Virchows Arch [Pathol Anat] (1985) 408:29–41

Virchows Archiv A

Multicentric angiosarcoma (Kaposi's sarcoma)

Light and electron microscopic and immunohistological findings of idiopathic cases in Europe and Africa and of cases associated with AIDS

Hans Jörg Leu and Bernhard Odermatt

Institut für Pathologie der Universität Zürich, Schmelzbergstrasse 12, Ch-8091 Zürich, Switzerland

Summary. Comparison of idiopathic Kaposi's sarcoma in Europe and Africa and Kaposi's sarcoma in connection with AIDS shows an identical morphological appearance in all three types. Ultrastructural and immunohistological investigations indicate that the tumour originates from the endothelial cells of proliferating capillaries and is therefore a vascular tumour. The clinical course and the sites of manifestation differ slightly in idiopathic cases and those occurring in connection with AIDS. This effect may be determined by the general condition of the patient, the state of immune deficiency and the influence of opportunistic infections.

Key words: Kaposi's sarcoma – AIDS – Ultrastructure – Immunohistology

Kaposi's sarcoma was first described by the Hungarian Moricz Kaposi in 1872. It is a rare multicentric skin tumour occurring in Europe and the USA. In some African countries, especially in South Africa, Tanzania and Uganda (Keen 1963; Cook 1963; Davies and Lothe 1963; Lothe and Murray 1963) this tumour occurs rather frequently and a subentity has been described in African children with involvement of lymph nodes (Davies and Lothe 1963; Lothe and Murray 1963).

In recent years the tumour has become widely known as a complication of AIDS. Its occurrence has significantly increased with the onset of the acquired immune deficiency syndrome (Curran 1983; Schwartz et al. 1983; Drew et al. 1982; Finkbeiner et al. 1982; Marmor et al. 1982). According to the literature about 30% of all clinically certified cases of AIDS are accompanied in later stages by the appearance of multicentric malignant skin tumours (Curran 1983). The histology of these lesions has been described as identical to that in idiopathic cases of Kaposi's sarcoma by Fink-

Offprint requests to: H.J. Leu at the above address

Table 1

	Idiopathic Kaposi's sarcoma 1969–1984	Kaposi's sarcoma in connection with AIDS 1983–1985
Number	4 (3 male, 1 female)	14 (all male, all homosexuals)
Age	55–77	22–65
Lethal outcome	3 (+1 in terminal state)	5
Localization		
Extremities	4	12
Thoracic wall	–	2
Gastrointestinal tract	–	4
Liver/Spleen	2	–
Lung	–	–
Lymph nodes	–	5
		3 with Kaposi's sarcoma 1 inguinal 1 axillar 1 cervical
		1 with generalized malignant lymphoma (centroblastic, diffuse, non-Hodgkin-type)
		2 with generalized lymphadenopathy (follicular hyperplasia, in one case combined with metastatic tumor tissue in one lymph node)

beiner et al. (1982). Until May, 1984 approximately 4700 cases of AIDS have been reported in USA, 360 in Europe and 30 in Switzerland (Vogt et al. 1984). According to the WHO these figures have since increased to more than 8000 in USA, 762 in Europe and more than 40 in Switzerland.

In order to elucidate the features of Kaposi's sarcoma, we performed light and electron microscopy of 14 cases occurring in connection with AIDS, of 12 idiopathic cases from Africa (collection of Prof. Rüttner, Director, Institute of Pathology, University of Zürich) and of 4 idiopathic cases from Switzerland. In some cases immunohistology was performed.

Material and methods

Our material is listed in Table 1.

Of the African cases only light microscopy could be performed and no information about age, sex and localization was obtainable. Of all the cases occurring in connection with AIDS and in one of the recent cases of idiopathic Kaposi's sarcoma in a white male of 72 years, light as well as electron microscopy and in some cases also immunohistological examinations were performed.

Routine staining procedures for light microscopy included hemalaun-eosin, van Gieson, and Gomori's stain for reticulin fibers. Electron microscopy was performed according to the routine method used at our institute: immediate fixation in phosphate-buffered glutaraldehyde, embedding in Epon 812, staining with uranyl-acetate and lead citrate, examination on a Philips EM 201.

