

Tumoral Macroglobulinosis of the Skin: *In Situ* Release of IgM

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Sir,

Waldenström's macroglobulinaemia is an uncommon B-cell lymphoproliferative disorder, characterized primarily by bone marrow infiltration and IgM monoclonal gammopathy (1). The plasmacytoid cells secrete monoclonal IgM, but a diagnosis of macroglobulinaemia can be made irrespective of IgM concentration. Skin involvement is rare, and most often non-specific, due to blood hyperviscosity and cryoglobulinaemia (2). However, two types of specific cutaneous disease have been described: (i) Cutaneous infiltration which is characterized by diffuse plaques and nodular lesions usually located on the face, but also on the trunk and the proximal extremities (3, 4). (ii) Macroglobulinosis of the skin, which is rarer and represents storage IgM lesions, and is characterized clinically by papules due to dermal IgM deposits on the elbows, knees and buttocks (5, 6). Tumour masses are secondary to a dense cellular infiltration, or to amyloid deposits. We report a case in which tumoral masses were numerous, mainly composed of IgM deposits secondary to *in situ* excretion.

CASE REPORT

This case was previously published in French (7) but without inclusion of electron microscopic investigations performed many years later.

In short, a 73-year-old woman presented with a haemolytic anaemia of 1 year's duration, with a positive direct Coombs test. Lymphadenopathies were present and a biopsy showed plasma cell infiltrate with intra-

and extracellular Russel bodies. She was treated with chlorambucil. She was referred to us for multiple acquired subcutaneous nodules, well limited, on the trunk and upper limbs, clinically resembling lipomas. The face was diffusely infiltrated. Serum protein electrophoresis showed monoclonal IgM $\mu\lambda$ (4.8 g/l). Medullary erythroblastosis was observed. The skin biopsy revealed a gelatinous and translucent material. In the dermis and the hypodermis, a lympho-plasma cell infiltrate was noted within an abundant amorphous PAS-positive substance. Staining for amyloid (Congo red, thioflavin T) and mucinosis (Alcian blue) was negative. Direct immunofluorescence showed a diffuse staining with IgM. The dermal substance was homogenized and electrophoresis revealed an IgM component.

Electron microscopy revealed a granular electron-dense structure with no fibrils in the dermis. The plasma cells were huge and filled with the granular substance (Fig. 1a). In some instances, the cell membrane was open and the cell discharged the material in the intercellular space (Fig. 1b, c).

DISCUSSION

Our case showed that immunoglobulins were locally secreted in the skin and that they represent the material of the tumour. IgM was directly released by abnormal plasma cells in the dermis, resulting in clinical tumours. The histopathological and immunofluorescence findings in our patient were similar to previous cases (5–8). Previous studies demonstrated amorphous or

