Light chain plasmacytoid lymphocytic lymphoma

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Summary

A case of plasmacytoid lymphocytic lymphoma characterized by the exclusive finding of a λ -light chain paraprotein, in the absence of heavy chains, is described. The immunoperoxidase study on bone marrow biopsy sections confirmed the production and secretion of the only λ -light chain.

Introduction

Waldenström's primary macroglobulinaemia (Waldenström, 1944) is characterized by serum IgM paraproteinaemia and pleomorphic infiltration consisting of lymphocytes, abnormal plasma cells and intermediate cell forms in the bone marrow and other tissues (McCallister *et al.*, 1967; MacKenzie and Fudenberg, 1972). This pathological picture has been termed 'plasmacytoid lymphocytic lymphoma' by Lukes and Collins (1975) in their classification system for non-Hodgkin's malignant lymphomas. However, an identical tumour cell morphology has been observed in some patients in whom the IgM serum paraprotein is absent (Child *et al.*, 1977; Tursz *et al.*, 1977; Levine *et al.*, 1980).

The patient now described presented with the cytohistological features of 'plasmacytoid lymphocytic lymphoma' but with a paraprotein belonging to the λ -light chain. Immunoperoxidase and electronmicroscopic studies are included in this report.

Case report

A 66-year-old woman presented in June 1979 with a 3-month history of progressive weakness and dyspnoea. Past history was unrevealing. Both the liver and spleen were found to be enlarged at physical examination; the liver extended 5 cm and the spleen 8 cm below the costal margin. Moderate generalized lymphadenopathy was present.

Laboratory data included: Hb 8.2 g/dl; platelets $80 \times 10^9/l$; leucocytes $5 \times 10^9/l$ with 58% neutrophils, 4% monocytes and 38% lymphocytes; ESR

4 mm/hr; BUN 80 mg/dl; uric acid 10.8 mg/dl; calcium 2.2 mmol/l. SGOT, SGPT, LDH, alkaline phosphatase, and bilirubin were within the normal range. Total serum protein was 52 g/l with specific values of IgG 7.9 g/l, IgA 0.5 g/l; IgM 0.34 g/l. Serum electrophoresis showed a sharp peak in the β region, which was immunochemically demonstrated to have λ chain specificity. Bence Jones proteinuria was 20 g/24 hr.

FIG. 1. Bone marrow aspirate showing infiltrate composed of lympho-plasmacytoid cells and small lymphocytes (May-Grünwald-Giemsa, $\times 400$).

A sternum bone marrow aspirate (Fig. 1) and an iliac crest needle bone marrow biopsy both revealed an extensive pleomorphic infiltrate mainly composed of plasmacytoid lymphocytic cells. Small lymphocytes with nuclei almost devoid of cytoplasm and

a few mature plasma cells were also seen. Rectal biopsy for amyloid was negative. There were no osteolytic lesions on skeletal films.

A diagnosis of plasmacytoid lymphocytic lymphoma with Bence Jones proteinuria and proteinuria was made and treatment with chlorambucil and steroids was started. This resulted in slow but progressive improvement.

Materials and methods

Electronmicroscopic studies

Marrow fragments were fixed for 1 hr in 2.5% glutaraldehyde in 0.5 M phosphate buffer at pH 7.2 and post-fixed in 1% osmium tetroxide. Ultra-thin sections prepared from Epon-Araldite-embedded material were stained with uranyl acetate and lead citrate and examined in a Philips EM 300 electron microscope.

Immunoperoxidase studies

Serial sections of Zenker's fixed bone marrow

specimens were examined for the presence of cytoplasmic immunoglobulins by the peroxidase-antiperoxidase (PAP) method, as described by Taylor (1976). All antisera and PAP complexes used were obtained from Dakopatts A/s. 3,3'-diaminobenzidine-tetra HCl (DAB) was purchased from BDH.

Membrane markers

Suspensions of mononuclear cells were obtained from peripheral blood by Ficoll-Hypaque density gradient centrifugation. The E-rosette test was used for identifying the T cells; surface immunoglobulins were identified by direct immunofluorescence staining using F(ab')₂ goat polyvalent and specific anti-immunoglobulin antisera obtained from commercial sources (Aiuti *et al.*, 1974).

Results

Ultrastructural findings

Electron microscope studies confirmed the light

FIG. 2. Bone marrow aspirate displaying the pleomorphic features of neoplastic lymphoid cells (TEM, $\times 18\,000$; bar represents 1 μm).

microscopy finding of cytological pleomorphism in the bone marrow. Small and medium-sized lymphocytoid cells dominated the bone marrow infiltrate picture (Fig. 2).

