Virchows Archiv A Pathol Anat (1989) 415:297–300

Virchows Archiv A
Pathological Anatomy and Histopathology

Case report

An immunohistochemically defined non-Hodgkin's lymphoma showing intercellular junctions

A case report

B.P. Eyden and M. Harris
Department of Histopathology, Christie Hospital & Holt Radium Institute, Manchester M20 9BX, United Kingdom

Summary. A rare example of pleomorphic B cell non-Hodgkin's lymphoma is described in which tumour cells possessed simple intercellular junctions.

Key words: Non-Hodgkin's lymphoma – Electron microscopy – Immunohistochemistry – Intercellular junction

Introduction

The diagnosis of lymphoma is usually based on classical histological methods supplemented by appropriate immunophenotyping using wax or frozen sections. Occasionally in addition, transmission electron microscopy is used, especially in unusual cases or cases with ambiguous immunohistochemical results. In such cases a major diagnostic criterion for the diagnosis of lymphoma is the absence of intercellular junctions (Ghadially 1985). Here, we document a non-Hodgkin's lymphoma of probable B cell lineage which exhibited frequent simple cell junctions.

Case report

A 30 year old Caucasian woman presented in April 1988 with lethargy, diarrhoea and lower abdominal discomfort. In June she developed an acute abdomen, requiring an emergency laparotomy. A 10 cm mass, arising from the pelvis and adherent to sigmoid colon and a loop of small bowel, was found and biopsied. A later laparotomy was performed for surgical debulking of residual tumour. The patient had no other tumour and no lymphadenopathy, and 4 months after initial presentation was receiving chemotherapy.

Materials and methods

The biopsy and resected tumour were fixed in buffered formalin and embedded in paraffin wax. 5 μm sections were stained with Haematoxylin and Eosin (H&E). Immunoperoxidase staining was performed on wax sections from the biopsy and frozen sections from the resected tumour as indicated in Table 1. For electron microscopy, formalin-fixed tissue from the biopsy was processed conventionally into epoxy resin.

Offprint requests to: B.P. Eyden

Results

The biopsy and resected tumour were histologically identical. The observations presented here refer to the biopsy except for frozen-section immunostaining results which are confined to the resected specimen. H&E sections showed a malignant tumour mainly of non-cohesive round cells (Fig. 1A). They were pleomorphic, ranging from small mono-nuclear cells to large cells with bizarre and lobed or multiple nuclei. Nucleoli were prominent. Immunohistochemical results (Figs. 1B, C) are shown in Table 1. Ultrastructurally, tumour cells had euchromatic nuclei (Fig. 2A) with moderate numbers of nuclear pockets (Fig. 2B). The abundant cytoplasm contained many lipid droplets, moderate numbers of mitochondria, a few rER cisternae and many polyribosomes but no other specialised cytoplasmic organelles. Some areas of cell surface had numerous long or short processes. Other smoother areas possessed simple junctions, either joining rounded processes to cells (Figs. 2A, B), or forming contacts between whole cells (Fig. 2A). Under low power they appeared sharply defined and electron-dense (Figs. 2A, B). At higher magnification (Fig. 2C), they were seen to be primitive structures, lacking filaments and including a quantity of electron-dense material beneath the apposed plasma membranes.

Discussion

Although the histological appearance of this tumour was not typical of non-Hodgkin's lymphoma

Table 1. Immunohistochemistry

	Antibodies[3]	Reactivity	Staining[5]
Initial biopsy[1]	anti-LCA(CD45)	most white cells	++
	L26	B cells	++
	4KB5(CD45R)	B cells	+
	UCHL1(CD45R)	T cells, granulocytes, histiocytes	−
	MAC387	monocytes, histiocytes	−
	anti-EMA	epithelial cells, plasma cells, some lymphoid cells	−
	CAM5.2	low molecular weight cytokeratins	−
	anti-desmin	smooth and striated muscle cells	−
	anti-S100 protein	Langerhans cells, IRCs[4], melanocytes, Schwann cells	−
Resected tumour[2]	anti-IgD/IgM/K/λ		−
	CD19	B cells	+
	Leu16(CD20)	B cells	+
	Pan B(CD19,22)	B cells	+
	T11(CD2)	T cells	−
	UCHT1(CD3)	mature thymocytes, peripheral T lymphocytes	−
	T1(CD5)	T lymphocytes	−
	T4(CD4)	helper/inducer T cells	−
	T8(CD8)	suppressor/cytotoxic T cells	−
	DRC-1	dendritic reticulum cells	−

