Generalized Eruptive Histiocytosis in an Infant

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Sir,

Histiocytoses are a group of disorders involving the proliferation and accumulation of cells derived either from Langerhans' cells (LC) or from the macrophage system. They can be grouped into LC or non-LC histiocytoses (1, 2). Clinical and pathological evaluations are essential for differential diagnosis of these entities.

Generalized eruptive histiocytosis (GEH) is a rare variant of non-LC. GEH is seen mainly in adults, but a few cases have been documented in paediatric patients. The disease has a benign, self-healing clinical course with hyperpigmentation.

The pathogenesis of GEH is unknown; previous studies suggest that the proliferation of histiocytes is a physiologically appropriate response to viral infection. We report here the clinical course of a 5-month-old girl with generalized erythematous papules, which was diagnosed as GEH.

CASE REPORT

A 5-month-old girl was brought to our hospital with diffuse and generalized discrete erythematous to brownish papules that had developed abruptly within a week. She had been well until 2 months of age, when the parents noticed a similar skin eruption of papules over the trunk and extremities. According to the parents, the lesions regressed partially with residual scaling and pigmentation in one week.

Approximately one week before the current presentation, the patient had recurrent formation of erythematous papules, 2–5 mm in diameter, which appeared first on the trunk and then spread to the extremities and face (Fig. 1). Despite the clinical progression, the skin lesions did not seem to cause any discomfort.

The patient was born to a healthy Taiwanese mother after an uncomplicated pregnancy. No skin lesions were noted at birth; the patient's growth and development had been normal. The patient's vaccination history was up to date and the family history was unremarkable.

On examination, the patient was active and well nourished. Multiple disseminated erythematous papules in crops were noted over the whole body with sparing of the mucous membranes. There was no palpable lymphadenopathy or hepatosplenomegaly. Laboratory tests were slightly abnormal, with mild leukocytosis (13,500/μl, normal 5,300–12,000/μl), elevated neutrophil (39.2%, normal 9.4–30.4%) and decreased lymphocytic count (54.2%, normal 55.6–82.6%), along with increased atypical lymphocytes (1%). The viral serologies were positive for high titre IgG-viral capsid antigen (VCA) (> 1:320) and negative for Epstein-Barr virus (EBV) nuclear antigen (EBNA) antibodies (< 1:20).

A skin biopsy was performed and revealed nodular infiltration of histiocytes intermingled with a few lymphocytes and multinucleated giant cells in the dermis; there was no evidence of epidermotropism or atypia (Fig. 2 A). Immunohistochemical study revealed that the histiocytes expressed CD68 as a marker for macrophage, but were negative for S-100 and CD1a (Fig. 2 B). Electron microscopy revealed dense and regular round oval bodies within the histiocyte cytoplasm without characteristic Birbeck granules. These results are most consistent with cutaneous infiltration by non-LC; correlating clinical presentation with the histological findings, the diagnosis of GEH was established. Subsequent follow-up after 6 months without active treatment showed clinical remission of the skin eruption with post-inflammatory hyperpigmentation.

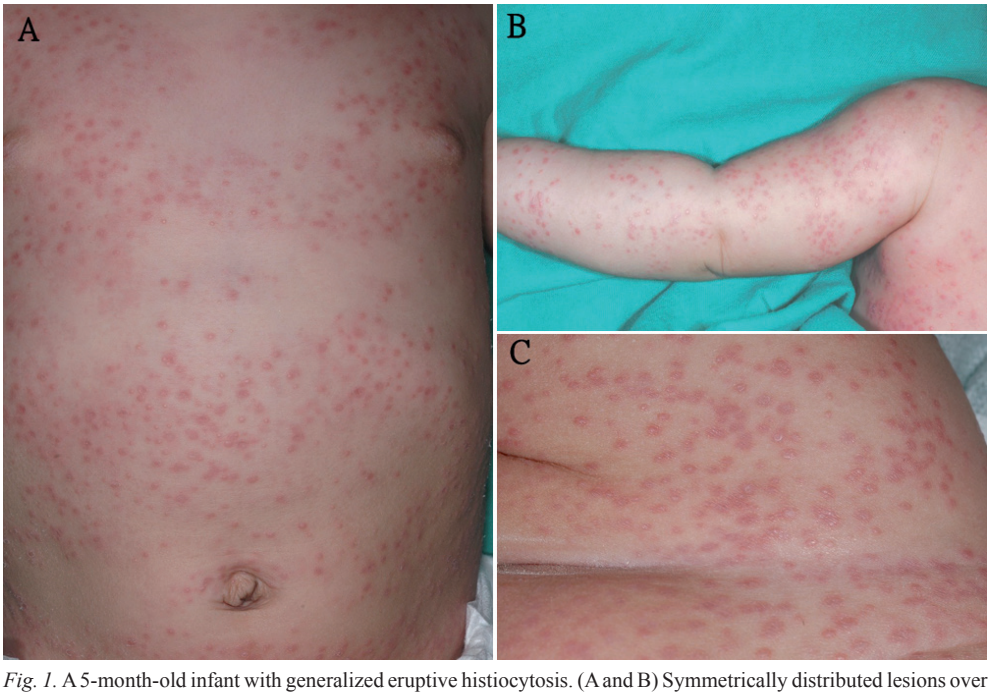

Fig. 1. A 5-month-old infant with generalized eruptive histiocytosis. (A and B) Symmetrically distributed lesions over the head, trunk and extremities. (C) Close-up of skin lesions showing erythematous papules and scales in crops.

