Kaposi's sarcoma in lymph nodes: histological study of lesions from 16 cases in Malawi

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SUMMARY Biopsy of lymph nodes containing Kaposi's sarcoma from 16 patients showed that the tumour is identical in appearance with that of Kaposi's sarcoma of the skin, regardless of the age of the patient or the mode of presentation. Spread of tumour along sinusoids throughout the lymph node was seen only in the cases of two children with generalised lymphadenopathy, but discrete deposits were present both in lymph nodes regional to skin lesions and in lymph nodes from patients who had presented with primary lymphadenopathy. The reaction of the remainder of incompletely involved nodes was variable. No transition was seen between Kaposi's sarcoma and malignant lymphoma.

Kaposi (1872) described the multiple pigmented haemorrhagic sarcoma of the skin, and later (Kaposi, 1894) he described a case with visceral involvement found at necropsy. Since then much attention has been focused on skin lesions, which are by far the commonest form. But numerous studies in several parts of the world—particularly in Africa, where the disease is common—have shown that lymph node and visceral lesions are by no means rare (Tedeschi *et al.*, 1947; Reynolds *et al.*, 1965; Slavin *et al.*, 1969; Bhana *et al.*, 1970). Unsuspected lymph node and visceral lesions may be found at necropsy in patients who clinically appeared to have only skin lesions (Templeton, 1972). Occasionally lymph nodes draining the site of a skin lesion are invaded by tumour (Bhana *et al.*, 1970). In addition, a primary generalised lymphadenopathic type of Kaposi's sarcoma is recognised. This is commonest in children and young adults and may be unassociated with any skin lesions. It is usually rapidly fatal (Dutz and Stout, 1960; Davies and Lothe, 1963; Slavin *et al.*, 1970).

This paper reviews the findings on biopsy of all lymph nodes containing Kaposi's sarcoma received at St Thomas's Hospital from Malawi between January 1969 and September 1975 inclusive. The histopathology of 159 cases of Kaposi's sarcoma of the skin and mucous membranes in patients in Malawi during the same period are discussed in a separate paper (O'Connell, 1977).

Material and methods

St Thomas's Hospital Medical School provides the only histopathological service for Malawi. The diagnosis has been made on sections of lymph nodes stained with haematoxylin and eosin. Additional sections of some nodes were stained with Perls' stain for iron, Gordon and Sweet's reticulin stain, periodic acid Schiff reagent (PAS), phosphotungstic acid haematoxylin (PTAH), Mallory's trichrome, and phloxine tartrazine. As with skin lesions, the tumours in lymph nodes were classified according to their histological pattern into those with a mixed pattern, a predominantly spindle cell pattern, and an anaplastic group. When possible the distribution of tumour deposits within the lymph nodes was examined and also any abnormalities in the unaffected portions of nodes or in adjacent nodes.

Results

A total of 168 biopsy specimens showing Kaposi's sarcoma from 159 patients were received during the period. Among them were 17 lymph nodes containing tumour from 16 patients (9 children and 7 adults). Two patients, cases 7 and 8, had both a skin and a lymph node lesion. Some of the clinical and histological features are summarised in Table 1.

The tumours were classified into mixed type, spindle cell predominant, or anaplastic types. The mixed type is composed of a pattern of interlacing bundles of spindle cells with abundant vascular slits containing red cells between adjacent tumour cells.

Table 1 Clinical and histological features in 16 cases of Kaposi's sarcoma in lymph nodes

Case no.	Age (years)	Sex	Histology type	Extent of node involvement	Clinical features
1	Adult	M	Mixed	Whole node	Multiple lymphadenopathy
2	3	M	"	" "	" "
3	20	M	"	" "	" "
4	2	F	"	Sinusoidal	" "
5	1	M	"	Whole node	" "
6	Adult	M	"	Peripheral discrete deposits	" "
7	39	M	"	Discrete deposits	Inguinal nodes + skin nodules
8	60	M	"	Peripheral discrete deposits	Scrotal nodules, chest wall nodules, and inguinal nodes
9	3	F	"	Sinusoidal spread	Multiple nodes and skin nodules
10	10	M	"	Whole node	Multiple lymphadenopathy and skin tumours
11	4	M	"	" "	Multiple lymphadenopathy
12	9	M	"	Discrete deposits	Inguinal lymphadenopathy
13	Adult	M	"	" "	Multiple lymphadenopathy
14	14	M	"	Whole node	Cervical node
15	6	F	Spindle cell predominant	Discrete	Inguinal lymphadenopathy
16	Adult	M	Mixed	Whole node	Axillary lymph node and widespread skin nodules

In the spindle cell predominant type vascular slits are very much less evident and the cellular component predominates. In the anaplastic group the tumour cells themselves are much more pleomorphic, not always spindle shaped, and the diagnosis is possible only if more typical areas are seen.

