Acute generalized exanthematous pustulosis with cytomegalovirus infection

Article *in* International Journal of Dermatology · November 1996

DOI: 10.1111/j.1365-4362.1996.tb00653.x · Source: PubMed

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congenita and hypotrichosis.[3,4] Feinstein et al.[3] reported that 5.4% of pachyonychia congenita were associated with SM and Cole[4] reported a case of SM associated with hypertrichosis. Our case was associated with congenital alopecia on the frontal scalp and it is not certain whether or not the congenital alopecia association with SM is coincidental.

The characteristic histopathologic findings of this disease are the presence of flattened sebaceous lobules within the cystic wall and acellular eosinophilic cuticles with a wavy configuration. Steatocystoma multiplex may arise in a sebaceous duct because the lining of the lumen is composed of an undulatory eosinophilic cuticle that is characteristic of the sebaceous duct.[5] Therefore, we think undulatory eosinophilic cuticles are important in diagnosing SM because we can differentiate other cysts by their origin such as a trichilemmal cyst (origin from the outer root sheath of follicle), epidermal cyst (origin from infundibulum), and vellus hair cyst (origin from infundibulo-isthmic junction or isthmus). In this case, the absence of the granular layer could rule out an epidermal cyst and vellus hair cyst.

CONCLUSIONS

Our case is unique in the following points: (1) multiple lesions of SM were only confined to the forehead and frontal scalp that are not common sites of this disease and (2) congenital alopecia on the frontal scalp is associated with this disease. We think our case was a distinct clinical variant of SM and we suggest that such a clinical variant of SM is sebocystomatosis.

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CAMEO

ACUTE GENERALIZED EXANTHEMATOUS PUSTULOSIS WITH CYTOMEGALOVIRUS INFECTION

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A 79-year-old woman had Alzheimer-type dementia, but no other noteworthy antecedents, and no history of drug intake. There was no personal or family history of psoriasis or other dermatoses. She was referred to the Dermatology Service because of a 2-day history with sudden appearance of a generalized skin eruption accompanied by a fever of 39°C and moderate pruritus. Examination revealed extensive, irregular, confluent erythematous macules, distributed mainly on the thorax, back, arms, and thighs, and smaller macules on the distal regions of the extremities. On these lesions were numerous whitish, nonfollicular pustules, 1 to 3 mm in diameter, that tended to coalesce, forming blisters in some areas (Fig. 1). The mucosa and the palmar and plantar areas were spared.

General physical examination revealed no findings of interest. There was no adenopathy or hepatosplenomegaly. Auscultation of the chest, chest roentgenogram, ophthalmoscopic examination, abdominal ultrasonography and electroencephalogram showed no pathologic changes. Computerized tomographic examination of the brain revealed generalized cortical-subcortical atrophy that was more intense in the right parietal region. The hemogram revealed microcytic anemia (hemoglobin 11g per dL) and leukocytosis (16,900 per mL) with neutrophilia (83%) and lymphopenia (6.8%). The erythrocyte sedimentation rate was raised (79/110 mm). Biochemical analyses of blood revealed slight increases in alka-

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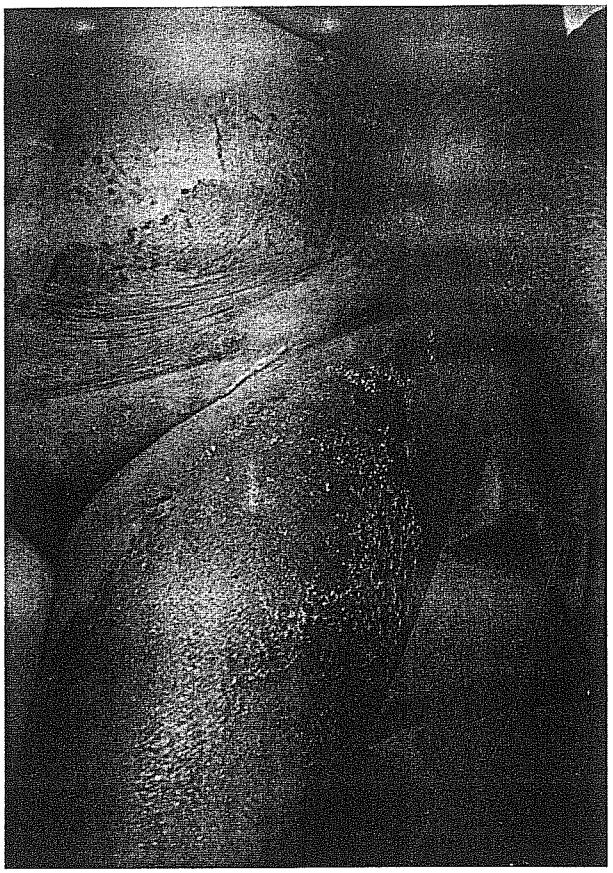

Figure 1. Small pustules on large erythematous macules and laminar desquamation on the abdomen, in a 79-year-old woman.

line phosphatase (362 IU per L, normal < 280 IU per L), gammaglutamyl transferase (48 IU per L, normal < 32 IU per L) and fibrinogen (558 mg per dL, normal < 400 mg per dL). Protein electrophoresis showed moderate hypergammaglobulinemia (22.6%, 1.53 g per dL, normal < 19.9%, 1.35 g per dL), without an increase in any single type of immunoglobulin. The T4/T8 lymphocyte ratio was 3.06. Serial blood bacterial cultures failed to grow pathogenic organisms. Specific cultures of material from the cutaneous pustules for bacteria and *Candida* sp. were negative.