[1] ABC technique on wax sections; [2] streptavidin technique on frozen sections; [3] all obtained from Dako except CAM5.2 and Leu16 (Becton-Dickinson) and UCHT1 (Unipath); [4] interdigitating reticulum cells; [5] ++ strongly positive, + weakly positive, − negative

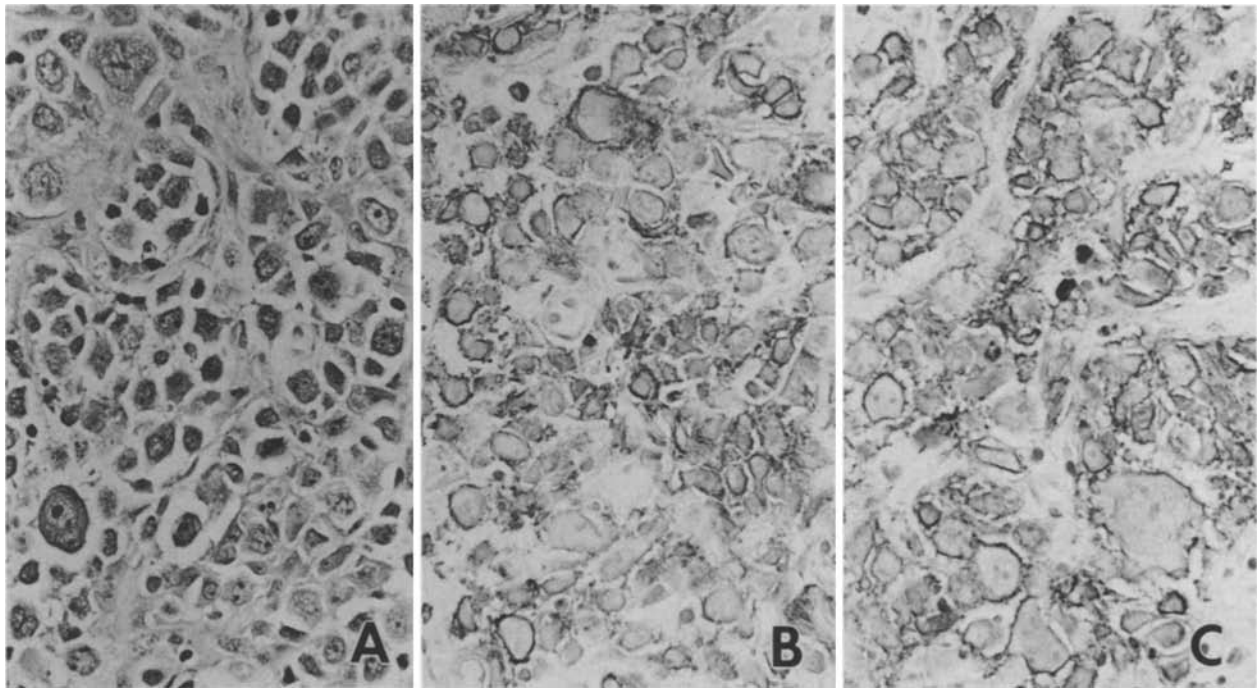

Fig. 1 A–C. Light microscopy of biopsy (all ×340). **A** H&E appearance showing pleomorphic non-cohesive cells. **B** and **C** Wax sections immunostained for LCA and L26 respectively. Note strong membrane staining

(NHL), the immunohistochemical results unequivocally indicate that this is the correct diagnosis. The LCA positivity, combined with positive staining for five B-cell markers and negative results with six T-cell markers, delineate this tumour as an NHL of B cell lineage. Negative results for low molecular weight cytokeratins, desmin and S100 protein argue against alternative diagnoses of carcinoma, myogenic tumour or malignant melanoma.

