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Factor XIIIa Expression in Juvenile Xanthogranuloma

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Dermal dendrocytes constitute the largest population among cells of dermatofibromas. In other histiocytic tumours, the exact nature of histiocytic cells is not known. We have searched for the presence of dermal dendrocytes in juvenile xanthogranulomas. The immunohistochemical study was performed on 9 juvenile xanthogranulomas. We used monoclonal or polyclonal antibodies: anti-XIIIa, HAM56, anti-S100, anti-NSE, anti-HLA-DR, anti-CD68 and anti-lysozyme. Phagocytic mononuclear cells (histiocytes, giant cells, Touton cells) did not express Langerhans' cell markers (S100, NSE ou HLA-DR). They weakly expressed markers of macrophages (CD68, lysozyme). There was a very strong binding by HAM56 and anti-XIIIa. This expression was more evident on xanthomatous and newly appeared tumours than on fibrous tumours. The largest population of juvenile xanthogranuloma cells appeared to be constituted by dermal dendrocytes. These cells are perhaps the key-cells of a continuum of benign tumours, from juvenile xanthogranuloma to dermatofibroma, with different stages corresponding to different proportions of dendrocytes, lymphocytes and fibroblasts. ***Key words: Dendrocyte; Histiocyte; Histiocytic tumour.***

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Juvenile xanthogranulomas (JXG) are histiocytic tumours of the skin. It is generally agreed (1, 2) that histiocytic tumours can be divided into two categories: Langerhans' cell histiocytosis (LCH) and histiocytoses related to other phagocytic mononuclear cell proliferations. In the first category, we usually find histiocytosis X and Hashimoto-Pritzker disease. In the second, there are various skin tumours, such as dermatofibromas, xanthoma disseminatum, multicentric reticulohistiocytosis, generalized eruptive histiocytoma, benign cephalic histiocytosis, papular xanthomas, JXG and fibroxanthoma.

We analyzed 9 non-X benign histiocytic tumours in order to better understand the origin of the proliferating cells.

MATERIAL AND METHODS

Patients included in our study were children or teenagers or young adults. They had been seen during the years 1988 to 1992. Our study included a total of 9 cases of JXG. The age of the lesions was from 3 weeks to 1 year. Hematoxylin and eosin-stained sections were observed histologically, and clinical data were obtained on all patients.

Paraffin blocks were cut at 5 mm and mounted on glass slides coated with an adhesive mixture. They were then deparaffinized in xylene and absolute ethyl alcohol, and endogenous peroxidase activity was quenched by immersion for 30 min in methyl alcohol containing 0.6% hydrogen peroxide. Following rehydration in graded ethyl alcohol solutions, distilled water, and phosphate-buffered saline (pH 7.4), the sections were incubated for 18 h at 4°C in moisture chambers, after application of primary antibodies. The latter, which are listed in Table I, included anti-XIIIa, anti-S100 protein, anti-NSE, anti-HLA-DR, anti-lysozyme, anti-CD68 and HAM56.

Detection of antibody binding was accomplished by subsequent incubation with biotinylated secondary antibodies and avidin-biotin-peroxidase complex (ABC) (3). Chromogenic development was obtained by immersion of all sections in 3,3-diaminobenzidine solution (0.25 mg/ml) with 0.003% hydrogen peroxide, for a maximum of 10 min. After counterstaining with Harris hematoxylin, slides were coverslipped with a synthetic mounting medium and examined by all authors independently.

Positive controls were represented by stock tissues known to contain the determinants of interest. Sections of all study cases were also incubated with irrelevant anti-keratin antibodies (polyclonal antibovine muzzle keratin, Dako; CAM 5.2 monoclonal antikeratins, Becton Dickinson) as negative controls. Sections were defined as immunohistochemically "positive" if distinct, crisp labelling was seen in at least 10% of lesional cells by all observers.

RESULTS

All the tumours included in this study were histologically typical and composed of polygonal cells, with or without spindle cells. These cells were arranged in a nodular fashion with thin septa of collagen between the cellular aggregates. Nuclei were vesicular with inconspicuous nucleoli; the cytoplasm was moderately abundant and variably eosinophilic, amphophilic or vacuolated. Most JXG contained Touton cells and giant cells. Other cells were lymphocytes and fibroblasts.

Most of the histiocytes were positively stained by HAM56 (Fig. 1), KP1 and anti-lysozyme antibodies. HLA-DR was only stained on lymphocytes and Langerhans' cells. CD1a, S100 protein and NSE were only expressed on Langerhans' cells.

