Generalized Eruptive Histiocytoma

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We report a case of generalized eruptive histiocytoma in a 30-year-old female who presented with widespread flesh colored papules in a symmetrical fashion on the trunks and arms. The lesions were characterized by histologically dermal proliferation of benign histiocytes which were immunohistochemically lysozyme positive, and electron microscopically, the cells had lysosomes in their cytoplasm. Individual lesions had spontaneously resolved over a period of six to eight months. (Ann Dermatol 2:(2) 113-116 1990)

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In 1963 Winkelmann and Muller" proposed "generalized eruptive histiocytoma" as a distinct clinical entity; an unclassified form of benign histiocytosis of the skin without systemic involvement occurring in healthy adults.

The major features are as follows: (1) multiple widespread, essentially symmetric lesions particularly involving the trunk and proximal portion of the extremities and rarely the mucous membranes; (2) distinct flesh-colored to bluish-red papular lesions without a tendency to group; (3) progressive development of new lesions without an antecedent history of trauma; (4) spontaneous resolution of lesions healing completely or with brown macules; (5) a benign histologic picture of mononuclear histiocytic cells.

The initial cases were reported only in adults, but later cases were reported in children. Special microscopic studies have demonstrated that this syndrome is a non-X and non-lipid histiocytosis.2,3,5

We herein present, a case of generalized eruptive histiocytoma in a 30-year-old female that met all of the above mentioned criteria.

REPORT OF A CASE

A female, aged 30 years, was presented with a cutaneous eruption of 2 months' duration. She first noticed a few flesh-colored, raised, non-itchy lesions on her chest and the flexor aspects of both arms. She is a housewife with no past history of any trauma, or infective or iatrogenic insults to the skin. She had no constitutional symptoms.

Examination of the skin revealed the presence of numerous, flesh-colored, discrete papules on her chest and arms. The scalp, hands, feet and external genitalia were completely spared as were the mucous membranes. The distribution was symmetrical. The lesions were 1 to 8 mm in size. When the involved skin was stretched, the papular masses were easily seen (Fig. 1, 2). There was no hepatosplenomegaly or lymphadenopathy. No other abnormality was detected on physical examination. Laboratory studies were essentially normal including urinalysis, serum lipid studies and routine hematologic studies.
**Generalized Eruptive Histiocytoma**

**Explanation of Figures**

**Fig. 1.** Discrete, flesh-colored papules on the chest

**Fig. 2.** Skin lesions on the flexor aspects of left arm

**Fig. 3.** Relatively well circumscribed proliferation of benign histiocytes in the reticular dermis (H & E stain, ×40).

**Fig. 4.** The principal cells of the infiltrate are histiocytes, with abundant, light, poorly limited cytoplasm (H & E stain, ×250).

**Fig. 5.** The infiltrating cells show diffuse light to brown staining in the cytoplasm (lysozyme stain, ×250).

**Fig. 6.** Electron micrograph of the dermal histiocytes showing a few lysosomes (arrowheads), microvesicles and mitochondria (×8,200).

A skin biopsy from nodules revealed a relatively well circumscribed proliferation of benign histiocytes in the reticular dermis without epidermal hyperplasia (Fig. 3). Touton giant cells were not noted. The individual cells were histiocytic in nature showing round to ovoid or bean-shaped vesicular nuclei and pale abundant cytoplasm with ill-defined cytoplasmic borders (Fig. 4). The mucopolysaccharides and lipid were not observed in the cells by special stains. Histochemical stains for lysozyme (muramidase, Dako 1:300, polyclonal) from paraffin section by immunoperoxidase method showed diffuse light to brown staining in the cytoplasm of the infiltrating cells (Fig. 5); however, S-100 protein stain (Dako 1:300, polyclonal) revealed only a few scattered weakly positive cells. Electron microscopic sections from paraffin embedded tissue revealed an irregular nuclear shape with a few lysosomes, microvesicles and microorganelles (Fig. 6). Neither Langerhans granules nor fat globules were noted in the proliferative cells. Myelin figures in vesicles were noted but active phagocytosis was not observed. All these findings suggested that those infiltrating cells were neither lipid-containing histiocytes nor Langerhans cells.

Six months after the onset of the eruption, each lesion began to regress spontaneously, and then, over the next few months, they completely disappeared without sequelae.

**DISCUSSION**

The main discussion points on this disease will be focused on its histogenesis, differential diagnosis, and the process of the dermal nodular infiltration and later spontaneous involution.

The histiocytic nature of generalized eruptive histiocytoma (GEH) in its histogenesis is quite believable by its immunohistochemical and electron microscopic findings: the presence of large numbers of lysosomes, no Langerhans granules, no microfilaments and positive for lysosomal enzymes, although phagocytic activity is not definite and active which is the most characteristic feature of histiocytes. Our case also revealed quite a few primary lysosomes in the proliferated cells with positivity for lysosomal enzymes although phagocytosis was not definite. Also, Birbeck granules were absent in main proliferating cells. These features suggested that its histogenesis is histiocytic in origin in its intermediate stage.

According to Muller et al., the enzyme pattern in GEH appears to be characteristic of all benign proliferative histiocytic diseases and the presence of hydrolytic enzymes in GEH cells indicates that might have phagocytic function. Caputo et al. reported, in their ultrastructural study, that the most typical cytoplasmic organelles in tumor cells in GEH were dense bodies and laminated-body structures, generally associated with lysosomal activity.

Differential diagnoses included juvenile xanthogranuloma, papular xanthoma, benign cephalic histiocytosis, multicentric reticuloendothelial xanthoma and granuloma annulare. Juvenile xanthogranuloma and papular xanthoma may be excluded in view of the color of the lesions and absence of both foamy lipid containing histiocytes and Touton giant cells. Benign cephalic histiocytosis may represent a problem in differential diagnosis because of its similar features of benign cephalic histiocytosis. Multicentric reticuloendothelial xanthoma was excluded from our consideration because of the type and distribution of lesions, the absence of arthritis and the lack of multinucleat-
ed giant cells.\textsuperscript{6} Granuloma annulare was excluded in view of the clinical appearance of the lesions and the lack of collagen changes with palisading histiocytes.

GEH is a distinctive clinical entity because of its clinical manifestation as a papular or nodular eruption at nearly the same time and stage which is followed by spontaneous resolution without any sequelae, although it may recur sometime later. These clinical courses suggested that GEH is reactive rather than in combination with hyperlipoproteinemia. But the primary initiating causes of proliferation in multiple foci and spontaneous regression are still not fully understood.

Whether the dermal histiocytes are infiltrated from blood origin or in situ proliferation of histiocytes in multiple foci is unknown. Although blood cells of histio-or monocytic lines are not increased in blood cell counts, local proliferation of histiocytes and epithelioid cells could be quite possible. This is suggested in various infections where initial infiltration of histio-or monocytic cell lines is followed by localized proliferation of histiocytic cells until causative factors are present, then there is spontaneous involution.

From a view of the literature,\textsuperscript{11} we think that a comprehensive study by immunohistochemistry and electron microscopy of all cases of histiocytic proliferation in the skin would be of great importance in extending our nosologic understanding of the complex problem of histiocytic proliferative disease and its differential diagnosis.

\textbf{REFERENCES}