Kaposi’s sarcoma: histopathological study of 159 cases from Malawi

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SUMMARY The histological features of 168 lesions of Kaposi’s sarcoma from 159 patients in Malawi, where the disease is commoner than elsewhere, were characteristic. All showed well-developed areas of tumour and could be grouped fairly readily into those with a mixed pattern, a predominantly spindle cell pattern, and an anaplastic group, though intermediate patterns were seen. Hyaline bodies were present in nearly all tumours of skin. The cell of origin of Kaposi’s sarcoma is uncertain and possibly has multipotential capabilities. Differential diagnosis may be difficult. Clinically the lesion may be confused with granuloma pyogenicum and may also be like it histologically. The presence of hyaline bodies and deposits of haemosiderin indicate Kaposi’s sarcoma. The spindle cell predominant type may be confused with leiomyoma, leiomyosarcoma, or fibrosarcoma. The presence of hyaline bodies and the formation of vascular channels between spindle cells point to a diagnosis of Kaposi’s sarcoma.

Since Kaposi (1872) described the multiple pigmented haemorrhagic sarcoma of the skin which bears his name cases have been reported in many parts of the world. Over the past 50 years it has become evident that the disease is commoner in parts of Africa than anywhere else. The histopathological features of the tumour in Africa have been described by a number of authors (Kaminer and Murray, 1950; Lothe, 1963; Slavin et al., 1969; Taylor et al., 1971). The histogenesis, however, remains uncertain and the disease presents problems in diagnosis in Britain, where it is rare.

This paper reports the histological features of the tumour in 159 patients in Malawi. Kaposi’s sarcoma forms 4.2% of all malignant tumours in that country (O'Connell et al., 1977).

Material and methods

Since 1968 St Thomas’s Hospital Medical School has provided the only histopathological service for the whole of Malawi. Specimens are forwarded from Government and mission hospitals to the Queen Elizabeth Central Hospital in Blantyre. There they are sorted, registered, and sent to London in weekly consignments. The slides from all cases of Kaposi’s sarcoma received between January 1969 and September 1975 have been reviewed.

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All cases were originally diagnosed on sections stained with haematoxylin and eosin. In selected cases additional sections were cut and stained with Perls’ stain for iron, Gordon and Sweet’s reticulin stain, periodic acid Schiff reagent, phosphotungstic acid haematoxylin, Mallory’s trichrome, and phloxine tartrazine. Clinical information was obtained from the pathology request form. In most cases the sex and approximate age of the patient were given, the site of the lesion, whether the lesions were single or multiple, and the sites of other lesions. Sometimes information was given about the presence of other diseases.

Results

During the period under review 171 biopsy specimens had been diagnosed as Kaposi’s sarcoma. Two of these were rejected as not being diagnostic and one was reclassified as a histiocytoma. The remaining 168, from 159 patients, were accepted as cases of Kaposi’s sarcoma. Biopsy specimens previously received from two of these patients had been rejected as being non-diagnostic. The sites of the tumours are shown in Table 1. Lesions in 17 lymph nodes from 16 patients are the subject of a separate report (O'Connell, 1977). The remainder of the lesions were in skin or mucous membranes and the biopsy findings are described here. Skin lesions numbered 147 and were from 141 patients. The
lesions were mostly on the limbs but some were on the trunk, head and neck, and external genitalia. Some of their histological features are summarised in Tables 2 and 3.

**Cellular Pattern**

Early lesions, described by Dörffel in European and American patients, are seldom subjected to biopsy in Africa. They will be discussed later. The lesions from Malawi all showed well-developed areas of tumour and could be grouped fairly readily into those with a mixed pattern, a predominantly spindle cell pattern, and an anaplastic group.

**Mixed group** (Fig. 1)

The typical lesion of Kaposi's sarcoma has a distinct histological appearance and is characterised by interlacing bundles of spindle cells and vascular channels. Some of the vascular channels within the tumour mass are well-formed arterioles or endothelial-lined capillaries but red cells also appear to lie in spaces between adjacent tumour cells. Where cellular bundles are cut longitudinally red cells appear to lie in slits between spindle cells. Where bundles are cut across, a sieve-like appearance results in which red cells lie in small holes between transversely cut tumour cells. Arterioles and capillaries as well as the channels between tumour cells are often dilated, so that the vascular nature of the tumour is immediately apparent. In such cases the tumour was classified as a mixed type—that is, a mixture of spindle cell proliferation and vascular channel formation.