DISCUSSION

Clinically, GEH has a polymorphous cutaneous eruption, varying from reddish papules to yellowish and brownish lesions in older lesions, distributed in discrete or cluster lesions over the whole body; the clinical course is usually benign and self-limited (3, 4). Benign cephalic histiocytosis is thought to be a localized

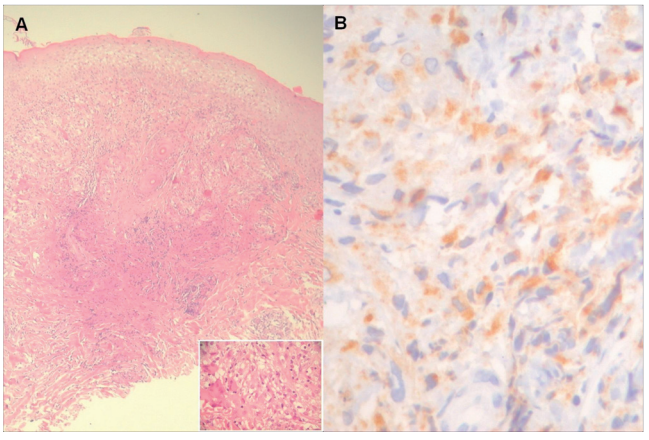

Fig. 2. (A) Skin biopsy showed nodular infiltration of inflammatory cell without epidermotropism: and (*inset*) dense histiocytic infiltration over the dermis with giant cells. (haematoxylin and eosin (H&E) ×200). (B) Immunohistochemical stain showing histiocytes positive for CD68 (×400).

variant of eruptive histiocytosis; however, clinical progression to GEH has been documented (5). The clinical progression for our patient is typical of GEH, with initial skin eruption over the trunk and extremities, and later progression to facial involvement.

Histological findings usually reveal benign features, with infiltration of histiocytes in the dermis, showing immunohistochemical markers for non-LC (CD68+, CD1a–, S100–). The presence of multinucleate giant cell is an unusual findings in GEH; however, its presence should not mitigate against the diagnosis. Recurrent cutaneous eruption is unusual for GEH. According to the parents, the skin lesions that appeared when the patient was 2 months old were the same as the lesions that occurred at 5 months of age.

Fewer than 50 cases of GEH have been reported in the literature and only nine paediatric cases have been reported (2, 6–10). There was an equal incidence for male and female, with age of onset ranging from 3 months to 5 years.

The developmental pathway of histiocytes is regulated by immunological mechanisms through different cytokines (11); histiocytes in GEH may represent the most immature end of the developmental pathway.

The aetiology of GEH in paediatrics is still unclear; however, isolated case reports postulated infections as a potential trigger for skin eruption. Matsushima et al. (6) described a paediatric case associated with rheumatic fever; Tamiya et al. (7) also reported a case of GEH following exanthema subitum. Virus-induced local immune alternation in the transformation of the non-LC histiocytosis has been postulated (12). EBV reactivation may occur due to immune suppression during pregnancy and is associated with a high maternal EBV viral capsid antigen IgG (VCAG) antibody in offspring. EBV may cross the placenta and cause foetal infection; however, serology is an indirect and non-specific measure of exposure to an infectious agent. Although there was no direct evidence of infection in our patient, we could not rule out an association of EBV infection with the development of GEH.

Non-LC histiocytosis includes a variety of conditions resulting from the neoplastic or reactive proliferation of mononuclear phagocytes/histiocytes. Pathogenesis of spontaneous regression remains unclear; Misery et al. (13) reported a case of infantile GEH with healing during summer, suggesting a possible role of ultraviolet exposure in the spontaneous regression. Tang et al. (14) took the concept forward by ultrastructural examination and noticed process of apoptotic degeneration in histiocytes, which may be responsible for its spontaneous regression.

Since GEH is self-limiting, no specific treatment is required; however, due to the rapidly progressive nature of cutaneous eruption in our patient, prompt confirmation of the diagnosis, along with in-depth counselling and reassurance was important in order to alleviate parents' anxiety. Complete systemic evaluation, including physical examination, whole-body radiographic skeletal survey, and abdominal ultrasound is also vital to prevent the need for further aggressive treatment.

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