Circulating Russell-Body-Containing Lymphoid Cells in an Immunocytoma Patient

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Immunoglobulin-containing inclusions in B-lymphoid cells are either globular/homogeneously electron dense or crystalline, with a variable periodic-acid Schiff (PAS) reaction. Globular-PAS-positive inclusions are often referred to as Russell bodies. We describe a case of immunocytoma (diagnosed on bone marrow biopsy) in which most of the peripheral circulating lymphoid cells contained in-tracytoplasmic inclusions exhibiting the cytochemical and ultrastructural characteristics of typical Russell bodies.

A 72-year-old male presented with a 3-week history of non-specific gastro-intestinal complaints, hepatomegaly, normocytic anaemia, IgM λ paraproteinaemia (11 g/l) and λ Bence Jones proteinuria. Bone marrow aspiration and trephine biopsy were obtained from the posterior iliac crest using Klima and Jamshidi needles, respectively. The biopsy was fixed in Zenkers' solution, decalcified and embedded in paraffin wax. Immunohistochemical stains were done using the avidin-biotin complex technique (Dako, Denmark), modified by treating the sections with 0.1% trypsin for 9 min at 37°C, blocking endogenous peroxidase with 1.5% H₂O₂ for 10 min and blocking non-specific binding with 5% skimmed milk buffer. The sections were stained for IgG, IgM, IgA, κ and λ (Dako, Denmark) and with LN2 and MB2 (Clonab, FRG). For electron microscopy, the blood was collected in lithium heparin and the buffy coat processed according to standard technique. Thin sections (60-90 nm) were studied with a Hitachi H-600 electron microscope. No other tissue was available for investigation. The patient was lost to follow-up shortly after the bone marrow investigation.

The blood count (Coulter STKS) showed: Hb 10.3 g/dl; WBC $13.4 \times 10^9/l$; platelets $253 \times 10^9/l$; lymphocytes $4.82 \times 10^9/l$; neutrophils $7.91 \times 10^9/l$ and monocytes $0.67 \times 10^9/l$, with 70% of the peripheral lymphocytes exhib-

iting prominent diastase-resistant PAS-positive inclusions (fig. 1). The lymphocyte population consisted of small well-differentiated cells, bigger lymphocytes with more cytoplasm and euchromatin and the occasional lymphoplasmacytoid cell. The marrow was hypercellular and interstitially infiltrated by a heterogeneous population of lymphoid cells, 64% containing inclusions and consisting predominantly of lymphocytes with some lymphoplasmacytoid cells, plasma cells and immunoblasts. Single cells with PAS-positive intranuclear inclusions (Dutcher bodies) and an increased background population of mast cells were also evident. Most of the

lymphoid cells reacted with the B-lymphoid markers MB2 and LN2. The presence of cytoplasmic IgM λ in the lymphoplasmacytoid and plasma cells (often containing the Russell bodies) was immuno-histochemically confirmed. The inclusions stained eosinophilic with haematoxylin and eosin but did not react with anti-IgM λ . Electron-microscope examination (fig. 2) showed lymphoid cells of different sizes, displaying nuclear and cytoplasmic heterogeneity. Homogeneously granular electron-dense material occurred within dilated rough endoplasmic reticulum in the majority of peripheral lymphoid cells. No filamentous, fibrillar, microtubular, microvesicular or paracrystalline internal structures were present. A well-developed Golgi apparatus was usually closely associated with the inclusions. The ribosomes and polyribosomes appeared normal and few profiles of rough endoplasmic reticulum (apart from the dilated cisternae containing the inclusions) were evident. The presence of cytoplasmic lipid droplets was a regular feature.

Russell bodies in tissue B-lymphoid cells are well described [1,2], but in circulating lymphoid cells they seem to be mostly restricted to patients with chronic lymphocytic leukaemia, usually without serum or urine paraprotein, although

Fig. 1. Peripheral blood film, a Two lymphocytes and a neutrophil. The lymphocytes, like the majority of lymphoid cells, exhibit what appears to be intracytoplasmic vacuoles on routine Romanowsky-stained blood smears. May-Grünwald-Giemsa. $\times 180$. b The vacuoles were subsequently shown to be PAS-positive intracytoplasmic inclusions. PAS stain. $\times 180$.

Fig. 2. Composite low-magnification electron microphotograph illustrating lymphoid cells in the peripheral blood, a A homogeneously granular electron-dense inclusion is present in the dilated perinuclear cistern. Note the few but large mitochondria and a nucleus containing peripheral dense marginated heterochromatin. $\times 5,800$ original magnification, b Lymphoid cell with relatively immature nucleus with increased eu-chromatin content and two prominent nucleoli. Note the extensively developed Golgi complex and single electron dense intracisternal inclusion. $\times 4,350$ original magnification.

$V_{\frac{1}{2}}^{\frac{1}{2}} > W < \frac{1}{2} W$

though a case of lymphocytic leukaemia exhibited plasma-cytoid differentiation of lymphocytes in a lymph node biopsy done later [3]. Three cases of immunocytoma described with circulating inclusion containing lymphocytes had overt lymphocytoses ($8.8-98.8 \times 10^9/l$) with 1-10% containing the inclusions, which were PAS negative and crystalline [4]. The inclusions of our case did not stain for IgM λ using the described method, but it is generally accepted that these inclusions represent condensations of intracisternal immunoglobulins and technical factors are probably responsible for inconsistent results [1, 3, 5, 6]. In the absence of an overt peripheral lymphocytosis and when many lymphocytes were small and well differentiated, this rare phenomenon provided morphological evidence of a circulating malignant component, which is a constant feature in Waldenström's macroglobulinaemia previously demonstrated by means of immunological techniques [7-9].

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