A few mature plasma cells were also seen. The nuclei were spheroid, medium-sized, and displayed a degree of chromatin margination. Occasional nucleoli were also seen. Eccentric arrays of well developed rough endoplasmic reticulum occupied the scanty cytoplasm, but these were less prominent than is usual in myeloma cells. The Golgi apparatus was poorly developed.

Intracellular immunoglobulins

Immunoperoxidase staining of bone marrow specimen sections showed all lymphoid cells to contain only λ -light chain (Fig. 3). Anti- γ , α , μ , δ , ϵ , and k antisera gave negative results.

FIG. 3. Bone marrow biopsy section stained for λ -light chain by the immunoperoxidase technique. The lymphoplasmacytoid cells are seen as uniformly dark brown in the original preparation (Haematoxylin counterstain, $\times 400$).

Membrane markers

When immunoglobulin class-specific fluorescent antisera were used, 85% of the peripheral mononuclear cells were stained by anti λ -antibodies, while only 5% stained for k chain. Ten per cent. of the peripheral blood lymphocytes were T cells as defined by spontaneous rosette formation with sheep erythrocytes (E-rosettes).

Discussion

The tumour morphology in this patient was

identical with the classical description of Waldenström's macroglobulinaemia.

The findings of an isolated λ -light chain paraproteinaemia and proteinuria without concomitant IgM M component were unexpected. The bone marrow biopsy immunohistochemical study confirmed the results of the serum and urine immunoelectrophoresis and revealed the presence of a monoclonal λ -light chain within the lymphoplasmacytoid cells and no μ or other heavy chain determinants. Moreover, it was demonstrated that 85% of the peripheral blood lymphocytes bore only λ -light chain on their surface.

So far as the authors know, only 2 similar cases have been analysed. In one, described by Tulliez, Elbaz and Tulliez (1979), the manifestations at presentation and the cytohistological picture were of Waldenström's disease, and the immunofluorescent studies confirmed that the only chain present in the plasmacytoid lymphocytic cells was the λ -light chain. In the other reported by Sun *et al.* (1979), the tumour morphology and immunohistochemical pattern were similar; however, the clinical picture at presentation was that of multiple myeloma (osteolytic lesions and hypercalcaemia). Levine *et al.* (1980) reported one patient (case No 7) in their recent series in whom the clinical picture at diagnosis was characterized by high levels of plasmacytoid lymphocytic cells in the peripheral blood associated with osteolytic lesions without either splenomegaly or lymphadenopathy. The only protein anomaly encountered was the presence of type k Bence Jones proteinuria. However, as no intracellular immunoglobulin study was carried out, it is not known whether the lymphoid cells were synthesizing and if there were non-secretory heavy chain determinants or not.

The pathological picture of 'plasmacytoid lymphocytic lymphoma' has been found also in patients with IgG (Resegotti, Palestro and Coda, 1977; Tursz *et al.*, 1977; Levine *et al.*, 1980), with IgA (Hijmans, 1975; Tursz *et al.*, 1977; Levine *et al.*, 1980), with IgE (Shirakura *et al.*, 1978) with monoclonal gammopathy, or without M component (Levine *et al.*, 1980).

Can plasmacytoid lymphocytic lymphomas, where monoclonal IgM serum is absent, be interpreted as variants of the classical Waldenström's macroglobulinaemia or can they be considered as myelomas with lymphoplasmacytic morphology as Sun *et al.* (1979) claimed for their patient? The last hypothesis is supported by Maldonado *et al.* (1966) who reported that myeloma cells may appear very lymphoid at light and electron microscopy. Kyle and Bayrd (1976) have also classified these disorders characterized by lympho-plasmacytic bone marrow infiltration and IgG type paraprotein

aemia as multiple myeloma; whereas Levine *et al.* (1980) and Tursz *et al.* (1977) maintain that the characteristic cell infiltrates in which lymphocytes and plasmacytoid lymphocytes predominate is clearly different from that seen in multiple myeloma.

The differences in definition are more apparent than real. Those cases in which there are intermediate characteristics between Waldenström's macroglobulinaemia and multiple myeloma may well reflect a block in the maturation of lymphocytes at a certain stage of their differentiation. Indeed, the target cell for malignant transformation in multiple myeloma may also be a B-lymphocyte and this could then be responsible for the malignant myeloma cell proliferation (Salmon and Seligmann, 1974; Mellstedt, Killander and Pettersson, 1977).

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