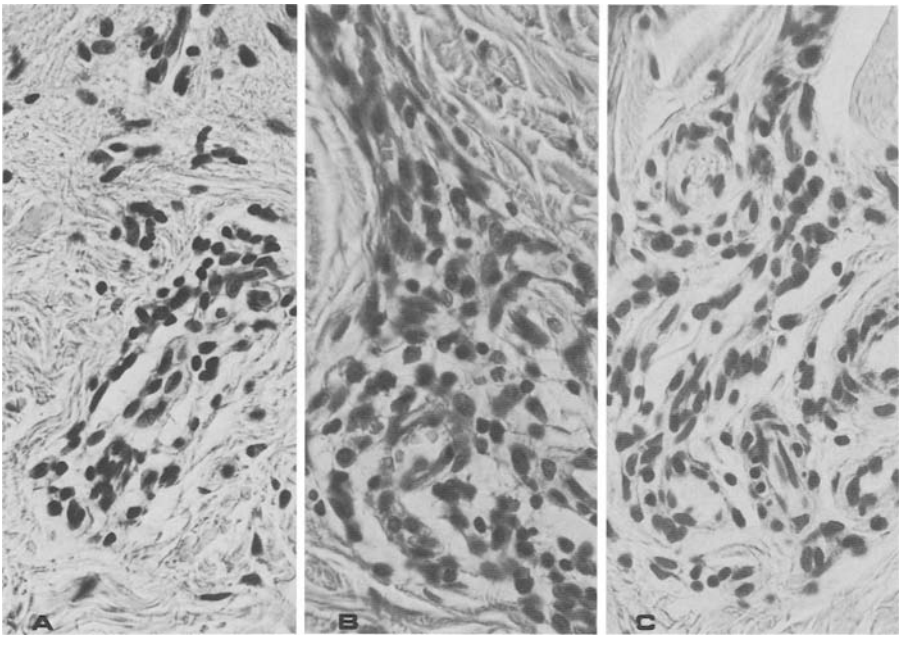

Fig. 1a–c. *Early lesions in Kaposi's sarcoma* 36 year-old homosexual with AIDS. HZ 5559/85. H & E, 300 ×. **a** Inflammatory stage with pericapillary lymphocyte infiltrate. Clear distinction between capillaries and connective tissue. Slight atypia of endothelial cells. **b** and **c** Invasion of atypical endothelial cells into surrounding tissue. Distinction of capillary walls from cell-rich surrounding tissue difficult

Immunological examinations. Staining for factor VIII and S-100 protein was performed using both Ortho and Biogenex histosets according to the manufacturers. The presence of keratin and desmin was tested by a modified method of Sternberger et al. (1970) using polyclonal rabbit antibodies against keratin, desmin (Dako) and lysozyme (Dako).

Results

Light and electron microscopy

Gross anatomy of the skin lesions shows bluish-brown, rather circumscribed patches, slightly elevated, usually 0.5–1 cm in diameter.

Light microscopy shows an intact epidermal layer. The lesions are situated in the corium, usually well separated from the epidermal layer, often circumscribed but usually ill-defined and never encapsulated, frequently spreading into the surrounding tissue. The elastic fibers of the corium are destroyed in the area of the tumour tissue. Early lesions consist of proliferating capillaries growing in the direction of the epidermal layer, mostly surrounded by some lymphocytes and plasmocytes. The endothelial cells are plump, their nuclei are enlarged, of irregular shape with dense chromatin. The reticulin sheath of the capillaries is frequently broken up and endothelial

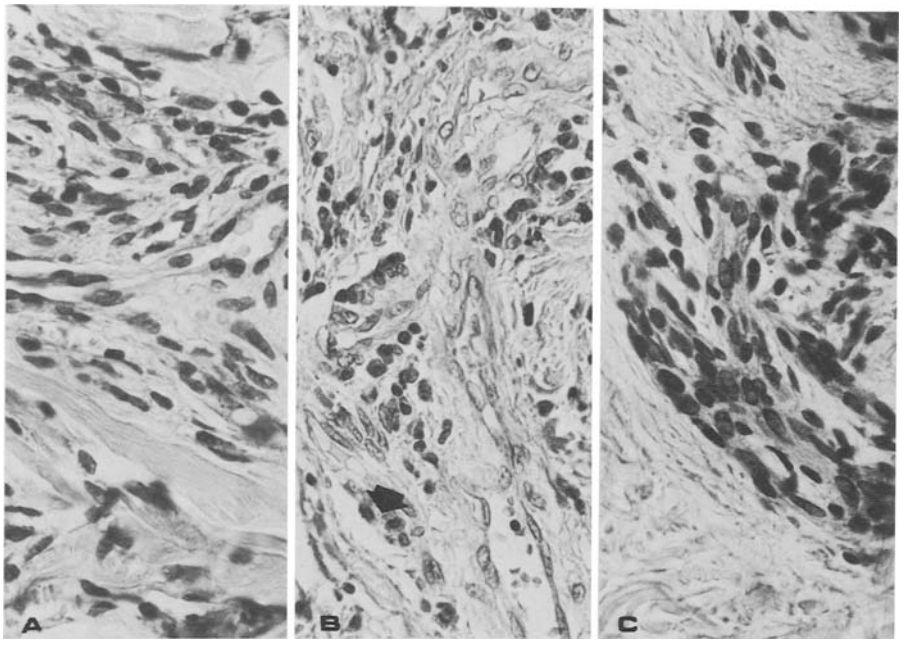

Fig. 2a–c. *Early lesions in Kaposi's sarcoma.* **a** Invasion of polymorphic, elongated tumour cells into the pericapillary tissue. 35-year-old homosexual with inguinal lymph node metastasis. HZ 24974/84. H & E, 300 ×. **b** Inflammatory cells around capillaries with proliferating endothelial cells, cell atypia and occasional mitotic figures. 50-year-old Bantu negro with skin lesions at the upper and lower extremities. HZ 10707/70. H & E, 125 ×. **c** Desintegration of the reticulin sheath and invasion of atypical endothelial cells into the surrounding tissue. 22-year-old homosexual with AIDS. HZ 6403/85. H & E, 300 ×

cells invade the surrounding tissue. Mitotic figures occur, but are infrequent (Figs. 1a–c, 2a–c). In several cases we have observed the development of such early lesions consisting solely of capillary proliferation into fully developed malignant vascular tumours of Kaposi's type. The characteristic lesions of Kaposi's sarcoma consist of three components: inflammatory cell infiltrates, proliferating capillaries with atypical polymorphous endothelial cells and a spindle-shaped cell-type around the capillaries. The angiomatous tumour component consists of vascular spaces of all sizes and shapes, lined by one to several layers of polymorphic endothelial cells which may be separated into the luminal spaces. The "stromal" tissue is built up of spindle-shaped cells with elongated blunt-ended nuclei. This tissue contains slits and clefts without endothelial lining which contain erythrocytes and deposits of haemosiderin. The mitotic rate of both these tumour cell types is low. The third component, the inflammatory infiltrate, consists of lymphocytes and plasmocytes which sometimes accompany the capillaries or may form follicular structures of even granulomatous appearance.