**Table 1** Site of tumour in 168 biopsies of Kaposi's sarcoma from 159 patients

<table>
<thead>
<tr>
<th>Site of tumour</th>
<th>No. of biopsies</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin only</td>
<td>145</td>
<td>139</td>
</tr>
<tr>
<td>Skin and lymph nodes</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Lymph nodes only</td>
<td>15</td>
<td>14</td>
</tr>
<tr>
<td>Nasal polyps</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Gingiva</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Eyelid*</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

*Visceral lesions also found at necropsy.

**Table 2** Histological features in 147 biopsies of Kaposi's sarcoma of skin grouped according to cellular pattern

<table>
<thead>
<tr>
<th>Cellular pattern</th>
<th>No. of cases</th>
<th>Single</th>
<th>Multiple</th>
<th>Frequent mitoses</th>
<th>Nodular</th>
<th>Mixed nodular and diffuse</th>
<th>Diffuse</th>
<th>Ulcerated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mixed</td>
<td>117</td>
<td>30</td>
<td>87</td>
<td>27</td>
<td>37</td>
<td>28</td>
<td>52</td>
<td>41</td>
</tr>
<tr>
<td>Spindle cell predominant</td>
<td>24</td>
<td>15</td>
<td>9</td>
<td>17</td>
<td>5</td>
<td>13</td>
<td>6</td>
<td>14</td>
</tr>
<tr>
<td>Anaplastic</td>
<td>6</td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>4</td>
</tr>
</tbody>
</table>

**Table 3** Situation in dermis of nodular and diffuse lesions of Kaposi's sarcoma

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Superficial or ulcerated</th>
<th>Deep</th>
<th>Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>Purely nodular</td>
<td>21</td>
<td>20</td>
<td>1</td>
</tr>
<tr>
<td>Purely diffuse</td>
<td>49</td>
<td>7</td>
<td>2</td>
</tr>
</tbody>
</table>

**Spindle cell predominant group** (Fig. 2)

In a smaller group of tumours vascularity was much less marked and the predominant feature was interlacing bundles of spindle cells. Vascular slits were never entirely absent and on closer examination areas

![Fig. 1](http://jcp.bmj.com/)

*Fig. 1* Solid area of tumour of mixed type. At the bottom bundles of spindle cells are cut longitudinally. At the top and in a small area in the lower left corner cells are cut transversely. The vascular nature is apparent with many red cells visible between adjacent tumour cells. (H and E × 275)
Kaposi's sarcoma: histopathological study of 159 cases from Malawi

showed a more diffuse area of tumour (Fig. 5). Sometimes the tumour was partly nodular and partly diffuse, and often a single lesion on clinical examination contained several nodules and plaques. These two distinct configurations were found in most tumours of mixed pattern. While some tumours of the predominantly spindle cell group were clearly nodular or diffuse most were classified as partly nodular and partly diffuse, often with a lobulated shape which was not clearly one or the other. The anaplastic group showed a much more varied growth pattern. The lesions were larger and often only part of the tumour was included in the section.

Well-defined nodules of tumour were about equally divided between those situated deep in the dermis at the level of the sweat glands and those situated immediately below the epidermis or ulcerating through it (Table 3). Diffuse plaques of tumour were much more likely to be situated superficially. Superficial nodules of tumour were sometimes polygonal with a rim of epidermis stretched over them. These often ulcerated and were covered with

**Growth Pattern**

Clinically, patients presented with either skin nodules or plaques. Histologically, nodules were well circumscribed, sometimes producing slight compression of the adjacent connective tissue but only occasionally a definite capsule (Fig. 4). Plaques of a mixed pattern were usually found. Mitoses tended to be more frequent in the predominantly spindle cell type though were seldom more than one per high-power field.

**Anaplastic group** (Fig. 3)

Tumours of this type were much less common. There was much greater cellular and nuclear pleomorphism than in the other two groups. Giant cells were sometimes found and several superficially resembled haemangioendotheliosarcoma. The tumours often showed marked vascularity but the more orderly pattern of spindle cells and vascular slits was found only in occasional areas. Mitoses were infrequent in three of the six tumours. The final diagnosis in this group was based on the finding of typical mixed areas and the presence of hyaline bodies in tumour cells (see below).

