Acral Persistent Papular Mucinosis (APPM) with Pruritus

A Case Report and Mast Cell Quantification

Sir,

Acral persistent papular mucinosis (APPM, French: mucinose papuleuse persistante acrale) was described as a new entity in the heterogeneous group of dermal mucinosis by Naeyaert & Kint in 1985 (1) and Rongioletti & Rebora in 1986 (2). Primary (metabolic) mucinosis is seen as diffuse forms in generalized or pretibial myxedema, lichen myxedematosus (papular mucinosis, scleromyxedema), reticular erythematous mucinosis, scleredema or storage diseases. Primary (metabolic) mucinosis as focal form is seen in follicular mucinosis, cutaneous mucinosis or in myxoid (synovial) cysts. Secondary (catabolic) mucinoses appear in connective tissue trauma, collagen-vascular diseases, in some cases with the L-tryptophan induced eosinophilia-myalgia syndrome, Degos' disease (papulosis atrophicans maligna) or in neoplasms (3,4). In 13 cases of APPM reported till today, flesh-colored or erythematous, mostly asymptomatic discrete papules occurred on the extremities. These lesions show slow progression up to 10 years in otherwise healthy persons without laboratory abnormalities (1, 2, 5–15, Table I). Mucinous deposits of mainly hyaluronic acid are found between collagen bundles particularly in the superficial, but also in the mid- and deep reticular dermis, accompanied by a slight increase of dermal fibroblasts (13). We report on the third symptomatic case with pruritus. We studied the possible association of APPM, mast cells and pruritus and present a mast cell quantification.

CASE REPORT

A 34-year-old woman in good health showed 5–10 red isolated partly excoriated papules of 2–4 mm in diameter, generally symmetric on the knees up to the extensor surface of the upper legs. After 2 years she was seen with about 50 papules spreading from the knees to the lower legs and the extensor surface of hands and arms with exaggerating pruritus (Fig. 1). There was no worsening after sun exposure.

Routine laboratory and studies for T3, T4, thyroid stimulating hormone and thyroid releasing hormone, serum protein electrophoreses and immunelectrophoreses, antithyroid antibodies and antinuclear antibodies, rheumatoid factor, HbsAg, TPHA and *Borrelia burgdorferi* IgG and IgM were normal. Ultrasound and scintigraphic examination of the thyroid gland showed struma diffusa I – II without hot or cold areas. No focal inflammation was found at a general check-up.

Results of histopathological examinations revealed no epidermal changes, only a slight lymphomonocytic infiltration around the superficial plexus with a discret edema of the stratum reticulare and papillare with mucinosis and proliferation of fibroblasts. Local antipruritics or corticosteroids, systemic antihistamines or hydroxyzine, UVA irradiation, intralesional triamcinolone injections or oral chloroquine administration were unsuccessful. PUVA therapy for 3 months decreased pruritus, but there was a slight progression.

A biopsy from a papule of the right upper leg of our patient was taken, and a biopsy of normal skin of another patient, of the same localization, was used as control. The specimens were fixed in 10% formalin, paraffin-embedded, processed in serial sections and stained with Giemsa. Connective tissue mast cells with the typical metachromatic granules were quantified per mm² of epidermis in a light microscopy (Orthoplan Leitz, 250x magnification).

In our patient with APPM an area of 76.4 mm² was counted and showed an average of 28.3 mast cells per mm². In the comparable specimen of the control only an average of 18.3 mast cells per mm² dermis was evaluated in an area of 33.9 mm².

DISCUSSION

Even if Naeyaert & Kint (1) and Rongioletti & Rebora (2) described APPM as a destinct new entity, Montgomery & Underwood (5) are credited with the first report, in 1953. They subsumed their case report under lichen myxedematosus as "Myxedema papulosum". With metachromatic staining they showed definite granules in a few cells, discussing whether these histiocytes should be classified as "true mast cells" or not (5, 16). Many mast cells were reported in punch biopsies from lesions by Aho; he did not, however, comment on pruritus (13). Rare mast cells in symptomatic papular eruptions were described by Crovato (12), while Montgomery et al. and Ravello et al. report on rare mast cells in asymptomatic APPM (5,7). In pretibial myxedema numerous mast cells are present and have therefore been suggested to be the source of the excess in hyaluronic acid (17). In patients with papular mucinosis (lichen myxedematosus) a serum factor was found to stimulate DNA synthesis in vitro and proliferation of normal human fibroblasts (18).