Histology is absolutely identical in the cases in connection with AIDS, in idiopathic cases from our country and in those from Africa (Fig. 3, 4). The same may be said of the tumour tissue occurring in visceral organs

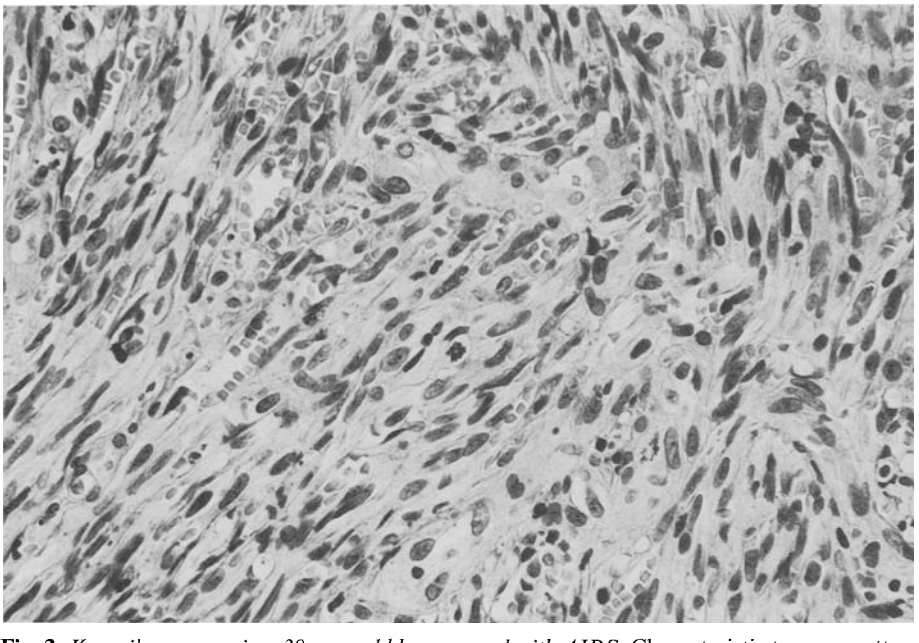

Fig. 3. *Kaposi's sarcoma in a 38-year-old homosexual with AIDS.* Characteristic tumour pattern with capillaries and "stromal" tissue of elongated cells. Several mitotic figures. HZ 3567/84. H & E, 300 ×

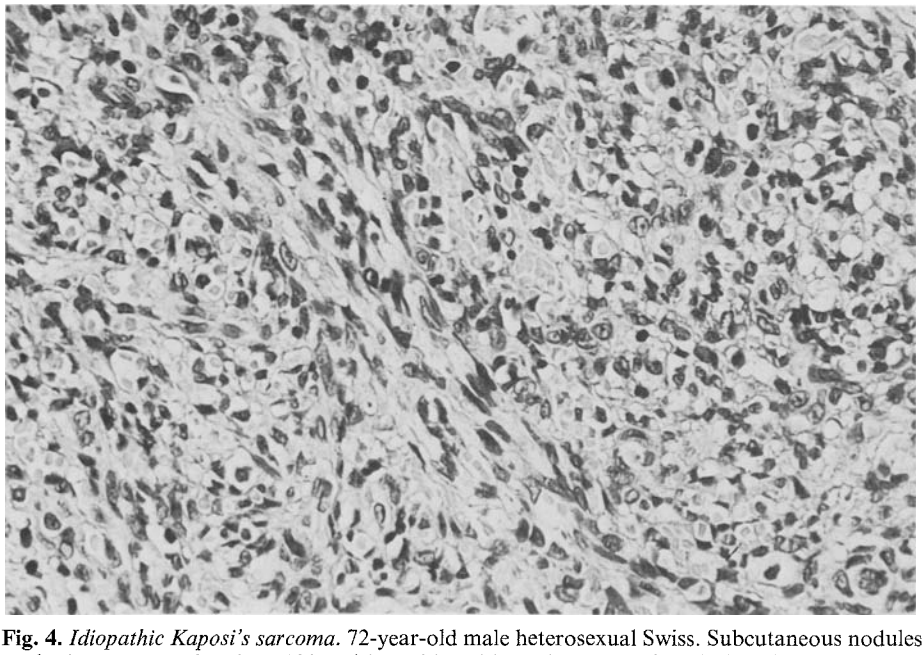

Fig. 4. *Idiopathic Kaposi's sarcoma.* 72-year-old male heterosexual Swiss. Subcutaneous nodules at the lower extremity since 1982 with rapid multicentric progression during the last months. Typical slits and clefts without endothelial lining containing erythrocytes. HZ 4352/84. H & E, 300 ×