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Fig. 2 **Spindle cell predominant type. Interlacing bundles of spindle cells are seen with very little vascularity in this field.** (H and E x 290)

Fig. 3 **Anaplastic type with greater cellular pleomorphism.** The tumour here resembles a haemangioendotheliosarcoma. Elsewhere more typical areas of Kaposi's sarcoma were seen. Hyaline bodies were found even in pleomorphic areas. (H and E x 170)
granulation tissue resembling a granuloma pyogenicum. Hyperkeratosis was seen over most superficial tumours and less often over the deeper ones.

Lesions with a spindle cell predominant pattern were more likely to be single than those with a mixed pattern and they were also more likely to ulcerate (Table 2). Fourteen of the 17 spindle cell predominant lesions with frequent mitoses were ulcerated. Anaplastic lesions also often presented as single ulcerated lesions. One patient with an anaplastic axillary skin lesion had a lesion on the hand which showed a typical mixed pattern on biopsy.

OTHER FEATURES
Hyaline bodies (Fig. 6) were seen in the tumour in almost all skin lesions. These are eosinophilic hyaline globules of varying sizes, usually smaller than a red cell but occasionally up to 10 μm in diameter. They are most numerous in the more vascular areas and are distinguishable from red cells by the fact that they appear as a cluster of globules of different sizes and that they stain bright red with the phloxine tartrazine stain. They also stain a dark bluish-black colour with PTAH, bright red with Mallory's trichrome, and are weakly PAS positive. They are very similar in appearance to Russell bodies but are clearly seen within tumour cells well away from any inflammatory reaction. Careful searching of the haematoxylin and eosin stained sections revealed hyaline bodies in 136

Fig. 4  Well-circumscribed nodule of tumour situated deeply in the dermis, producing slight compression of adjacent connective tissue. (H and E × 17)

Fig. 5  Large diffuse plaque of tumour (H and E × 22)
of the 147 biopsy specimens. Further sections of negative cases were stained with phloxine tartrazine and hyaline bodies were then found in another six cases.

The amount of inflammation in and around skin lesions was extremely variable and was clearly affected by ulceration. However, chronic inflammatory cells, particularly plasma cells, were seen in non-ulcerated lesions both within and around the tumour in a number of cases. They were particularly marked in ulcerated spindle cell predominant lesions well away from the ulcerated surface.

As described above, arterioles and well-formed endothelial-lined capillaries were seen within the tumour mass. Endothelial-lined capillaries could also be seen disappearing into and merging with tumour spindle cells. In some tumours other vascular features were seen. Tumour was sometimes seen in very close relationship to a large vessel, giving the appearance of having replaced its wall. In other lesions large vessels within a tumour were surrounded by a clear space devoid of tumour. Outside the tumour dilated endothelial-lined channels were seen in the dermis. These were most numerous between nodules of tumour and the epidermis and sometimes they were stretched around the edge of a well-defined nodule forming part of its boundary (Fig. 7).

Perls’ stain showed a variable amount of haemosiderin. Occasionally solid nodules or plaques of tumour showed iron deposition throughout, but most showed none or only a small amount at the periphery. Haemosiderin was more abundant in the early, less well-developed lesions nearby in the dermis. In sections containing several nodules and plaques some were completely free of iron and others showed moderately heavy deposition throughout.

Trichrome stains showed that some tumours contained virtually no collagen and others contained a large amount. Individual cells were often surrounded by delicate collagen fibres which helped to line some of the vascular slits. Reticulin stains also showed the tendency for fibres to surround individual tumour cells.