Glycosaminoglycans in the granula of mast cells are responsible for the typical metachromatic staining which can be shown by Giemsa or toluidine blue (19,20). This is used to localize and quantify mast cells (21). Mast cell counts differ widely depending on the localization, for example 18.3 mast cells per mm² on the leg and 147.5 mast cells per mm² on the face. Depending on

Table I. *Clinical characteristics of the enrolled patient and previous investigations of APPM*

Author	Cases f/m	Pruritus	Duration until reported (years)
Montgomery et al. 1953 (5)	38 f	–	10
Woerdeman 1960 (6)	19 m	not known	3
Naeyart et al. 1985 (2)	66 f	+	2
Rongioletti et al. 1986 (1)	40 f	–	0,5
	41 f	–	5
Ravella et al. 1987 (7)	56 f	–	6
Berbaum et al. 1987 (8)		–	?
Royer et al. 1988 (9)	55 m	–	0,5
Flowers et al. 1989 (10)	42 f	–	6
Cribier et al. 1990 (11)	77 f	–	?
Crovato et al. 1990 (12)	46 f	+	3
Aho et al. 1991 (13)	24 f	not known	2
Coulson et al. 1992 (14)	56 m	–	0,5
Fosko et al. 1992 (15)	40 f	–	1
Our case 1993	34 f	+	2

f (female)
m (male)
+ with pruritus
– without pruritus
? not mentioned

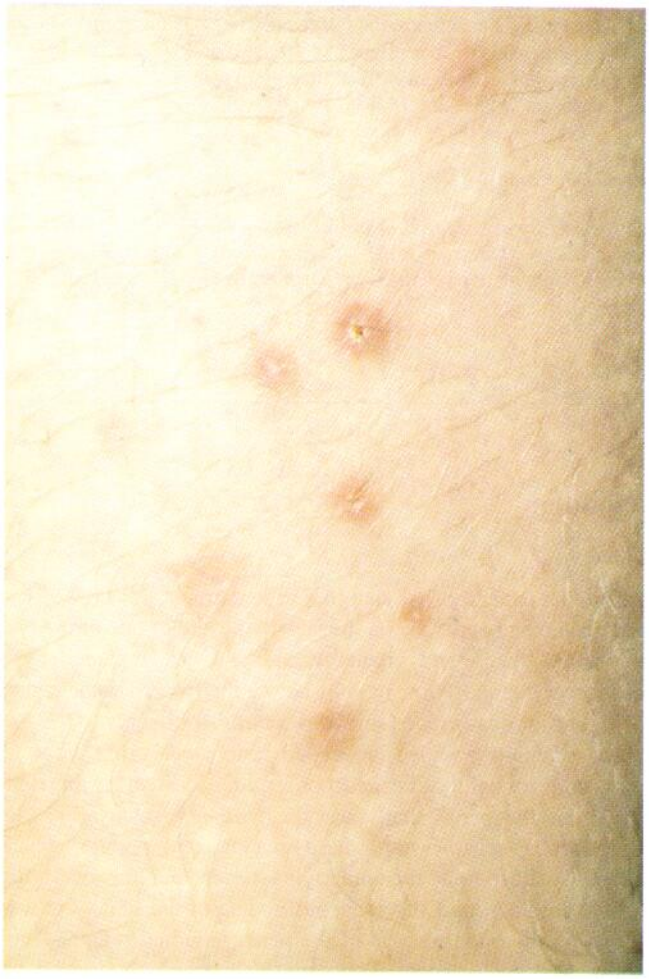

Fig. 1. Detail of the typical flesh-colored to erythematous isolated papules, partly excoriated, on the right leg in patient with APPM.

sun exposure irradiated skin shows an average of 66.3 mast cells per mm^2 compared to 27.2 mast cells per mm^2 in skin of the same skin area not exposed to the sun (22). In APPM we saw a higher mast cell count than in the control with the same sun exposure habits with the routine Giemsa staining of granula-containing mast cells. The real mast cell count could be even higher if one considers the fact that pruritus in our case of APPM led to the degranulation of metachromatic mast cell granules, leading to activated or "phantom" mast cells (21).

The histologic evaluation reveals fibroblast proliferation, which could be a second proof of a connection between APPM, mast cells and pruritus in our special case. Mast cells are studied in processes of fibrosis, because they interact with many cells in the skin, including fibroblasts (23). Histamine, one of the soluble mediators that mast cells secrete, stimulates fibroblast growth (24). In contrary heparin, the major component of connective tissue mast cell granules, may block the activity of fibroblast growth factor (25). So in APPM with pruritus the proper balance of histamine and heparin seems disturbed.

The typical clinical features as well as the histology, together with the absence of systemic abnormalities and serum paraprotein, support the diagnosis of APPM (13). According to Naeyaert et al., the classification of lichen myxedematosus of Montgomery & Underwood (5) should be modified. They prefer the term APPM because of its clinical usefulness and therefore classify the DPLM into a) APPM, b) annular lesions and c) less characteristic forms (26). Nevertheless, clinical differences such as sex preference (females) and the symmetric isolated topography of the papules, which spares face and trunk, remain, indicating APPM to be a distinct clinical entity (2,27). Furthermore APPM should be divided in an asymptomatic form and a symptomatic form with pruritus. More research has to be carried out concerning mast cells in the entity of APPM with pruritus in comparison to the asymptomatic form of APPM.

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