Significance of a ‘starry sky’ in lymphosarcomata in Britain

J. GOUGH

From the Department of Pathology, University of Manchester

SYNOPSIS Four cases of lymphosarcomata are described in which the histological pattern was identical to that seen in Burkitt’s lymphoma. The anatomical distribution was dissimilar in that the disease predominantly affected the reticulo-endothelial system. The arrangement of the histiocytes and lymphoid cells in these tumour groups is similar to that of macrophages and lymphocytes in rosettes seen in leucocyte cultures under certain conditions, and it is suggested that an immunological factor may be responsible for these appearances.

Attention has recently been drawn to the historical similarity between Burkitt’s tumour and a number of human and animal lymphomas. A proportion of cases of childhood lymphosarcoma in the United States have been found to show the characteristic histology of a ‘starry sky’ appearance produced by a uniform background of lymphoblasts studded with large phagocytic histiocytes (Gall, 1960; O’Conor, Rappaport, and Smith, 1965; Dorfman, 1965). In addition the anatomical distribution of the disease was similar to that of the African lymphoma (O’Conor, 1961; Burkitt, 1962) in that an abdominal presentation was particularly common, and peripheral lymph nodes were less frequently involved initially than in adult lymphosarcoma. Similar cases have also been seen in Britain (Wright, 1964; Baskerville, Hunt, and Lucke, 1966; Seed, 1966) and histologically indistinguishable lymphomata have been reported in cats and dogs (Bras, Murray, and McDonough, 1965; Baskerville et al., 1966; Lukes, Parker, Bell, McBride, and Madill, 1966; Squire, 1966). These observations have stimulated a further search for lymphosarcomata showing this histological picture.

MATERIAL

A review of 50 biopsies and 14 necropsies has been made from patients diagnosed as suffering from lymphosarcoma at the Manchester Royal Infirmary during the period 1951-1966 for the purpose of selecting those cases in which the histological appearances were those of the Burkitt lymphoma (O’Conor and Davies, 1960; Wright, 1963). The appearances were seen in four lymph node biopsies but not in any of the necropsy material. It should be noted that few children are admitted to the Infirmary, and consequently that there are only two cases below the age of 12 in this series.

RESULTS

The clinical data are summarized in the table. Only in case 3, in which the parotid gland was involved, did the disease initially present outside the reticulo-endothelial system. This patient also had a leukaemic blood picture, the white cell count being 13,000/c.mm., of which 30% were primitive lymphoid cells. Patients 1 and 2 had been treated initially by radiation and patients 3 and 4 by nitrogen mustards. Three of the patients have died, the duration of the disease being within the range generally found in lymphosarcomata. No necropsy examination was possible on any of these patients.

The histology of a lymph node biopsy from each patient showed a starry-sky appearance resulting from the presence of large histiocytes, many of which are engaged in phagocytosis of nuclear debris and occasionally whole lymphoid cells, amidst a back-
ground of poorly differentiated lymphocytes in which mitotic figures were present to a variable degree (Fig. 1). Occasional histiocytes are often seen in lymphosarcomata but a starry-sky appearance was present throughout the entire sections of the tumours described here.

**DISCUSSION**

Whilst these tumours showed a histological pattern identical to that of the Burkitt lymphoma the disease predominantly affected the reticulo-endothelial system in contrast to the extrarecticular sites in the African lymphoma (O’Conor and Davies, 1960; Burkitt, 1962). If Burkitt’s tumour is defined in terms not only of its histology but also of its anatomical distribution the tumours described here cannot be regarded as examples of the Burkitt lymphoma, but rather as lymphoblastic lymphosarcomata showing an identical histological pattern to that of Burkitt’s tumour. Phagocytosis by histiocytes is not exclusive to the Burkitt tumour and has been seen in other lymphomata (Diamondopoulos and Smith, 1964) and in lymph nodes showing reactive hyperplasia. However, the arrangement of the component cells in Burkitt’s lymphoma and in these lymphosarcomata is so characteristic that it probably represents some distinctive biological property common to both tumour groups, such as degeneration or an immunological phenomenon.

There is some circumstantial experimental evidence which suggests that an antigenic factor may be operating. In certain cultures of lymphocytes or lymphoid tissue rosettes are seen consisting of a large central macrophage surrounded by a ring of lymphocytes. This ‘peripolesis’ has been seen in cell cultures from patients with rheumatoid arthritis (Bartfeld and Juliar, 1964) and systemic lupus erythematosus (Marmont and Damasio, 1965), in cultures containing leucocytes from two donors (Maclaurin, 1965; McFarland, Heilman, and Moorhead, 1966), and less frequently in unstimulated cultures (Maclaurin, 1965, Fig. 2). It has also been seen in explants of lymph nodes and spleen obtained from rabbits subjected to antigenic stimulation or skin homografting (Sharp and Burwell, 1960), and has been described in a bone marrow smear from a patient with idiopathic thrombocytopenic purpura (Naiman and Oski, 1965). In the cultures the lymphocytes surrounding the macrophages show D.N.A. synthesis and transformation to a blastoid form (McFarland et al., 1966). The rosettes therefore appear to be associated with immunological reactions, and although the functional relationships between the cells is not entirely clear, the transmission of a stimulatory substance from macrophage to lymphocyte appears likely.

It is possible that the histiocytes in Burkitt’s lymphoma represent a reaction to degenerating tumour cells, but the presence of large numbers of histiocytes is not a general feature of necrotic tumours. Alternatively, the starry sky may signify an immunological phenomenon, in view of the fact that there is a resemblance between the arrangement of the cells in Burkitt’s tumour and the appearance of the rosettes of lymphoid cells and macrophages.
seen in the various situations described. The rosettes appear to arise as a result of antigenic stimuli, so if the macrophages of the rosettes and those of the tumours can be regarded as analogous, then circumstantial evidence is provided that the African lymphoma is antigen induced as suggested by Burkitt and Davies (1961). It could also mean that the lymphosarcomata described in this paper, by virtue of their similar histology, may also have been induced by a virus or other antigenic stimulus.

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