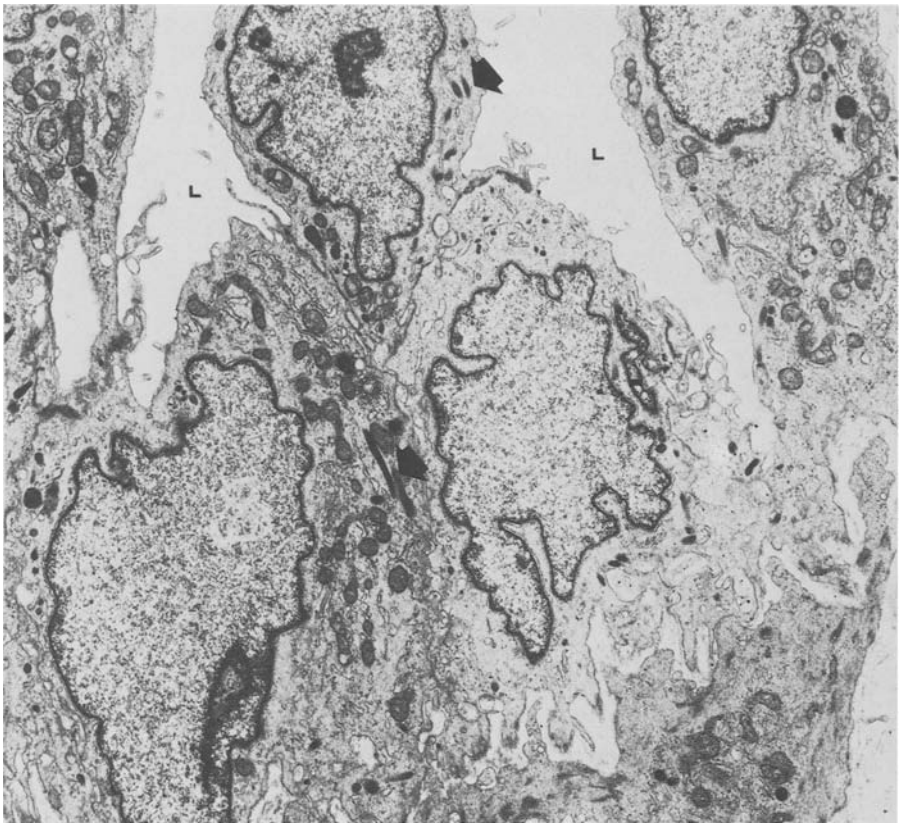

Fig. 5. *Ultrastructure of Kaposi's sarcoma.* 57-year-old homosexual with AIDS. Proliferating endothelial cells growing into the capillary lumen. Large, irregularly shaped nuclei. Typical Weibel-Palade bodies in the cytoplasm. Nr. 3692/83. Phosphate-buffered glutaraldehyde, 8400 ×, *L* = Lumen

or in lymph nodes. The only difference may be observed in the cases from Africa which may show skin tumours of advanced stages. These may be very large, rather circumscribed and may include the epidermal layer (ulceration of skin).

Electron microscopy

The capillary spaces are lined by irregular, plump, polymorphous tumour cells with enlarged nuclei of irregular shape and prominent nucleoli. These cells are often arranged in multiple layers with occasional detachment into the lumen. Characteristic endothelial organelles such as Weibel-Palade bodies, multivesicular bodies, tonofilaments, tight junctions and basement membrane are regularly found. There is no clear distinction between these endothelial cells and the cells which lie outside the vascular channels. Very

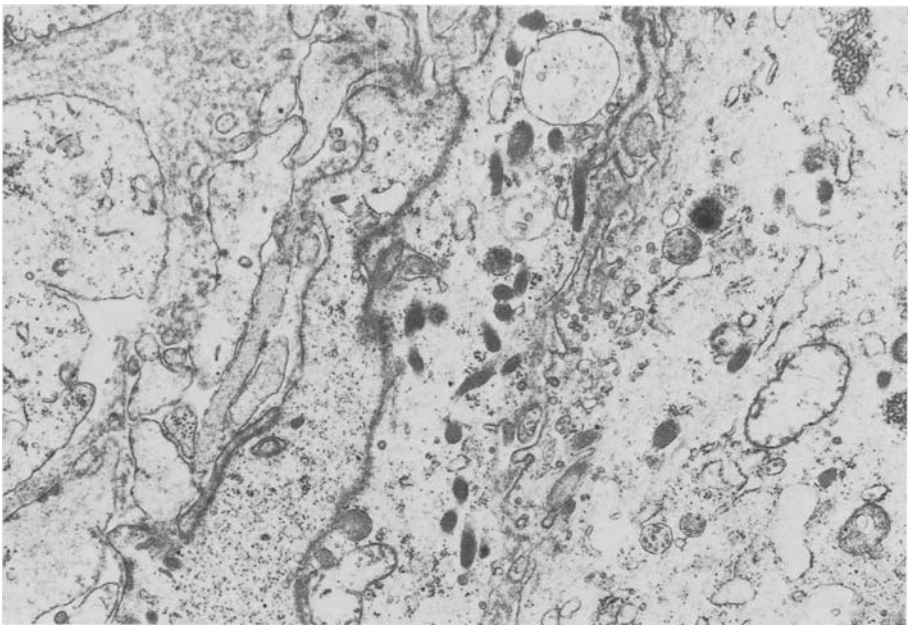

Fig. 6. *Ultrastructure of Kaposi's sarcoma.* Same case as 5) Elongated "stromal" tumor cells with Weibel-Palade bodies in the cytoplasm. Nr. 4382/84. Phosphate-buffered glutaraldehyde, 18100 ×

often the basement membrane is lacking and endothelial cells invade the perivascular area. These cells still strongly resemble endothelial cells but only rarely contain Weibel-Palade bodies. Further distant from the capillaries the tumour cells possess an elongated shape with oval or spindle-shaped blunt-ended nuclei containing a dense rim of chromatin. The cytoplasm is scarce and contains only few organelles, usually dilated rough-surfaced endoplasmatic reticulum, numerous mitochondria and free ribosomes. Mitotic activity is low. Between the "stromal" tumour cells some extravasated erythrocytes and siderophages are regularly detected. At the borders of the tumour tissue, clusters of macrophages and plasmocytes accumulate (Leu 1984) (Fig. 5–8).

