A case of Lennert's lymphoma

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SUMMARY A 73-year-old man who presented with a tonsillar mass and generalised lymphadenopathy died two months after admission to hospital. The appearances in the surgical biopsy material resembled those of Lennert's lymphoma, while the necropsy findings were those of a diffuse lymphocytic lymphoma composed mainly of cells with small nuclei showing only slight irregularity. The implication of these findings in relation to the nature of Lennert's lymphoma are briefly discussed.

The name Lennert's lymphoma has been applied to a form of malignant lymphoma with a high content of epithelioid histiocytes which was first described by Lennert and Mestdagh in 1968. At that time they believed it was a form of Hodgkin's disease in which diagnostic Reed-Sternberg cells were hard to find. Since then Lennert *et al.* (1975) have changed their views and include the lesion in their classification of the non-Hodgkin's lymphomas, referring to it as 'lympho-epithelioid cellular lymphoma'. To date the only detailed report of a series of cases in the English literature has been by Burke and Butler (1976) based on 15 patients from the MD Anderson Hospital. Of the six patients who had died, necropsy material was available in only three, and in none of these was there definite evidence of lymphoma at necropsy. This case is reported because of the small number of necropsy studies and because of the striking difference in the appearance of the lymphoma in the surgical biopsies and necropsy material.

Case report

A 73-year-old-man, who had recently lost 12 kg in weight, was admitted to Ninewells Hospital in March 1976 complaining of difficulty in swallowing. His previous medical history included two mild episodes of coronary thrombosis and tonsillectomy in 1932. At endoscopy a mass was found in the right tonsillar region and a biopsy was taken. The histological appearances were difficult to interpret but suggested a malignant lymphoma, possibly Hodgkin's disease. After the biopsy the patient was transferred for social reasons to another hospital

where he was found on examination to have numerous enlarged cervical lymph nodes and a lesser degree of bilateral inguinal lymphadenopathy. The liver was enlarged to four fingerbreadths and the spleen was just palpable. Investigations carried out included: Hb 10.5 g/dl; Hct 0.33; MCHC 32 g/dl; WBC $3.2 \times 10^9/l$; platelets $250 \times 10^9/l$; aspartate transaminase 28 IU/l (normal range 5-40); alkaline phosphatase 14 King Armstrong Units (normal range 8-13); total bilirubin 9 μmol ; cholesterol 4.2 mmol/l; total protein 74 g/l; albumin 31 g/l.

In order to make a more definite diagnosis a biopsy was taken from a cervical lymph node. This showed a malignant lymphoma whose appearance was not that of Hodgkin's disease but which did not readily fit into any definite category, although there were features which suggested the possibility of immunoblastic lymphadenopathy. At this time the patient was suffering from a severe chest infection which was being treated with antibiotics, and the immunoglobulin levels were as follows: IgG 23 700 mg/l (normal range 7000-18 000); IgA 13 680 mg/l (normal range 500-4500); IgM 1000 mg/l (300-2500); serum protein electrophoresis showed beta gamma bridging. Because of the clinical evidence of widespread disease the patient was treated with the COPP regime after recovering from his chest infection. He received a single dose of 800 mg of cyclophosphamide and 2 mg vincristine intravenously and was started on oral procarbazine 150 mg and prednisone 80 mg daily. Initially his condition improved and there was a marked reduction in the size of the lymph nodes and spleen, but subsequently he became severely breathless due to the formation of a tension pneumothorax which was relieved by needling. His condition, however, deteriorated due to the development of a severe chest infection and he died about two months after his first admission to hospital and six days after starting chemotherapy.

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SURGICAL SPECIMENS

The following special staining methods were used where indicated: periodic acid-Schiff reagent, methyl green pyronin, Ziehl-Neelsen, Gomori's periodic acid methanamine silver.

The tonsillar biopsy measured $3 \times 2 \times 1$ cm and was covered by squamous epithelium. The underlying tissues were heavily infiltrated by cells of many different types. In places the pattern was granulomatous, containing pink-staining, spindle-shaped cells with the appearance of epithelioid histiocytes forming ill-defined granulomata with occasional multinucleated Langhans' giant cells (Fig. 1). In other parts of the tonsillar biopsy the histiocytes, a few of which were binucleate, formed small clusters or were distributed fairly uniformly among a variety of other mononuclear cells, which included lymphocytes, plasma cells, and mononuclear cells with larger pale-staining nuclei, some of which had prominent nucleoli (Fig. 2). Numbers of mitotic figures were seen and a few of the larger mononuclear cells had pyroninophilic cytoplasm. No

Reed-Sternberg cells were identified and stains for acid-fast bacilli and fungi were negative.