Fifteen of the 17 lymph nodes showed the mixed pattern. Vascular slits were plentiful and filled with red cells. Endothelial-lined channels and small blood vessels within the tumour were often dilated so that the whole tumour appeared extremely vascular. The lymph node tumours were often but not always more vascular than skin lesions of mixed pattern and the histological features were essentially the same (Figs. 1, 2). Mitoses were infrequent. Two lymph nodes, both from the same patient, a 6-year-old girl (case 15), showed a predominantly spindle cell pattern with little vascularity. Mitoses, however, were infrequent. None of the lymph nodes examined showed an anaplastic pattern. In cases 7 and 8 (a man of 39 and a man of 60 respectively) a biopsy of a skin nodule and a lymph node were done at different times. In both cases the skin nodule and the lymph node showed tumour of identical mixed type appearance. The skin tumours showed no histological evidence of aggression or unusual mitotic activity.

In sections stained with haematoxylin and eosin clusters of eosinophilic hyaline bodies from about 1 to 10 μ m in size have often been found in Kaposi's sarcoma within spindle cells and in vascular slits. Their nature is uncertain. They resemble Russell bodies in their staining characteristics, though they are found well away from any inflammatory infiltrate. They are particularly well seen with phosphotungstic acid haematoxylin and phloxine tar-

trazine, and have been noted in almost all skin lesions from Malawi. They were seen in sections stained with haematoxylin and eosin in 12 of the 17 lymph nodes. Further sections were stained with PTAH and phloxine tartrazine and, altogether, hyaline bodies were found in 14 of the 17 nodes.

Perls' stain showed virtually no iron in the unaffected portions of the lymph nodes. Heavy iron deposition was often seen at the periphery of tumour deposits. Iron deposition within the tumour varied from none at all in some areas to moderately heavy deposition in others. Reticulin stains confirmed the observations of others (Lothe, 1963; Lee, 1968) that a delicate reticulin framework surrounded almost every cell. The amount of collagen demonstrated by Mallory's trichrome was extremely variable but some was present in almost all areas of tumour, often surrounding single cells and sometimes lining portions of vascular channels.

In eight biopsies the lymph nodes were totally or almost totally replaced by tumour, so that it was impossible to comment on the pattern of involvement. In the remaining nine biopsies from eight patients some lymphoid tissue remained. In two cases tumour was evenly distributed throughout the lymph node, predominantly along the sinusoids. Bands of tumour surrounded primary and secondary lymphoid follicles, which sometimes showed hyperplastic germinal centres (Fig. 3). In the other seven biopsies tumour deposits were more localised. In two of these (cases 6 and 8) the deposits were obviously situated peripherally (Fig. 4). Case 8 was an inguinal node from a patient with a histologically proved scrotal lesion. The patient in case 6 presented with multiple lymphadenopathy. Peripheral deposits of

Fig. 1

Fig. 1 *Kaposi's sarcoma in lymph node. Note interlacing bundles of spindle cells separated by vascular slits containing red cells. Some are cut longitudinally and some transversely. Appearance is identical with that seen in skin lesions. (H and E $\times 170$)*

Fig. 2

Fig. 2 *Kaposi's sarcoma in lymph node. Note extreme vascularity with many dilated, blood-filled channels. (H and E $\times 68$)*

Kaposi's sarcoma were seen and the remainder of the node was occupied by a malignant lymphoma of diffuse lymphoblastic type. In the remaining five cases the tumour deposits in the node, though discrete, were too large to be able to say whether their origin was peripheral or not.

In some nodes even very large tumour deposits were nodular and very sharply demarcated from the remaining lymphoid tissue (Fig. 5). In other nodes localised deposits had begun to infiltrate adjacent areas of the node along the sinusoids. Both patterns were sometimes seen in the same lymph node.

The appearances of unaffected portions of lymph nodes are summarised in Table 2. Almost all tumour deposits showed some degree of plasma cell predominant inflammatory response at the margins, even when they occupied almost the whole node. Some nodes showed no reactive changes. Others showed follicular hyperplasia, sinus hyperplasia, or both (Figs 6, 7).

Table 2 *Reaction of unaffected portion of lymph nodes to tumour deposits*

Reaction	No. of cases
Follicular hyperplasia	5
Sinus hyperplasia	2
Plasma cell reaction around tumour	14
No plasma cell reaction	1
No reaction in remaining node	2

Discussion

This review of biopsy findings confirms that the appearances of Kaposi's sarcoma in lymph nodes are identical with those of Kaposi's sarcoma in the skin. As observed by others, the histology of a tumour from a child with generalised lymphadenopathy and a rapidly fatal outcome appears to be no more aggressive than the skin lesions of a middle-aged man with

Fig. 3

Fig. 4

Fig. 5

Fig. 3 *Predominantly sinusoidal spread of tumours surrounding follicles with hyperplastic germinal centres. (H and E $\times$ 68)*

Fig. 4 *Peripherally situated deposits of tumour. (H and E $\times$ 8)*

Fig. 5 *Large, well circumscribed nodule of tumour in lymph node. (H and E $\times$ 4)*

Fig. 6 *Lymph node with well circumscribed tumour. Pronounced follicular hyperplasia apparent in remainder of node. (H and E $\times 26$)*

Fig. 7 *Well circumscribed tumour with sinus hyperplasia in uninvolved portion of node. (H and E $\times 22.5$)*

Fig 8. Kaposi's sarcoma (arrowed) extending along sinusoids showing vascular reactive hyperplasia. It is difficult to know where tumour ends and reaction begins. (H and E $\times$ 100)

Fig. 9 Kaposi's sarcoma and malignant lymphoma. The malignant lymphoma in the lower left corner (bounded by arrowheads) and Kaposi's sarcoma above and to the right are distinct tumours. Darkly staining plasma cells (arrowed) are numerous in the junctional zone. (H and E $\times$ 400)

an indolent course over many years (Lothe, 1963; Slavin *et al.*, 1969; Templeton, 1972).

