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POEMS Syndrome and Multiple Angioproliferative Lesions Mimicking Generalized Histiocytomas

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A case of POEMS syndrome and Castleman's multicentric disease is reported. Multiple long-standing cutaneous lesions, histologically similar to histiocytomas, were the initial manifestation of POEMS syndrome. A high incidence of angiomatous lesions associated with POEMS syndrome has already been established. To our knowledge, this report is the first report to associate multiple angioproliferative lesions mimicking generalized histiocytomas with POEMS syndrome. ***Key words: Crow-Fukase syndrome; dermatofibroma.***

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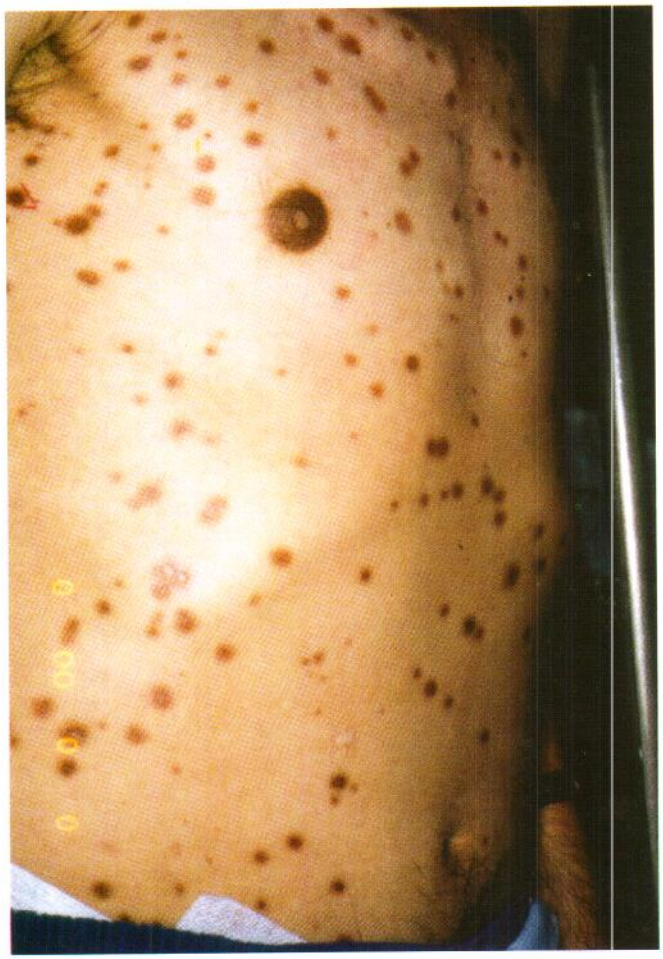

Fig. 1. Multiple scattered dermatofibroma-like lesions on the patient's trunk.

POEMS syndrome is a multisystemic disorder involving polyneuropathy, organomegaly, endocrinopathy, plasmacytoma and haematopoietic disorders, and diverse cutaneous lesions (1). Initial cutaneous manifestations, although non-specific, help diagnose in the majority of cases. The most frequent signs are hyperpigmentation, oedemas, hypertrichosis, sclerosis and skin haemangiomas (2, 3), the latter usually multiple, eruptive and tuberous angiomas. In the Japanese series, 24% to 44% of all patients with POEMS syndrome have angiomatous lesions (4). Although histological descriptions are seldom given, when pathological examinations are carried out, lesions have been commonly reported as mature capillary hemangiomas (5). Recently, Chan et al. (4) have described a peculiar histological form of angioma associated with POEMS syndrome which has been named glomeruloid hemangioma.

Castleman's disease is a benign localized lymphoid hyperplasia. Multicentric presentation is usual, with diffuse lymphadenopathy, hepatosplenomegaly and haematological features, such as anaemia and hypergammaglobulinaemia. It has also been reported in associaton with POEMS syndrome (2, 6).

On the other hand, Smith & Wilson-Jones (7) described a benign vascular lesion, clinically resembling Kaposi's sarcoma, and histologically similar to a dermatofibroma. These lesions were named multinucleated cell angiohistiocytomas (MCAH) and were not found to be related to any systemic disease (7, 8).