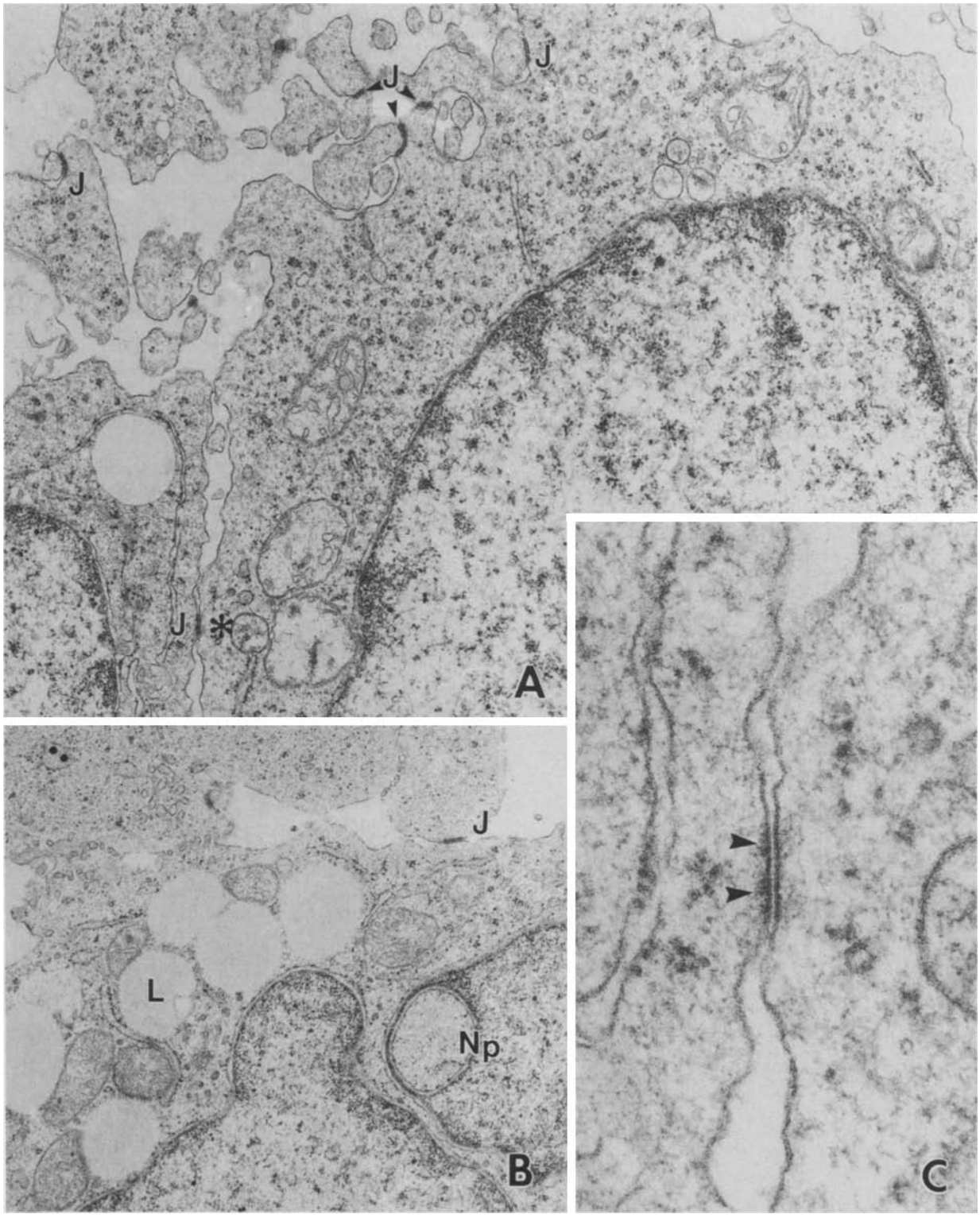

Fig. 2. Ultrastructure of biopsy. **A** Tumour cells and processes attached by sharply delineated junctions (J) (×19600). **B** Simple junction mediating attachment of a cell process to a cell displaying a nuclear pocket (Np) and abundant lipid (L) (×8600). **C** Detail of asterisked area of **A** showing primitive nature of junction: arrowheads, dense material adherent to apposed plasma membranes (×98000)