The cervical lymph node, which measured $2 \times 2 \times 1.5$ cm, showed a similar appearance to the tonsillar biopsy but without the striking epithelioid granulomatous areas, the histiocytes being distributed singly or in small clusters.

In both the cervical node and the tonsillar biopsy the lymphocytic component, which was overshadowed, and to some extent obscured by the other cells present, consisted of lymphocytes with small nuclei showing little sign of nuclear grooving or cleavage (Fig. 3). There was no evidence of periodic acid-Schiff positive interstitial material.

NECROPSY

The immediate cause of death was extensive pneumonia affecting both lungs associated with an empyema in the left pleural cavity. The liver weighed 1130 g and the spleen 170 g. There was no evidence of any tonsillar mass and the largest lymph node found measured 0.6 cm diameter.

Histological examination showed the architecture of the lymph nodes examined to be replaced by

Fig. 1 Tonsillar biopsy showing ill-defined granulomata containing spindle-shaped epithelioid histiocytes. On the left is a Langhans' giant cell. Haematoxylin and eosin $\times 215$

Fig. 2 Another part of the tonsillar biopsy showing pale staining histiocytes distributed singly or in small clusters and a background of mononuclear cells. Note the binucleate histiocyte with prominent nucleoli (arrow). *H and E* $\times 215$

Fig. 3 Cervical lymph node showing lymphocytes, most of which have small round nuclei and pale staining histiocytes and mononuclear cells, some of which have prominent nucleoli (arrow). *H and E* $\times 320$

diffuse sheets of cells, most of which had round nuclei only a little larger than those of mature lymphocytes (Figs 4 and 5). Occasional mitoses were found and in places there was invasion of the pericapsular fatty tissue. There was extensive infiltration of the portal tracts in the liver by cells with a similar appearance (Fig. 6), and the bone marrow was also infiltrated. The uniform nature of the infiltrate was in marked contrast to that seen in the surgical biopsies, particularly the absence of pink-staining epithelioid histiocytes. In the spleen there was marked periarterial fibrosis and haemosiderin deposition producing a confusing picture, making it difficult to be certain whether an abnormal cellular infiltrate was present.

Discussion

It was only in retrospect after the paper by Burke and Butler (1976) appeared that the diagnosis of Lennert's lymphoma was considered, and review of the tonsillar biopsy and cervical node confirmed that they showed the features they describe, in

particular, the presence of large numbers of epithelioid histiocytes and a variety of other cell types.

In their detailed discussion of the clinical and pathological features of Lennert's lymphoma Burke and Butler (1976) comment on the incidence of tonsillar and pharyngeal involvement, as do Lennert and Mestdagh (1968), and this was a prominent feature in our case.

The pleomorphic appearance of the infiltrate in Lennert's lymphoma makes the distinction from mixed-cellularity Hodgkin's disease difficult and may, as in our case, suggest a diagnosis of Hodgkin's disease.

Typical Reed-Sternberg cells are, however, scanty or not present in Lennert's lymphoma, and this is the most useful distinguishing feature. In the lymph nodes the epithelioid histiocytes occur in small clusters, but as in our case, a more granulomatous pattern with Langhan's giant cells may be seen in the tonsillar lesions (Todd and Michaels, 1974; Burke and Butler, 1976).

Immunoblastic lymphadenopathy also has histological similarities to Lennert's lymphoma but is

Fig. 4 Lymph node removed at necropsy showing loss of the normal architecture and a diffuse infiltrate of small lymphocytes. Note the absence of epithelioid histiocytes and the very uniform appearance compared with the surgical biopsies. H and E $\times 130$

Fig. 5 A higher power view of the lymph node in Fig. 4 shows the uniform appearance of most of the infiltrating lymphocytes. *H and E* $\times 600$

Fig. 6 A portal tract in the liver showing a dense lymphocytic infiltration. *H and E* $\times 320$

characterised by marked vascular proliferation, amorphous periodic acid-Schiff positive interstitial material, and, in most cases, polyclonal gammopathy (Lukes and Tindle, 1975). Polyclonal gammopathy may also be present in some cases of Lennert's lymphoma (Burke and Butler, 1976). Our patient had raised IgG and IgA levels, which, however, may have been related to infection and liver involvement by lymphoma.