We report a patient with POEMS syndrome and Castleman's multicentric disease, and multiple maculopapular lesions resembling histiocytomas.

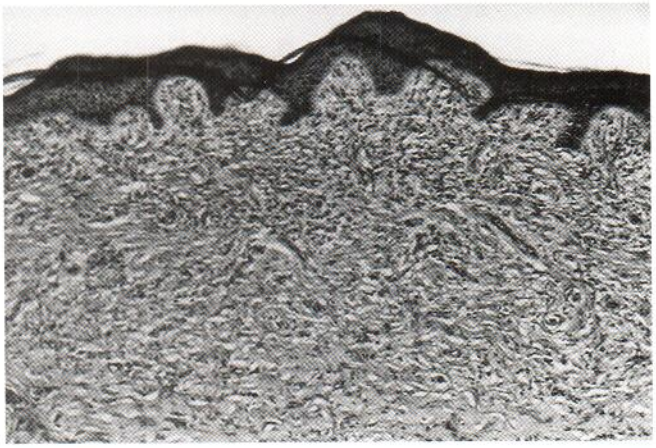

Fig. 2. Histological study of the first biopsy specimen. Moderate small vessel proliferation and diffuse infiltrate in the upper dermis (HE, 100×).

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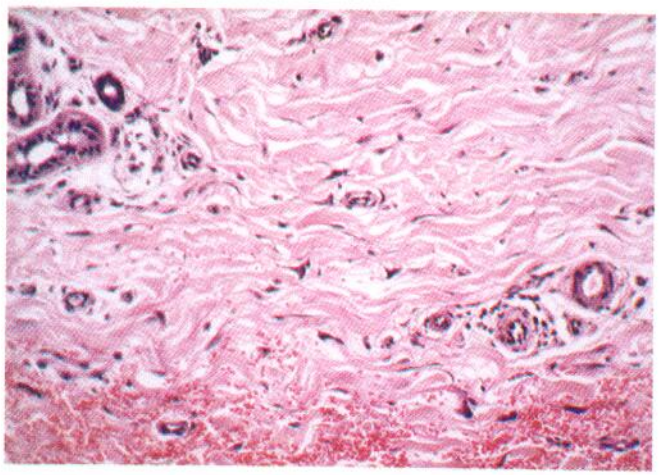

Fig. 3. Detail of Fig. 2. Isolated multinucleated cells with starry configuration in the deeper dermis (HE, 200×).

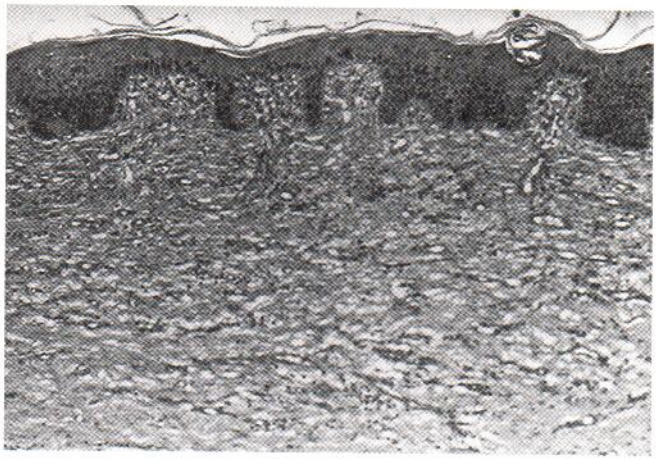

Fig. 4. Histological study of the second biopsy. Intense capillary proliferation and diffuse lymphocytic infiltrate in the upper dermis (PAS, 200×).

CASE REPORT

In 1988, a 42-year-old male with intermittent abdominal pain, long-lasting dysarthria, and paresthesia of the arms was admitted to our hospital due to a new attack of abdominal pain. He complained of acute pain localized predominantly on his right hemiabdomen, vomiting and diarrhoea during the previous 3 days. Other symptoms were weight loss, asthenia, anorexia, impotence coeundi, polydipsia and polyuria.