The electron microscopic findings are again identical in all types of Kaposi's sarcoma.

Viral inclusions could not be detected with certainty in the tumour cells of skin, visceral and lymph node manifestations. The elongated "stromal" cells with blunt-ended nuclei resemble smooth muscle cells in the light microscope. However, electron microscopy does not reveal any characteristics of smooth muscle cells. No myofilaments of actin type with densities and attachment points, no micropinocytotic vesicles and no basement membranes suggest any relationship to smooth muscle cells. Ultrastructurally these cells outside the vascular channels do not permit an identification further than that of a "primitive mesenchymal cell". (Fig. 7, 8).

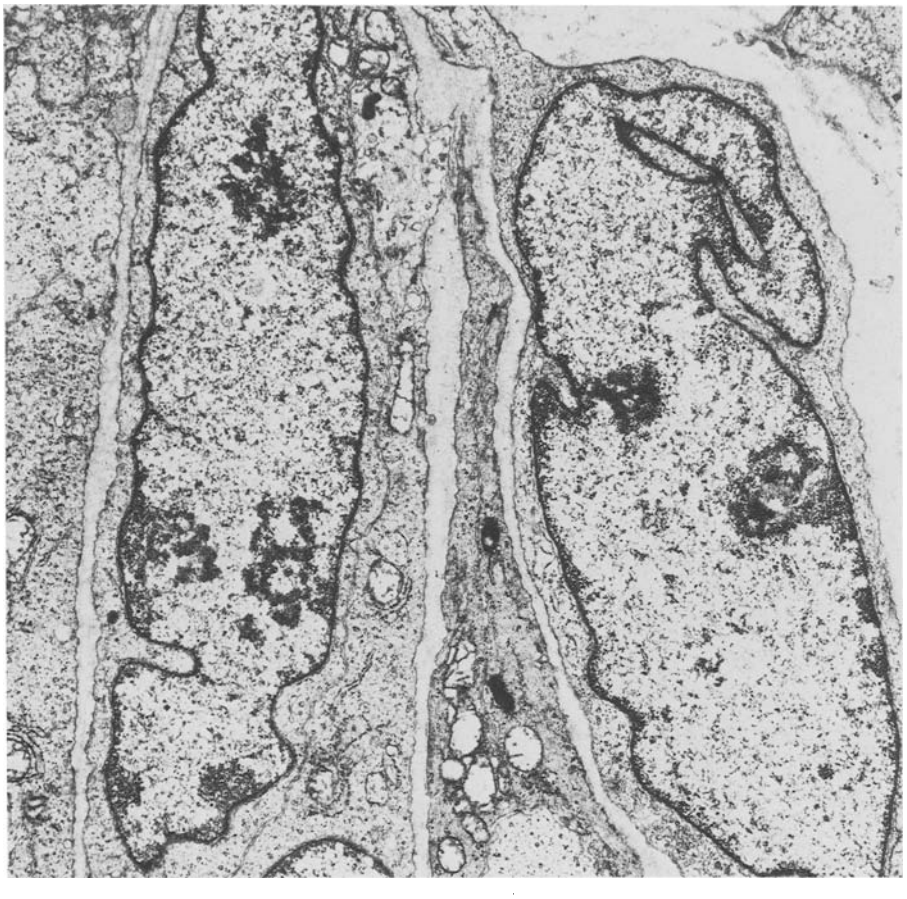

Fig. 7. *Ultrastructure of Kaposi's sarcoma.* 38-year-old homosexual with AIDS. "Stromal" tumor cells. Primitive mesenchymal cells resembling fibroblasts with irregularly shaped, blunt-ended, enlarged nuclei. No Weibel-Palade bodies. No characteristics of smooth muscle cells. Nr. 4134/84. Phosphate-buffered glutaraldehyde, 11900 ×

Immunohistology

Factor VIII is found irregularly. It is commonly present in the endothelial cells of the more or less differentiated capillaries, especially in the angiomatous parts of the tumour. It may be lacking in the cells of the solid tumour areas outside the blood vessels (spindle-shaped parts of the tumour). But even in these elongated cells within the solid tumour tissue, we have frequently found distinct presence of factor VIII, either in singular cells or in entire cell groups. The staining may be feeble or prominent.

Lysozyme is always present in some cells of the inflammatory infiltrate, of early lesions as well as of advanced cases, but negative in the actual tumour cells.

Desmin and cytokeratin are always negative in the tumour cells of clearly endothelial type as well as in the elongated "stromal" tumour cells.