Factor XIIIa was expressed in cytoplasm of giant cells, Touton cells and dendritic cells in the dermis (Fig. 2). This expression was negative on Langerhans' cells, lymphocytes, keratinocytes, Merkel cells, melanocytes and endothelial cells. The labelling was stronger on newly appeared and xanthomatous tumours than on fibrous tumours.

Table I. *Immunohistochemical reagents used in this study*

Reagent	Antibody type	Source	Dilution
Anti-S100 protein	Polyclonal	Dako	1:100
Anti-NSE	Polyclonal	Dako	1:50
Anti-HLA-DR	Monoclonal	Dako	1:20
Anti-CD68 (KP1)	Monoclonal	Dako	1:800
Anti-XIIIa	Polyclonal	Behring	1:200
HAM56	Monoclonal	Enzo	1:100
Anti-lysozyme	Polyclonal	Dako	1:100

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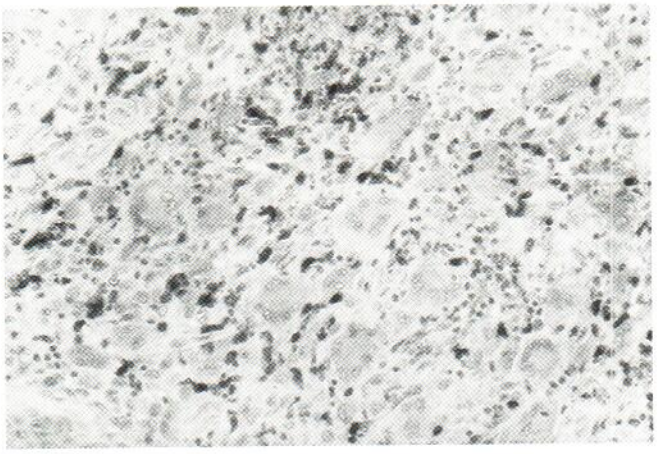

Fig. 1. HAM56 staining in JXG.

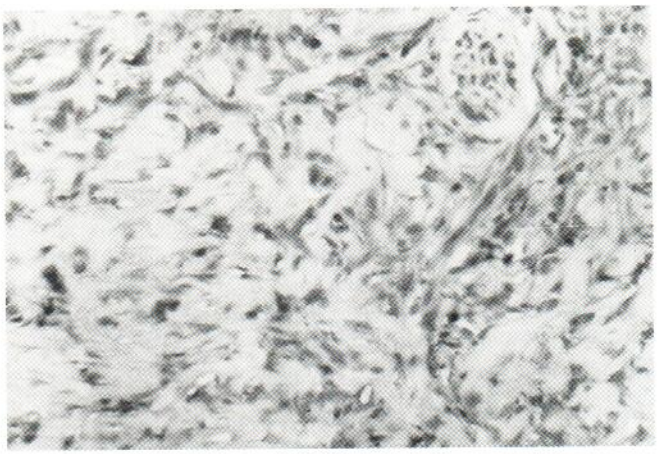

Fig. 2. Expression of factor XIIIa in JXG.

DISCUSSION

This study showed that the dermal infiltrate of JXG is mainly composed of factor XIIIa+ cells, suggesting that these cells may be derived from dermal dendrocytes. The expression of factor XIIIa has previously been reported but only in one case (4). Stainings by HAM56 are usual on these tumours (5). But expression of lysozyme or CD68, which are markers of macrophages, is inconstant (6). CD1a, S100 protein and NSE, markers of Langerhans' cells, like HLA-DR are not expressed on JXG Touton cells, giant cells, foam cells or dendritic cells in the dermis (7).

Dermatofibromas seem to be a proliferation of dermal dendrocytes (8). The contention that diverse benign histiocytic tumours of the skin represent varying stages of the same evolutionary process is not new. In a review of xanthogranulomatous proliferations involving several organs, Cozzutto and Carbone (9) observed several histologic phases, which included all stages from early JXG to very fibrous tumours. The authors suggest that, although the tumours of this group are conceptualized as unrelated by some observers, they may represent different stages of one unifying process. More recently, Tahan et al. (10) reviewed 34 cases of JXG and expanded the definition of this entity to include xanthomatous, fibrohistiocytic and transitional variants in addition to classical forms. Marrogi et al. (11), in a survey of 60 benign histiocytic tumours of five categories (xanthomatous JXG, classic JXG, transitional JXG, histiocytoma and dermatofibroma), showed that the histological appearance was related to the duration of clinical lesions. Their findings further support the notion that there is a continuum with xanthomatous JXG at one end and dermatofibroma at the other. Similar opinions have been expressed by Helwig (12), and our study seems to confirm this hypothesis.

Proliferations of dermal dendrocytes may represent a great spectrum of "histiocytic" tumours of the skin. Various histological appearances should be related to the duration.

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