**MUCOUS MEMBRANE TUMOURS**

Four lesions of mucous membranes all showed a typical mixed histologic pattern. Two patients pre-

![Fig. 6 Kaposi's sarcoma showing cluster of hyaline bodies in a tumour cell. (For the purposes of photography 1 μm sections were cut from tissue fixed in paraformaldehyde and stained with methylene blue). × 720](http://jcp.bmj.com/)

![Fig. 7 Dilated endothelial-lined channels are seen between a nodule of tumour and the epidermis. Some are stretched around the edge of a nodule forming part of its boundary. (H and E × 180)](http://jcp.bmj.com/)
sent with large nasal polyps composed almost entirely of Kaposi's sarcoma. In one of these well-circumscribed nodules were present. One section of tumour of the gum of an 8-year-old child was also obviously from a large lesion. Two pieces of tissue between 2.0 cm and 3.0 cm in diameter did not include the whole lesion. The fourth biopsy was of a well-circumscribed nodule 1 cm in diameter from the palpebral conjunctiva of a 4-year-old child. Tissue from this child, taken later at necropsy, showed Kaposi's sarcoma of mixed pattern in lymph nodes and in small bowel. Hyaline bodies were seen in all four cases.

Discussion

The histology of these well-developed lesions of Kaposi's sarcoma received from Malawi accord closely with descriptions and photographs of lesions from other African countries. Lothe (1963) emphasised the essential features of interlacing bundles of spindle cells and vascular channels. Schmid (1973), in Tanzania, described a predominantly angioblastic group and a predominantly fibroblastic group. Taylor et al. (1971), in Uganda, divided their material into three histological groups virtually identical with those described here. Their groups were labelled mixed cell, mononuclear, and anaplastic. In the mixed cell pattern they described clumps of large, pale-staining, histiocytic-like cells with minute vascular slits lying between the interlacing bundles of spindle cells.

Histiocytes have been seen in electron microscopy of Kaposi's sarcoma (Pepler and Theron, 1962; Hashimoto and Lever, 1964; Niemi and Mustakallio, 1965) but from light microscopy descriptions and our own electron microscopy observations the predominant cell type seems the same whether seen in longitudinal section in spindle cell bundles or in cross section giving a sieve-like appearance. The difference in histological groups lies in the relative sparsity of vascular channels between tumour cells in the spindle cell predominant type.

It must be emphasised that although these lesions have been classified according to their overall appearance a continuous spectrum exists. Intermediate patterns are seen and are difficult to allocate to a particular type. At the extreme spindle cell predominant end of the spectrum it is difficult to sustain a diagnosis of Kaposi's sarcoma unless more vascular areas are found. The tumours may be confused with other connective tissue tumours such as fibrosarcoma or leiomyosarcoma. In occasional patients with such lesions a positive diagnosis of Kaposi's sarcoma may be impossible from the first biopsy, the diagnosis being established only by the subsequent clinical course or from biopsy of other lesions.

Dörffel (1932), describing lesions in patients from Europe and America, suggested that the evolution of a skin lesion passed through several phases—a predominantly inflammatory phase, a phase of capillary endothelial proliferation, an angiomatous phase, an angiosarcomatous phase, and finally an involutionary phase. Templeton (1972) observed that the haemorrhagic and granulomatous lesions are seldom seen in Africans. He suggested that this was partly owing to delay in seeking treatment and partly because skin pigmentation masks the early lesion, when change in skin colour is an important early sign in white patients.

Nevertheless in the Malawi lesions areas were seen adjacent to well-formed nodules of tumour which would correspond to the early stages of Dörffel's description (Figs. 8, 9, 10). The dermis showed increased collagenisation, dilatation of capillaries, and a heavy perivascular inflammatory infiltrate of lymphocytes and plasma cells with plasma cells predominating. In some areas capillaries appeared to be surrounded by more than one layer of cells and

![Fig. 8 Early change in the dermis near well-formed lesions of Kaposi's sarcoma. Note heavy collagenisation, dilated vascular channels, and a perivascular inflammatory infiltrate. (H and E × 170)](http://jcp.bmj.com/)

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K. M. O'Connell
Differential Diagnosis

Clinically, Kaposi's sarcoma may be confused with granuloma pyogenicum and they may also be alike histologically with plump, uniform capillary endothelial cells resembling Kaposi's spindle cells. Lee (1968) has described clinical and histological differences between these two lesions and emphasised that the presence of hyaline bodies in Kaposi's sarcoma is a useful feature in differential diagnosis. The nature of these bodies is uncertain. They tend to be more numerous in more vascular areas, which are the areas most likely to resemble granuloma pyogenicum, and it has been suggested that they are lysosomal degenerative bodies. Lee also noted that, unlike granuloma pyogenicum, haemosiderin was often deposited in and around the Kaposi lesion. As noted above, ulcerated lesions from Malawi sometimes showed tissue near the surface indistinguishable from granuloma pyogenicum and only in the depths of the lesion were more solid areas of spindle cell proliferation evident. As in Uganda (Lee, 1968), granuloma pyogenicum is a common lesion in Malawi. Sixty-three cases were diagnosed in the period under review.