In our case the most striking feature at necropsy was the uniform appearance of the infiltrate in the lymph nodes, liver, and bone marrow, which was purely lymphocytic. Although the lymph nodes were not grossly enlarged their normal architecture was effaced. This feature and the density of the infiltrate in the portal tracts and bone marrow leave little doubt as to its neoplastic nature.

While caution must be exercised in the interpretation of lymphoreticular tissue at necropsy most of the lymphocytes appeared to have round or slightly irregular nuclei only a little larger than normal lymphocytes, and resembled those seen in the tonsillar and cervical lymph node biopsies. Burke and Butler (1976) have also commented on the uniform appearance of the nuclei of the lymphocytes in their cases of Lennert's lymphoma, which distinguish them from those in a typical, poorly differentiated lymphocytic lymphoma, which is made up of cells whose nuclei have a variable appearance and may show angulation and indentation (Sheehan and Rappaport, 1970). They also differ from the cells of the follicular centre type of lymphoma described by Lukes and Collins (1974) which is of B-cell origin and is made up of small cleaved cells.

In our patient the monomorphous infiltrate at necropsy with the appearance of a diffuse lymphocytic lymphoma contrasted with the polymorphous infiltrate in the surgical biopsies. Occasionally two forms of non-Hodgkin's lymphoma or Hodgkin's disease and non-Hodgkin's lymphoma may co-exist in the same patient (Kim and Dorfman, 1974). While this possibility is difficult to exclude in our case we think it is unlikely.

Three of the cases reported by Burke and Butler (1976) were found to have splenic or abdominal node involvement at staging laparotomy and the histology was similar to that elsewhere. Necropsy material was available from three of their cases. Specimens from two patients treated by chemotherapy showed enlarged nodes replaced by fibrous material, and in none of the necropsy material was there definite evidence of lymphoma.

Benign epithelioid histiocytes, similar to those in Lennert's lymphoma, are a common finding in Hodgkin's disease, especially in the lymphocytic

and/or histiocytic type (Lukes, 1971). In Hodgkin's disease it is suggested that with the lymphocytes they represent a response by the host to the neoplastic process (Lukes and Butler, 1966) and the same might apply to the histiocytes in Lennert's lymphoma. In Hodgkin's disease progression of the disease is often marked by an increase in the number of Reed-Sternberg cells and a decrease in the proportion of lymphocytes and histiocytes, and this change may also be seen after therapy (Lukes and Butler, 1966).

Although our patient did not receive a full course of chemotherapy there was a marked reduction in the size of the lymph nodes, and we suggest that the histological appearances at necropsy may have reflected the effects of therapy which had suppressed the non-neoplastic elements, in particular, the reactive histiocytes which were present in the biopsy material. Whether the appearance of the nodes would have come to resemble that described by Burke and Butler (1976) if the patient had survived is a matter for conjecture, but there was no sign of any of the dense fibrous material which was a prominent feature in their two patients who were treated with chemotherapy.

The epithelioid granulomata, which were such a striking feature in our case and in other examples of Lennert's lymphoma, are also well described in Hodgkin's disease (Kadin *et al.*, 1970) and occur less frequently in non-Hodgkin's lymphomas (Dorfman and Kim, 1975). Braylan *et al.* (1977) have recently described three unusual cases of malignant lymphoma in which there was extensive epithelioid granuloma formation, which caused difficulties in diagnosis, and they discuss the pathogenesis of epithelioid granuloma formation in malignant lymphomas. As in our case, there was no evidence of infection or generalised sarcoidosis in their cases, and they conclude that the cause of the granuloma formation is unknown.

At present it is uncertain whether Lennert's lymphoma is a distinct form of lymphoma, or whether it is a variant of some other entity, such as Hodgkin's disease or immunoblastic lymphadenopathy (Burke and Butler, 1976; *Lancet*, 1976). Our findings suggest that in some cases, at least, Lennert's lymphoma may be a variant of lymphocytic lymphoma.