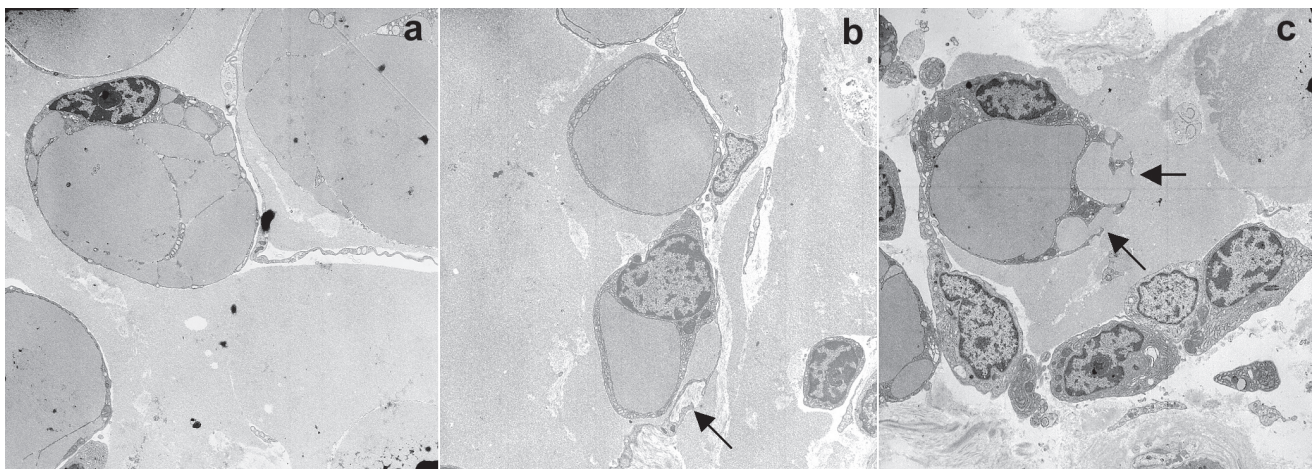


Fig. 1. Electron microscopy (x1980) of infiltrating plasma cells in the dermis. (a) Non-secreting cells with peripheral vacuoles, (b) opening of a vacuole (arrow) and (c) opening of several vacuoles (arrows).

granular but never filamentous material (5, 6). In one case, electron microscopic study revealed linear non-branching fibrils with peculiar striations different from amyloidosis (8). Both types of deposits were observed by Lipsker et al. (9) by immunoelectron microscopy to demonstrate IgM deposition in the lesions of macroglobulinosis.

Our case is quite original because electron microscopy clearly showed non-secreting plasma cells in the dermis, and secondary excretion of the granular material either by rupture of the cell membrane or by fusion of the cell layers leading to a hole in the membrane. We did not observe apoptotic cells or remnants of dead plasma cells. Thus it is suggested that in our case, non-secreting plasma cells were passively releasing immunoglobulins secondary to their cytoplasmic congestion.

REFERENCES

- Owen RG, Treon SP, Al-Katib A, Fonseca R, Greipp PR, McMaster ML, et al. Clinicopathological definition of Waldenström macroglobulinemia: consensus panel recommendations from the Second Workshop on Waldenström macroglobulinemia. *Semin Oncol* 2003; 30: 110–115.
- Libow LF, Mawhinney JP, Bessinger GT. Cutaneous Waldenström's macroglobulinemia: report of a case and overview of the spectrum of cutaneous disease. *J Am Acad Dermatol* 2001; 45: S202–S206.
- Gottron H, Korting G, Nikolowski N. Die makroglobulinmische retikuläre Hyperplasie des Haut. *Arch Klin Exp Dermatol* 1960; 210: 176–201.
- Bureau Y, Barrière H, Bureau B, Litoux P, de Galassus G. Les localisations cutanées de la macroglobulinémie de Waldenström. *Ann Dermatol Syph* 1968; 95: 125–137.
- Hanke CW, Steck WD, Bergfeld WF, Valenzuela R, Weick JK, Young JR, et al. Cutaneous macroglobulinosis. *Arch Dermatol* 1980; 116: 575–577.
- Mascaro JM, Montserrat E, Estrach T, Feliu E, Ferrando J, Castel T, et al. Specific cutaneous manifestations of Waldenström macroglobulinemia. A report of two cases. *Br J Dermatol* 1982; 106: 217–222.
- Fayol J, Bernard P, Bordessoule D, Vire O, Malinvaud G, Bonnetblanc JM. Localisations cutanées spécifiques au cours du myélome multiple et de la macroglobulinémie de Waldenström. *Ann Dermatol Venereol* 1985; 112: 509–516.
- Lowe L, Fitzpatrick JE, Huff JC, Shanley PF, Golitz LE. Cutaneous macroglobulinosis. A case report with unique ultrastructural features. *Arch Dermatol* 1992; 128: 377–380.
- Lipsker D, Cribier B, Spohner D, Boehm N, Heid E, Grosshans E. Examination of cutaneous macroglobulinosis by immunoelectron microscopy. *Br J Dermatol* 1996; 135: 287–291.