Similar cells appeared between vessels. As tumour cells became more numerous inflammatory cells became relatively fewer and vascular channels appeared between spindle cells. Lesions at different stages formed a spectrum of appearances up to the well-formed plaque or nodule, which corresponded to the mixed pattern angiomatos stage or spindle cell predominant angiosarcomatous stage.

 Clinically, some skin nodules involute and disappear even while further nodules are appearing and the disease progressing. Degenerative changes in tumour cells, increasing collagenisation, and endarteritis of vessels have been described and have been said to reflect involution (Kren and Jadassohn, 1933; Lever, 1954; Lothe, 1963). Biopsy of one nodule from Malawi followed mustine therapy and so the nodule could reasonably be assumed to be regressing. A thick fibrous capsule surrounded the nodule, which contained a large, central hyalinised area. In between were areas of tumour showing a mixed pattern where tumour cells appeared quite healthy. This picture may be very different from that of a lesion undergoing spontaneous regression.

**Fig. 9** Inflammatory infiltrate more pronounced. Minimal spindle cell proliferation. (H and E × 275)

**Fig. 10** Early Kaposi's sarcoma. Inflammation still prominent, proliferation of spindle cells is evident, some vascular channels have more than one layer of cells surrounding them, and spindle cells are seen between vascular channels. (H and E × 275)
The spindle cell predominant type may be confused with tumours such as leiomyoma, leiomyosarcoma, or fibrosarcoma. The Kaposi spindle cell has a pale oval nucleus with rounded or bluntly pointed ends. One or two small nucleoli may be seen in some cells but prominent nucleoli are not a feature. Where collagen is prominent cells and their nuclei tend to be thinner and more elongated. Under light microscopy the cells may resemble smooth muscle cells quite closely. The cytoplasm of the Kaposi cell has a uniform eosinophilic, more solid appearance than that of a fibroblast, though it may not always be easy to define cell boundaries. The two most helpful features in Kaposi's sarcoma are the presence of hyaline bodies and the formation of vascular channels between spindle cells, the latter best seen where bundles of spindle cells are cut transversely. In other tumours small artefactual spaces may be seen between tumour cells. In Kaposi's sarcoma these holes are more obviously rounded channels, with the nuclei of adjacent cells curved round the edge.

The anaplastic group are more difficult to diagnose. The tumour cells themselves are more pleomorphic with fewer spindle cells. The Malawi group most often resembled haemangioendotheliosarcoma, but unless typical areas are found a wide variety of other diagnoses may be suggested.

The cause of Kaposi's sarcoma and the cell of origin are still uncertain. Electron microscopy, tissue culture, and enzyme histochemistry have not completely resolved the problem. Electron microscopy studies have led to observations of similarities to endothelial cells, pericytes, macrophages, fibroblasts, and smooth muscle cells (Hashimoto and Lever, 1964; Niemi and Mustakallio, 1965). Histochemistry has revealed an absence of staining characteristics of mature cells of many of these types. Nevertheless, the predominant characteristic of the Kaposi cells is the propensity to form vascular channels. Lothe (1963) has shown alkaline phosphatase-positive endothelial cells lining some of the dilated vascular structures adjacent to the tumour and entering into the periphery but the central solid areas of tumour were negative.

This study of biopsy specimens from Malawi confirms that most cases of Kaposi's sarcoma have an appearance distinct from other vascular or soft tissue tumours but that some cause considerable diagnostic problems. Biopsy of a very early lesion may show insufficient spindle cell proliferation to distinguish a tumour from an inflammatory lesion. This seems to be a greater problem in biopsy of lesions from Europeans. However, problems may occur if the tissue is from a too superficial part of the lesion so that the main part is missed. Ulcerating lesions may show superficially only inflammatory granulation tissue indistinguishable from granuloma pyogenicum.

Finally, in a few cases, perhaps because of multipotential capabilities of the tumour cells as well as their immaturity, vascular channel formation may be minimal and a wide variety of tumours simulated by the anaplastic variant.

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