Pathologic studies with hematoxylin-eosin staining in a sample of affected skin showed an epidermis of normal thickness with subcorneal pustules containing neutrophils, some of which were degenerated, and mild surrounding spongiosis (Fig. 2). The papillary dermis showed marked edema and vasodilatation with endothelial swelling, extravasation of erythrocytes, and perivascular and dermal accumulation of neutrophils and some eosinophils. Staining with periodic acid-Schiff and Gram stains revealed no microorganisms. Direct immunofluorescence failed to detect deposits of immunoglobulin or complement.

We investigated titers of antibodies against *Salmonella typhi, S. paratyphi A* and *B, Brucella, Treponema pallidum, Mycoplasma pneumoniae*, enterovirus, Epstein-Barr virus, varicella zoster, and hepatitis B. In all cases the results were negative or not significant; however, in two blood samples collected 15 days apart, studies with anti-CMV antibodies (ELISA, Behring Institute, Germany) revealed a positive result for IgM, seroconversion of IgG antibodies from 1/160 to 1/640, and the presence of low avidity IgG antibodies. Careful examination of a number of histologic sections failed to detect cytomegalic cells. They were stained with anti-CMV monoclonal antibody p65 (Gull, USA) and no cell was marked.

The clinical signs and symptoms cleared without treatment 7 days after hospital admission, leaving a generalized laminar desquamation that persisted for 4 days. The patient was discharged in good general health after 17 days in the hospital.

DISCUSSION

Acute generalized exanthematous pustulosis (AGEP) was defined by Beylot et al. in 1980,[1] and characterized in detail by Roujeau et al. in 1991.[2] This rare disease is manifested as an erythematous-pustulous eruption, an acute course, and occurring mainly in response to systemic medication. The most noteworthy clinical and pathologic features of AGEP are: 1) acute start after ingestion of the drug and rapid disappearance in < 15 days after medication is discontinued, without recurrence; 2) numerous sterile, nonfollicular pustules, < 5 mm in diameter, appearing on a background of a generalized erythema; 3) fever > 38°C; 4) neutrophilia of peripheral blood; 5) histologic finding of subcorneal pustules associated with one or more of the following: a) dermal edema and variable signs of vasculitis, b) eosinophils in the superficial dermis, and/or c) focal keratinocytic necrosis. Although AGEP is currently considered a type of toxic skin reaction, some cases have been attributed to viral infection.[2,3]

The clinical and pathologic findings in our patient are compatible with the generally accepted features of AGEP[2] and, together with the results of complementary studies, rule out other dermatoses that can occur with

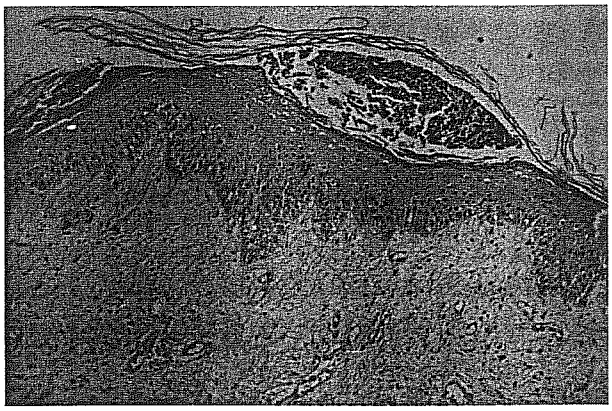

Figure 2. Histologic finding of subcorneal pustules with polymorphonuclear neutrophils, marked dermal edema, dilated capillaries, polymorphonuclear cell infiltrate and extravasation of erythrocytes. (hematoxylin and eosin, original magnification ×22)

erythema and pustules (e.g., pustulous psoriasis, subcorneal pustulous dermatosis, microbial pustulosis, pemphigus foliaceus, miliaria pustulosa, toxic epidermal necrolysis, and pustulous eruption of necrotizing vasculitis).

The condition is usually triggered by drug administration, particularly by beta lactam[1,4,5] and macrolide antibiotics,[1,2] and less frequently by other drugs.[2,4,6–14] It is thus considered a type of toxic dermatitis but an acute enterovirus infection has also been reported to cause AGEP.[2,3] The pathogenic mechanism of AGEP is currently unknown,[4] although type III[5] and delayed (type IV) hypersensitivity have been implicated.[15]

Cytomegalovirus is a DNA virus of the herpes virus family.[16] On occasions, CMV infection is accompanied by cutaneous manifestations such as infantile acropapulosis, perineal ulcerations,[17,18] hyperpigmented nodules or plaques, generalized maculo-papular and purpuric exanthema,[19] or vesiculo-ampullous lesions. Histologic studies sometimes reveal characteristic cytomegalic cells in the endothelium, with large intranuclear inclusions surrounded by a clear halo.[16,20]

Studies of serologic tests for viruses in our patient gave conclusive evidence of an acute infection by CMV, concomitant with the development of AGEP and no proof of direct CMV infection of the skin (similar to the exanthem of infectious mononucleosis). Previous studies make no mention of an association between AGEP and acute CMV infection. Although the possibility of casual association between CMV infection and AGEP exists, the clinical, pathologic, and laboratory findings were insufficient to rule out an etiologic relation between CMV infection and AGEP in our patient.

This report is a novel contribution to the list of agents that may trigger AGEP. We agree with Rouchouse et al.,[3] that AGEP should be considered before aggressive treatment is started in patients with generalized pustulosis and that virologic studies be done in patients with a clinical and histologic picture compatible with AGEP to confirm or reject the association with CMV.

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