Bhana *et al.* (1970) found lymph node involvement in 16 out of 48 consecutive cases of Kaposi's sarcoma in adults. They suggested that the appearance of incompletely involved nodes varied according to whether the gland was regional to skin disease or whether it came from a patient with primary lymphadenopathy. In the former, deposits were often adjacent to the subcapsular sinus, analogous to lymph node metastases from carcinomas. By contrast, in primary lymphadenopathy the tumour appeared to develop in the medulla of the node and expand from within. The only lymph node in this series which was obviously secondary to a skin lesion was in case 8, where discrete peripheral deposits were seen. In the other lymph node with localised peripheral tumour deposits the coexistence of malignant lymphoma made interpretation difficult. The two cases with a uniform predominantly sinusoidal distribution of tumour were both from children with multiple lymphadenopathy. However, in some of the patients presenting with primary lymphadenopathy there were discrete deposits of tumour in the lymph node. These were sometimes single and sometimes multiple.

Lubin and Rywlin (1971) described changes in the uninvolved portions of lymph nodes containing deposits of Kaposi's sarcoma. The most striking feature was follicular hyperplasia with pronounced hypervascularity of the germinal centres and some increase in the vascularity of the interfollicular areas. The other striking feature was a heavy plasma cell infiltration of the medullary cords. They describe transition between Kaposi's sarcoma and the hypervascular follicular hyperplasia. In the nodes from Malawi hypervascularity of germinal centres was present where surrounding Kaposi's sarcoma was just beginning to invade the follicle. Otherwise reactive centres appeared no different from those seen in lymph nodes reacting to a wide variety of stimuli. In general, the lymphoid follicles seemed to be the areas most resistant to being engulfed by tumour. Two cases with sinus hyperplasia showed marked hypervascularity of the sinusoids extending some distance from localised tumour deposits, and in these it was difficult to be sure where tumour ended and reaction began (Fig. 8).

The relationship of Kaposi's sarcoma to the reticuloendothelial system is of continuing interest. Dörfel (1932) believed that Kaposi's sarcoma was a neoplasm of the reticuloendothelial system. Mild lymphocytosis or monocytosis and reports of atypical monocytes in the blood have been noted in some cases, but in most the leucocyte count has been normal (Reynolds *et al.*, 1965). Kaposi's sarcoma is

seen increasingly in association with reticuloendothelial neoplasms, Hodgkin's disease, lymphosarcoma, chronic lymphatic leukaemia, and myeloma (Reynolds *et al.*, 1965). This association is much less common in Africa, though a number of cases have been reported (Thijs, 1957; Uys and Bennet, 1958; Lothe, 1963; McKinney, 1967; Slavin *et al.*, 1969).

Usually the two neoplasms have been quite distinct. Lothe reported two cases from Uganda in which the tumours were present in adjacent tissues. In one case a lymph node contained both Kaposi's sarcoma and lymphosarcoma. In the other the adrenal cortex showed adjacent Hodgkin's disease and Kaposi's sarcoma. Occasionally the tumours have merged, particularly in lymphoma or leukaemic infiltration of the skin (Sacks and Gray, 1945), and in one South African case the authors hinted at a transition between Kaposi's sarcoma and Hodgkin's disease (Uys and Bennet, 1958). In the lymph node in this series containing both Kaposi's sarcoma and lymphosarcoma spindle cells ran a short distance into the lymphoma in some areas but the appearance did not suggest any transition between the two. Plasma cells were numerous in the junctional zone (Fig. 9).

Recently, in an attempt to correlate immunological and histological findings, Warner and O'Loughlin (1975) put forward the interesting hypothesis that Kaposi's sarcoma is a by-product of an immunological response to a primary tumour, probably a lymphoma. They suggest that vascular proliferation is an integral part of the immunological response but that it later becomes self-perpetuating. They draw an analogy with angioimmunoblastic lymphadenopathy. Many of the tumour deposits in the Malawi lymph nodes were quite advanced and, unlike in the skin, adjacent early lesions were not seen. It was therefore difficult to be sure of the site or mode of origin of the tumour. However, clearly the mode of spread of the tumour and the reaction of the remainder of the node were variable. There appeared to be no transition between lymphoma and Kaposi's sarcoma, and only in the two lymph nodes showing hypervascular sinus hyperplasia was there any appearance of transition between reactive changes and tumour.

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