Physical examination showed a thin man, with hypertrichosis, a low hair line, sclerodermiform skin, and hypo-hyperpigmented macules on his lower extremities. Other signs were acropachy, bilateral Dupuytren, generalized hypotrophy, polyadenopathy, hepatomegaly with splenomegaly and global arreflexy.

Multiple (more than 50), individualized, consistent, maculopapular, brown-violaceous lesions were observed on the trunk and proximal part of the upper extremities. The patient stated that these lesions had appeared more than 20 years earlier as a generalized, asymptomatic eruption (Fig. 1).

Histological studies, performed on different occasions, of two lesions from the right arm revealed different histological patterns.

The first biopsy, taken in 1988, showed a moderate proliferation of small vessels in the upper and mid dermis, with moderate diffuse infiltrate of lymphocytic cells. Prominent connective interstitial tissue cells were present among the vessels. In the deeper areas, multinucleated cells with irregular and angular cytoplasm were detected. They had two or three nuclei and less cytoplasm than the foreign body giant cell type (Figs. 2 and 3).

An immunohistological study using the following markers was carried out: FVIIIRA, Ulex aeuropeus (UEA-1), FXIIIa, Vimentine, Desmin, protein S-100, alpha$_1$-antitrypsin and leukocyte common antigen. The results are summarized in Table I. This biopsy was interpreted as histiocytoma.

The second biopsy, taken in 1991, showed a different histological pattern. Epithelial hyperplasia and marked proliferation of small capillary and venous vessels, in combination with angiectasis, were present in the upper and mid dermis. A diffuse lymphocytic infiltrate, mainly of perivascular location, was also seen. It was diagnosed as a capillary hemangioma in regression (Fig. 4).

DISCUSSION

Cutaneous angiomas are one of the main cutaneous signs associated with POEMS syndrome (2, 4, 5, 9, 10). They are usually multiple, eruptive and distributed superficially on the trunk and proximal areas of the extremities.

From a histological point of view, different forms of mature capillary hemangiomas have frequently been described, although a cavernous type (11), a glomeruloid pattern (4), immature cases (3) and erythrophagocytosis phenomena (2) have also been observed. Furthermore, different types of angiomas may coexist in the same patient, suggesting that they may represent the same type of lesion in different stages of development, or different degrees of endothelial proliferation resulting from contact with unknown angiogenic stimuli (9).

One of the biopsy samples from our patient was diagnosed as capillary hemangioma, characteristic of POEMS syndrome. The other biopsy sample was diagnosed as histiocytoma. Some histological and immunohistological findings were similar, although non-conclusively, to multinucleated cell angiohistiocytoma (MCAH) (Table I) (7). MCAH has been defined as an angiohistiocytic lesion with a histological pattern similar to

Table I. *The results of an immunohistological study of the first biopsy specimen.*

UEA-1 = Ulex aeuropeus; Alpha-1-CT = Alpha$_1$-antitrypsin; LCA = leukocyte common antigen.

	Specification	First biopsy
FXIIIa	Fixed dendritic cells of connective tissue	Interstitial cells negative multinucleated cells negative
FVIIIRA	Vascular endothelia	Capillaries positive
Vimentine	Connective tissue cells, capillaries, nerves, inflammatory cells	Inflammatory cells positive, multinucleated cells positive, Capillaries positive
UEA-1	Vascular and lymphatic endothelia	Capillaries positive
Alpha-1-CT	Macrophages and neutrophils	Negative
Desmin	Muscular cells	Negative
S-100	Nerves, Langerhans' cells, melanocytes	Negative
LCA	Leukocytes	Lymphocytic cells

histiocytoma, with prominent vessels, diffuse histiocytic infiltration and multinucleated cells with a characteristic immunohistochemical pattern. MCAH has been reported as brown-violaceous papules, grouped on the limbs of a middle-aged female (7).

To our knowledge, generalized histiocytomas and MCAH have not yet been associated with any systemic process, to POEMS syndrome or Castleman's disease, although both entities are frequently associated with cutaneous angiomas. It is possible, however, that the lesions could initially have been angiomas which slowly regressed, some resembling sclerosant hemangiomas with prominent vascularization, and some resembling histiocytomas, with some histological features of MCAH.

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