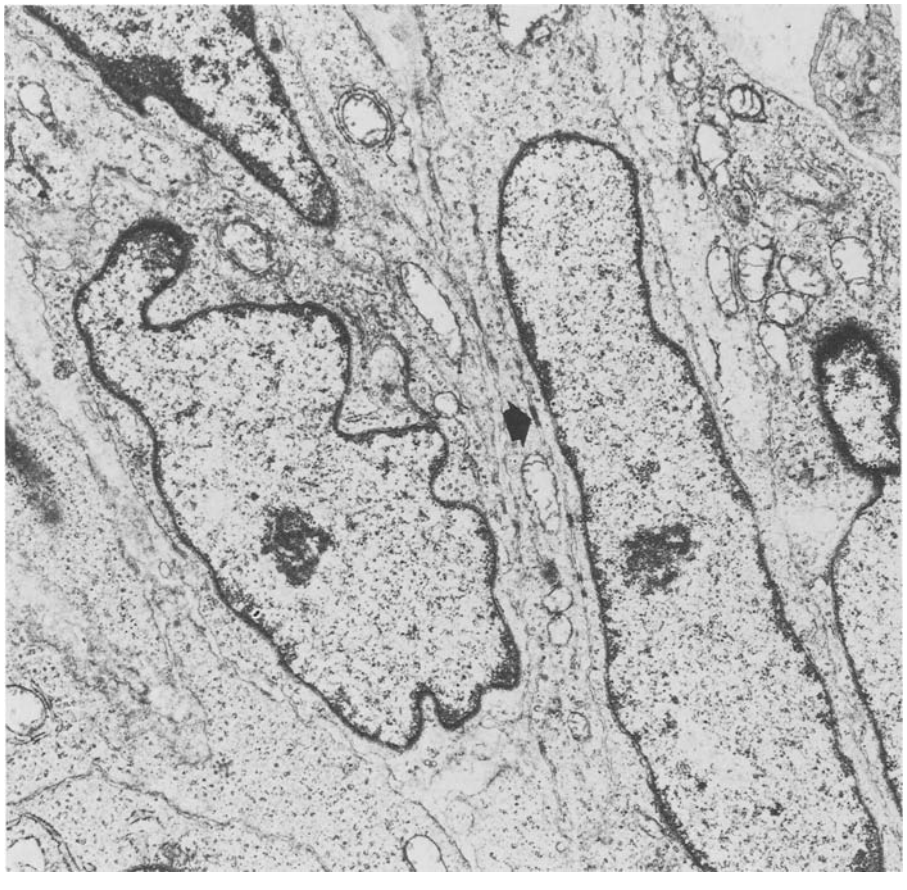

Fig. 8. *Ultrastructure of Kaposi's sarcoma.* Same case as 7) "Stromal" tumor cells: primitive mesenchymal cells without characteristics of smooth muscle cells. Very few organelles. No Weibel-Palade bodies. Occasional tight junctions indicate relationship to endothelial cells (*arrow*). Nr. 4128/84. Phosphate-buffered glutaraldehyde, 11900 ×

S-100 is constantly negative in all tumour cells. As a proof for the validity of the reactions for Desmin and S-100, we considered a positive reaction in the smooth musculature of arrectores pilorum and in nerves of the subcutaneous tissue respectively.

Clinical and epidemiological observations

Cases of idiopathic Kaposi's sarcoma in Africa include two types: Type 1 is predominant in adults. It initiates with singular or multiple skin nodules, mostly at the lower extremities. They grow at variable speed ranging from a slow progression to a fulminating course (Cook 1963). They may ulcerate. Singular nodules may even disappear spontaneously (Cook 1963). Internal involvement may occur, occasionally after as long as 20–30 years. These manifestations may be situated anywhere and metastases may occur in lymph nodes and viscera (Keen 1963, Murray and Lothe 1963). Type 2

has been described in African children. It initiates in and mostly remains restricted to lymph nodes, occular tissue and salivary glands (Davies and Lothe 1963). According to Davies and Lothe (1963) and also to our (limited) experience histology of the tumour is identical to that of skin nodules in the ordinary Kaposi's sarcoma.

Idiopathic Kaposi's sarcoma in Africa may affect any age group.

The cases of idiopathic Kaposi's sarcoma in Europe usually involve the higher age groups (50–70 years according to Rothman 1963). They also begin with with one or several nodules situated at the extremities. Growth is usually slow, metastases occur late and are preferentially localized in liver and spleen. Occasionally progression may be fast. Involution of tumour nodes has been described (Rothman 1963).

Kaposi's sarcoma in connection with AIDS has a slightly different course. It usually sets in with multiple disseminated small bluish-brown patches and spots which soon develop into nodules of usually not more than 1–2 cm. Their development and spread is fast, from the lower and/or upper extremities they soon spread on to the skin of the rump. In 4 out of our 14 cases tumours of the gastrointestinal tract developed after a short period. In one case a simultaneous malignant lymphoma of diffuse centroblastic type occurred. The internal involvement of the tumour is lethal. Internal manifestations or metastases may develop anywhere.

Discussion

Morphology of the lesions in Kaposi's sarcoma of idiopathic cases from Europe and Africa and of cases associated with AIDS is identical. This includes the primary skin lesions, the visceral manifestations and the metastases in lymph nodes and elsewhere. The histological pattern is characterized by its biphasic appearance. The primary skin manifestations are represented by multiple nodular tumours in the corium below an intact epidermal layer. The nodules may be circumscribed but not encapsulated or may be ill-defined with infiltration of the surrounding connective tissue.

