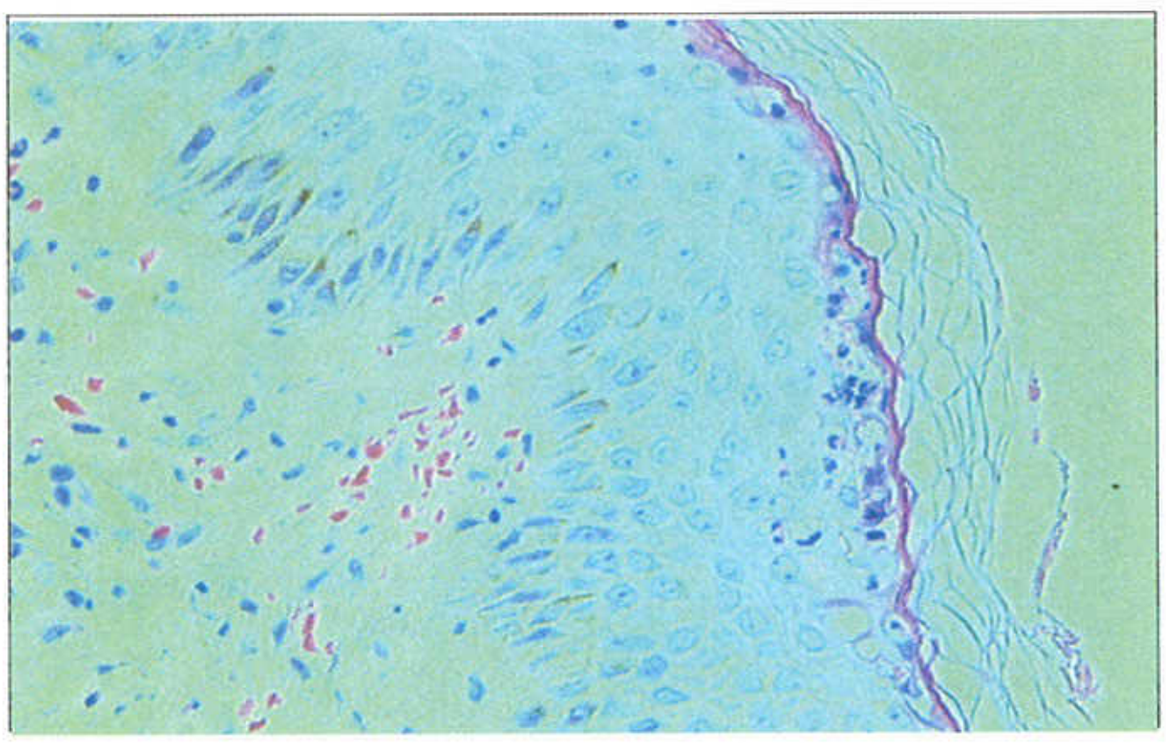

Fig. 3-c Close-up view of subcorneal spongiform pustule (x40)

morphic, last longer and recurs. Arthritis is associated in 32% of the cases, and drugs are rarely implicated in the etiology. The involution of the condition is slower, taken between 10 and 14 days (Table I) [3]. The etiopathogenesis is still obscure. In some studies, serum conversions for enterovirus and hepatitis B and Epstein Barr virus were observed [3,8]. Pharmaceutical drugs are the origin of 90% of the cases, among which the most important are antibiotics, especially beta-lactam and macrolides. Cases due to antibiotic use usually occur within a short span of time - less than 24 hours - after the administration of the medication. Other prescription drugs may take an average of 18 days to bring the patient to the clinical picture described [3]. The etiopathogenesis may be explained by the occasional existence of leukocytoclastic vasculitis, which evokes an Arthus-like hypersensitivity mechanism [10]. This could account for the surrounding immune complexes introduced by the infection or drug. Clinically, lesions begin on the face and, within a few hours, they spread to the trunk and limbs, or begin to arise in intertriginous areas [4]. After that there is annular desquamation for a few days, possibly accompanied by polymorphic lesions, especially purpuric lesions on the legs and feet. The mucous membranes are affected in 25% of the cases [8,9,11,12]. The clinical presentation in our patient started with erythematous lesions on the face and flexures then spread to become generalized, similar to what has been described in the literature [1,2]. the pustules spread over 72-hour period of time. In addition to fever there was single erosive lesion on the buccal mucosa thus coinciding with the description of AGEP [3,4]. There was regression of the condition after discontinuation of medication and initiation of corticosteroid treatment. Nevertheless, there was no a clinical recurrence of the eruption during 6 weeks of follow up. There were also concomitant normal laboratory parameters. Hypersensitivity reactions to paracetamol are rare. In laboratory tests leukocytosis, neutrophilia and eosinophilia may be observed. Hypocalcemia may also be found, mainly in the cases accompanied by hypoalbuminemia. Transitory renal failure may occur[2,3]. In some cases there is a momentary increase in aminotransferasis. The cultures of pustule are negative[3,12]. in our patient, leukocytosis with neutrophilia, eosinophilia and sterile culture of pustules were observed. The histopathological changes presented in this case were compatible with the diagnosis of AGEP. These changes included the presence of spongy pustules and necrosis of keratinocytes, eosinophil-rich intraepidermal pustules, perivascular infiltrate with eosinophils and leukocytoclastic vasculitis with fibrinoid deposit. Histologically, the differential diagnosis from pustular psoriasis is made by the presence in the latter of hyperplasia of the epidermis and papilloacanthosis[3,7]. The clinical presentation, the histological characteristics, the chronological relation with administration of paracetamol and, above all, the quick resolution of the condition following the interruption of medication, all these met the criteria for diagnosis of AGEP in our patient[1,4].

TABLE 1 COMPARISON OF CLINICAL, LABORATORY AND HISTOPATHOLOGY ASPECTS OF AGEP AND PUSTULAR PSORIASIS.

Characteristics	Acute Generalized Exanthematous Pustulosis	Generalized Pustular Psoriasis
Age	Adults	Adults
Cause	Drugs; viral infection	Respiratory tract infection
Clinical Characteristics	Numerous confluent Generalized, diffuse On erythematous skin	Confluent pustules On erythematous Skin
Fever	High	Prolonged
Leukocytosis	Yes	Yes
Course	Self-limited	Recurrent
Histology	Spongy, subcorneal Pustules, leukocytoclastic Vasculitis, eosinophils	Spongy, subcorneal Pustules, psoriasiform acanthosis

AGEP = Acute Generalized Exanthematous Pustulosis; GP = Generalized Pustular Psoriasis

Conclusion

We reported a rare case of acute generalized exanthematous pustulosis following the administration of paracetamol with clinical and pathological findings matching with this specific entity. Fever, leukocytosis and the quick resolution of the condition following the interruption of medication, met the criteria for diagnosis of AGEP. We conclude that acute generalized exanthematous pustulosis is important as differential diagnosis of pustular eruptions.

References

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