The occurrence of cell junctions in NHL is sparsely documented. It is best established in interdigitating reticulum cell (Rabkin et al. 1988) and dendritic reticulum cell (Monda et al. 1986) lymphoma. In our case, the former is excluded by negative staining for S100 protein and the latter by negative staining with anti-DRC1, as well as by ultrastructural features: the smoothly contoured, rounded or ovoid nuclei and the long, undulating cytoplasmic processes of dendritic reticulum cell lymphoma (Monda et al. 1986) are absent from our case. These lymphomas are extremely rare and are arguably not strictly comparable with neoplasms of true lymphocytes, and the occurrence of cell junctions in the latter has only occasionally been described. In a number of cases the diagnosis has been based on histology and electron microscopy alone (Kojima et al. 1973; Imai et al. 1980) and is therefore not fully established. A true histiocytic lymphoma with simple junctions was described by Thomas et al. (1984), the diagnosis resting on histology, positive staining for lysosomal enzymes and electron microscopy, but again, this was not a lymphocytic neoplasm.

As an incidental finding in 60 large-cell mediastinal lymphomas, Perrone et al. (1986) found three exhibiting cell junctions. These were LCA positive and although positive staining for cytokeratin was also found in the series, this was judged to be due to residual epithelial cells, and their illustration supports this. We have used a far more comprehensive panel of immunohistochemical markers to demonstrate that in an occasional case of unequivocal NHL primitive cell junctions can be found. We have used the term *junctions* rather than *paired subplasmalemmal densities* (Quinonez and Simon 1988) because in most instances these structures are the sites of closest approach of the adjacent plasma membranes; and where, only short distances away, cell surfaces begin to separate. The appearances, therefore, are of true contacting devices. The finding of such junctions is important diagnostic information since it indicates that in problem cases a diagnosis of non-Hodgkin's lymphoma should not be rejected solely as a result of finding intercellular junctions by electron microscopy.

Acknowledgements. We would like to thank Daxa Chauhan and Julie Cook for technical and photographic assistance in electron microscopy.

References

Erlandson RA (1981) Diagnostic Transmission Electron Microscopy of Human Tumours. Masson, New York, p 111

Ghadially FN (1985) Diagnostic Electron Microscopy of Tumours, 2nd ed. Butterworths, London, pp 74–75

Imai Y, Kasajima T, Terashima K, Dobashi M, Matsuda M (1980) Non-hodgkin malignant lymphoma with special reference to desmosome-like junctions. Acta Pathol Jpn 30: 195–217

Kojima M, Imai Y, Mori N (1973) A concept of follicular lymphoma. A proposal for the existence of a neoplasm originating from the germinal center. GANN Monog Cancer Res 15:195–207

Monda L, Warnke R, Rosai J (1986) A primary lymph node malignancy with features suggestive of dendritic reticulum cell differentiation. Am J Pathol 122:562–572

Perrone T, Frizzera G, Rosai J (1986) Mediastinal diffuse large-cell lymphoma with sclerosis. A clinicopathologic study of 60 cases. Am J Surg Pathol 10:176–191

Quinonez G, Simon GT (1988) Cellular junctions in a spectrum of human malignant tumors. Ultrastruct Pathol 12:389–405

Rabkin MS, Kjeldsberg CR, Hammond ME, Wittwer CT, Nathwani B (1988) Clinical, ultrastructural immunohistochemical and DNA content analysis of lymphoma having features of interdigitating reticulum cells. Cancer 61:1594–1601

Thomas P, Said JW, Rosenfelt FP, Heifetz LJ (1984) True histiocytic lymphoma: an immunohistochemical and ultrastructural study of two cases. Am J Clin Pathol 81:243–248

Received February 6, 1989 / Accepted March 28, 1989