The two main components consist of:

a) vascular channels with endothelial cells which contain enlarged nuclei of irregular shape proliferating into the vascular lumen as well as into the surrounding tissue through the partially destructed reticulin sheath. The ultrastructure of these cells shows all the characteristic organelles of a normal endothelial cell, i.e. Weibel-Palade bodies, multivesicular bodies, tight cell junctions and basement membrane. Immunohistology reveals the regular presence of factor VIII.

b) Intervascular "stromal" cells with spindle-shaped, blunt-ended, enlarged nuclei. Some of these elongated cells possess characteristics of endothelial cells such as Weibel-Palade bodies, tight junctions, basement membrane and factor VIII, but the majority are primitive mesenchymal cells resembling fibroblasts with scarce organelles (mitochondria, rough-surfaced endoplasmatic reticulum and ribosomes). No characteristics of smooth muscle cells such as myofilaments of the actin type with attachment points

and densities are present. Immunohistology does not indicate the presence of desmin, cytokeratin or S-100. Occasionally there are cells of similar appearance which show phagocytosis of erythrocyte fragments or siderosomes.

Further components of the tumour are: extravasated erythrocytes and haemosiderin, often lying in slits and clefts without endothelial lining, and inflammatory cells (lymphocytes and plasmocytes) often focally accumulated in the border areas of the tumour. The mitotic activity of the tumour cells is usually low to moderate.

In several cases we had the opportunity to observe the development of sarcomatous skin lesions from their very beginning as singular brown-blue spots to multicentric tumours of skin and viscera with or without lymph node metastases. Histologically the earliest visible alterations consist of proliferating capillaries in the corium with surrounding lympho-plasmocytic infiltrates. These alterations which correspond to the early inflammatory stage of Kaposi's sarcoma in Africans (Schmid 1973), do not yet indicate characteristics of a malignant tumor. The earliest symptom of neoplastic growth is indicated by enlargement of the nuclei with atypia of their shape in the endothelial cells, partial desintegration of the reticulin sheath of the capillaries and beginning invasion of endothelial cells into the surrounding tissue. At this stage the tissue between the capillaries still consists of normal collagen fibers and sweat glands. Later on the collagen fibers are replaced by a cell-rich tumour tissue of elongated cells with blunt-ended nuclei of irregular size and shape. The elastic fibers and the sweat glands of the corium have also disappeared in these areas.

It has been suggested that Kaposi's sarcoma might be a tumour of the reticulo-endothelial system (Reynolds et al. 1965; Schmid 1973; Safai and Good 1980; Safai et al. 1980; Scully 1982). The perithelial participation has been stressed by Roulet (1963). Murray and Lothe (1963) have mentioned the pericyte, the Schwann cell of the adventitia or a perivascular undifferentiated mesenchymal cell as possible source of origin of the spindle-shaped tumor cells outside the capillary channels. Modern immunohistological investigations, however, support the assumption that the tumour originates from the vascular endothelial cells. Some of the spindle-shaped tumor cells contain factor VIII. The lack of cytokeratin, desmin and S-100 excludes the derivation from epithelial, smooth muscle or Schwann cells. Two possibilities still remain: the tumour cells may originate from a primitive mesenchymal cell with partial differentiation into endothelial cells or the vascular endothelial cells may dedifferentiate into primitive tumour cells. Von Albertini (1974) believed that highly differentiated cells are not able to develop malignant neoplasias and that vascular tumours such as angiomas and angiosarcomas derivate from primitive mesenchymal tissue. The observation that endothelial cells with all the ultrastructural characteristics of this cell type invade the surrounding stromal tissue and during this process seem to loose more and more of their ability to produce factor VIII, together with the disappearance of the ultrastructural characteristics speaks more in favour of a de-differentiation of endothelial cells into malignant tumour cells.

In the cytoplasm of the tumour cells we did not detect particles which could be identified without doubt as virus. Attempts to demonstrate viral antibodies in the tumour cells by immunohistochemical reactions were not made due to the technical difficulties of such examinations.

The clinical behaviour of Kaposi's sarcoma is not universally identical. The tumours in patients suffering from AIDS are usually multicentric from the beginning. They spread with considerable speed in spite of a low mitotic activity and soon comprise the entire lower and upper extremities and also the rump. Primary manifestations may include the gastrointestinal tract and metastases in lymph nodes (mostly inguinal and axillary) may occur at an early date. The outcome is usually lethal within months. The opportunistic infections which are characteristic in these cases, are probably adding to the rapid deterioration of the condition. Of the 12 cases of AIDS which underwent autopsy at our Pathology institute, 50% did not have malignant neoplasias. The other 6 cases had Kaposi's sarcoma and one of these had an additional malignant lymphoma.

Kaposi's sarcoma in elderly Europeans without AIDS is rare. Its course is slowly progressive, the primary manifestations are less numerous and often remain restricted to the skin of the extremities for a long period. Metastases occur late and seem to be perferably localized in spleen and liver. In our four cases the clinical behaviour was that of an ordinary malignant soft tissue tumour. None of the opportunistic infections which are characteristic for AIDS have been observed.

According to the literature (Keen 1963; Rothman 1963) the behaviour of Kaposi's sarcoma in Africans is ambivalent. The tumour may cause death from internal involvement and/or metastases in a short time or may remain more or less stationary over decades. A subentity of the tumour comprises the lymph nodes of children but histologically this type of tumour is indistinguishable from the ordinary Kaposi's sarcoma (Davies and Lothe 1963). As consultants of the Pathology Institute of Tanzania, several members of our institute had the opportunity to study African cases of Kaposi's sarcoma. But apart from biopsy or autopsy material we do not possess sufficient information about clinical data to offer an opinion on the clinical behaviour of this tumour in Africans.