The most recent report concerning Lennert's lymphoma appeared in the Case records of the Massachusetts General Hospital (Tindle and Long, 1977). The patient was a 60-year-old woman who subsequently died, but details of the necropsy histology were lacking. In the discussion Tindle refers to 36 cases of what she describes as the 'Lennert lesion', which included a heterogeneous group of conditions among which was one case of Hodgkin's

disease, seven examples of immunoblastic lymphadenopathy, and 10 non-Hodgkin's lymphomas. In the three non-Hodgkin's lymphomas, in which cell surface marker studies were performed, most of the lymphocytes formed E-rosettes, suggesting a T-cell origin. Unfortunately we were unable to carry out surface marker studies in our case, but, as already indicated, the lymphocytes did not resemble small cleaved cells which are known to be of B-cell origin (Lukes and Collins, 1974). To add to the confusion reference is also made by Long to 121 cases of 'lymphoepithelioid-cell lymphoma' collected by Noel and Lennert. Forty-five were considered to be Hodgkin's variants, 36 were described as lymphogranulomatosis X, and in 40 no definite diagnosis was made.

In conclusion, we agree with Burke and Butler (1976), who express their uncertainty as to the exact nature of Lennert's lymphoma, in particular, its recognition as a separate disease entity, and we hope that future publications, particularly those describing cases studied using newer immunological methods, will clarify what at present is an area of much uncertainty and confusion.

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References

- Braylan, R. C., Long, J. C., Jaffe, E. S., Greco, F. A., Orr, S. L., and Berard, C. W. (1977). Malignant lymphoma obscured by concomitant extensive epithelioid granulomas: report of three cases with similar clinicopathologic features. *Cancer*, **39**, 1146-1155.
- Burke, J. S., and Butler, J. J. (1976). Malignant lymphoma with a high content of epithelioid histiocytes (Lennert's lymphoma). *American Journal of Clinical Pathology*, **66**, 1-9.
- Dorfman, R. F., and Kim, H. (1975). Relationships of histology to site in the non-Hodgkin's lymphomata: a study based on surgical staging procedures. *British Journal of Cancer*, **31**, supplement, II, 217-220.
- Kadin, M. E., Donaldson, S. S., and Dorfman, R. F. (1970). Isolated granulomas in Hodgkin's disease. *New England Journal of Medicine*, **283**, 859-861.
- Kim, H., and Dorfman, R. F. (1974). Morphological studies of 84 untreated patients subjected to laparotomy for the staging of non-Hodgkin's lymphomas. *Cancer*, **33**, 657-674.
- Lancet (1976). The Lennert lymphoma. **2**, 507.
- Lennert, K., and Mestdagh, J. (1968). Lymphogranulomatosen mit konstant hohem Epithelioidzellgehalt. *Virchows Archiv Abt. A Pathologische Anatomie*, **344**, 1-20.
- Lennert, K., Mohri, N., Stein, H., and Kaiserling, E. (1975). The histopathology of malignant lymphoma. *British Journal of Haematology*, **31**, supplement, 193-203.
- Lukes, R. J. (1971). Criteria for involvement of lymph node, bone marrow, spleen, and liver in Hodgkin's disease. *Cancer Research*, **31**, 1755-1767.
- Lukes, R. J., and Butler, J. J. (1966). The pathology and nomenclature of Hodgkin's disease. *Cancer Research*, **26**, 1063-1081.
- Lukes, R. J., and Collins, R. D. (1974). Immunologic characterization of human malignant lymphomas. *Cancer*, **34**, 1488-1503.
- Lukes, R. J., and Tindle, B. H. (1975). Immunoblastic lymphadenopathy: a hyperimmune entity resembling Hodgkin's disease. *New England Journal of Medicine*, **292**, 1-8.
- Sheehan, W. W., and Rappaport, H. (1970). Morphological criteria in the classification of the malignant lymphomas. *Proceedings of the 6th National Cancer Conference*, pp. 59-71. J. B. Lippincott, New York.
- Tindle, B. H., and Long, J. C. (1977). Fever, lymphadenopathy and splenomegaly in a 60-year-old woman. (Massachusetts General Hospital, Case record 30-1977). *New England Journal of Medicine*, **297**, 206-211.
- Todd, G. B., and Michaels, L. (1974). Hodgkin's disease involving Waldeyer's lymphoid ring. *Cancer*, **34**, 1769-1778.

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Addendum

Since this manuscript was accepted for publication Klein *et al.* (1977) have reported two cases of 'Lennert's lymphoma' with transformation to malignant lymphoma, histiocytic type.

Reference

- Klein, M. A., Jaffe, R., and Neiman, R. S. (1977). 'Lennert's lymphoma' with transformation to malignant lymphoma, histiocytic type (immunoblastic sarcoma). *American Journal of Clinical Pathology*, **68**, 601-605.