It is possible that here again the general condition, the state of the immune defence system and opportunistic infections may influence the duration of the disease.

It may be assumed that a common deficiency of the immune system is responsible for the development of multicentric malignant vascular tumours of Kaposi's type. The attempts to demonstrate a direct tumour induction by a virus have so far failed to give convincing and indubitable results. The fact that transplant recipients under longterm immunosuppression frequently develop malignant neoplasias is a further indication of an indirect induction. It is yet unknown whether a singular factor such as a retrovirus is causing the immune deficiency or whether different aetiological factors may initiate the disease. Opportunistic infections and the general condition of the affected individual may determine course and outcome of the disease.

Acknowledgements. We are indebted to Prof. Dr. J.R. Rüttner, Director, Institute of Pathology, University of Zürich and PD Dr. med. J. Schneider, Institute of Pathology, University of Zürich, former lecturer at the Institute of Pathology, Tanzania, for the African cases of Kaposi's sarcoma, Mrs. Irmhilt Schade for the electron microscopic preparations, Mrs. S. Homberger and Miss Ch. Dovale for immunohistological examinations (supported by a grant from the EMDO-Stiftung), Mr. Häberlin and Mr. Näf for phototechnical contributions, Mrs. S. Saremaslani for the examinations for factor VIII.

References

Albertini A von (1974) Histologische Geschwulstdiagnostik, 2nd edn. G. Thieme, Stuttgart, p 415

Cook J (1963) The clinical features of Kaposi's sarcoma in the East African Bantu, In: Ackerman LV, Murray JF (eds) Symposium on Kaposi's sarcoma, S. Karger, Basel, p 75

Curran JW (1983) AIDS-two years later. New Engl J Med 309:609–611

Davies JNP, Lothe F (1963) Kaposi's sarcoma in African children. In: Ackerman LV, Murray JF (eds) Symposium on Kaposi's sarcoma, S. Karger, Basel, p 81

Drew WL, Miner RC, Ziegler JL, Gullet JH, Abrams DI (1982) Cytomegalovirus and Kaposi's sarcoma in young homosexual men. Lancet 11:125–127

Finkbeiner We, Egbert BM, Groundwater JR, Sagebiel RW (1982) Kaposi's sarcoma in young homosexual men. Arch pathol Lab Med 106:261–264

Keen P (1963) The clinical features of Kaposi's sarcoma in the South African Bantu. In: Ackerman LV, Murray JF (eds) Symposium on Kaposi's sarcoma, S. Karger, Basel, p 67

Leu HJ (1984) Zur ultrastrukturellen Morphologie und Histogenese des Kaposi-Sarkoms bei AIDS. Vasa 13:107–113

Lothe F, Murray JF (1963) Kaposi's sarcoma. Autopsy findings in the African. In: Ackerman LV, Murray JF (eds) Symposium on Kaposi's sarcoma, S. Karger, Basel, p 116

Marmor M, Friedman-Kien AE, Laubenstein L, Byrum RD, William DC, D'Onofrio S, Dubin N (1982) Risk factors for Kaposi's sarcoma in homosexual men. Lancet 1:1083–1086

Reynolds WA, Winkelmann RK, Soule EH (1965) Kaposi's sarcoma: a clinicopathologic study with particular reference to its relationship to the reticuloendothelial system. Medicine (Baltimore) 44:419–443

Rothman S (1963) Remarks on sex, age and racial distribution of Kaposi's sarcoma and on possible pathogenetic factors. In: Ackerman LV, Murray JF (eds) Symposium on Kaposi's sarcoma, S. Karger, Basel, p 13

Roulet FCh (1963) Comments on the possible histogenesis of the cellular components of the so-called "Haemangiosarcoma Kaposi". In: Ackerman LV, Murray JF (eds) Symposium on Kaposi's sarcoma, S. Karger, Basel, p 147

Safai B, Good RA (1980) Kaposi's sarcoma: a review and recent developments. Clin Bull 10:62–69

Safai B, Miké V, Giraldo G, Beth E, Good RA (1980) Association of Kaposi's sarcoma with second primary malignancies: possible etiopathogenetic implication. Cancer 45:1472–1479

Schmid AH (1973) Kaposi's "sarcoma" – a tumor of vascular origin? Vasa 2:207–214

Schwartz RA, Kardashian JF, McNutt NS, Crain WR, Welch KL, Choy SH (1983) Cutaneous angiosarcoma resembling anaplastic Kaposi's sarcoma in a homosexual man. Cancer 51:721–726

Scully RE, Mark EJ, McNeely BU (1982) Case reports of the Massachusetts General Hospital. New Engl J Med 306:657–668

Sternberger LA, Hardy Ph Jr, Cuculis JJ (1970) The unlabeled antibody-enzyme method of immunochemistry. J Histochem Cytochem 18:315–333

Vogt M, Lüthy R, Oelz O, Ferber T, Bettex J-D, Joller H, Joller P, Frick P, Siegenthaler W (1984) Erworbenes Immunmangelsyndrom (AIDS) in der Region Zürich. Schweiz Med Wochenschr 114:1314–1326

Accepted July 8, 1985