

AN ULTRASTRUCTURAL STUDY OF AFRICAN ENDEMIC KAPOSI'S SARCOMA

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Abstract: An ultrastructural study of African endemic Kaposi's sarcoma (KS) of the skin and lymph nodes revealed an irregularity of blood vascular tissues and prominent diapedesis of erythrocytes in the early stage of the disease. In the advanced stage, incomplete blood capillary structures covered with primitive mesenchymal cells were observed. Erythrophagia was frequently seen. These results suggest that KS cells are derived from primitive mesenchymal cells which may differentiate to immature endothelial cells.

INTRODUCTION

KS is now thought to be a reversible hyperplasia at least at its inception and gradually progresses towards a true neoplasm at an advanced stage (Brooks, 1986; Itakura *et al.*, 1986). KS cells are characterized by spindle-shaped cells forming slit-like structures. On the histogenesis of KS cells, several hypotheses about original cells have been suggested by ultrastructural studies; vascular endothelial cell (Hashimoto and Lever, 1964; Ramos *et al.*, 1975), lymphatic endothelial cell (McNutt, *et al.*, 1983), Schwann cell (Pepler and Theron, 1962) and mesenchymal cell (Harrison and Kahn, 1978; Leu and Odermatt, 1985; Weich *et al.*, 1991; Kostianovsky *et al.*, 1992). However, the histogenesis of KS cells still remains obscure.

We performed an ultrastructural study of African endemic KS and discussed the histogenesis of KS cells.

MATERIALS AND METHODS

Materials:

Four cases of KS were obtained at Rift Valley Provincial General Hospital in Nakuru and Nyanza Provincial General Hospital in Kisumu, in Republic of Kenya. Clinical data and relevant information were recorded as accurately as possible.

Light microscopy:

Each specimen was prepared with hematoxylin-eosin stain (H. E.), periodic acid-Schiff reaction, Azan-Mallory's stain, and silver impregnation for reticulin fibers.

Histological growth pattern and cellularity were determined.

Ultrastructural studies:

Small pieces of formalin-fixed, paraffin embedded specimens were refixed in 2.5% glutaraldehyde, post-fixed in 2% osmium tetroxide, dehydrated in graded ethanol solutions, and embedded in Epon 812. Sections were observed with a JEM-100CX transmission electron microscope.

RESULTS

Light microscopy:

The clinical aspects and histological features of the four cases are shown in Table 1. According to the predominant histological features, two types of growth patterns; a granulation tissue type and a spindle cell/fibrosarcoma type were recognized. The former was characterized by an angioproliferative process with edema and an inflammatory cell infiltration, but less cellular (Figure 1). This type was seen in Case 1, at an early stage of the disease. The latter (in Case 2-4, at an advanced stage) was classified as a spindle cell/fibrosarcoma type. This type showed a high cellularity, but its cellular atypism and mitotic figures were not prominent (Figure 2).

Electron microscopy:

In the case of granulation tissue type, endothelial cells were arranged with no continuity and basal lamina were fragmented. Diapedeses of erythrocytes were prominent. Fibroblastic cells appeared between these capil-

Table 1 Clinicopathological findings of African Endemic Kaposi's sarcoma

Case	Age(yr)	Sex	Site of Location	Histological type	Cellularity
1	38	M	skin of leg	G	+
2	53	M	skin of leg	S	+++
3	10	M	scrotum	S	++
4	4	M	axillary lymph nodes	S	+++

G: granulation tissue-like type

S: spindle cell/fibrosarcoma-like type

laries (Figure 3). In the case of spindle cell/fibrosarcoma type, incomplete blood capillary structures were covered with the enlarged and irregular-shaped cells. The nuclei of the cells had irregular membrane with fungating

(powdery) chromatin and small nucleoli. These cells had abundant cytoplasm with few organelles and no Weibel-Palade bodies. Diapedeses of erythrocytes and erythrophagia were also observed (Figure 4).

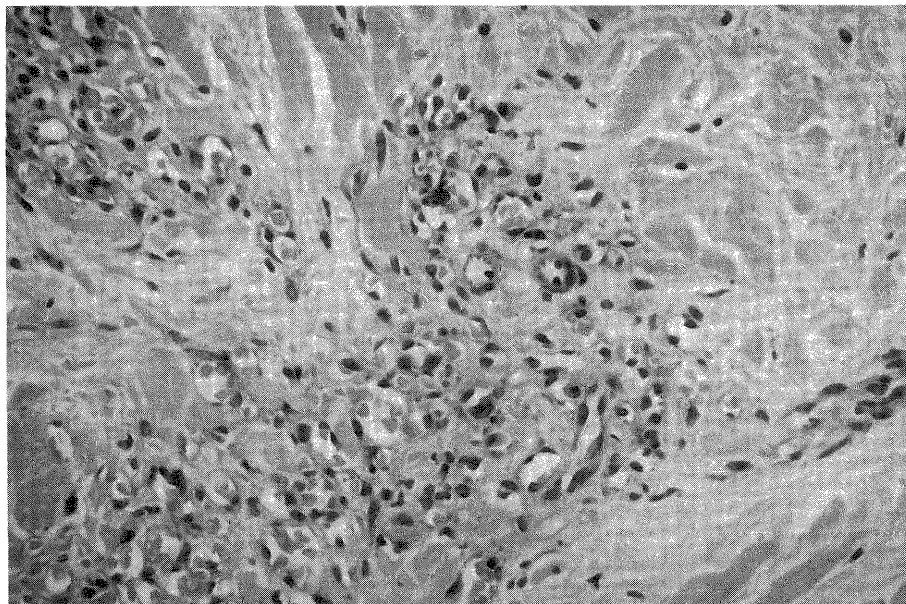


Figure 1 Case 1. Granulation tissue type of KS. The lesion is characterized by an angioproliferative process with an inflammatory cell infiltration. (H.E. $\times 100$)

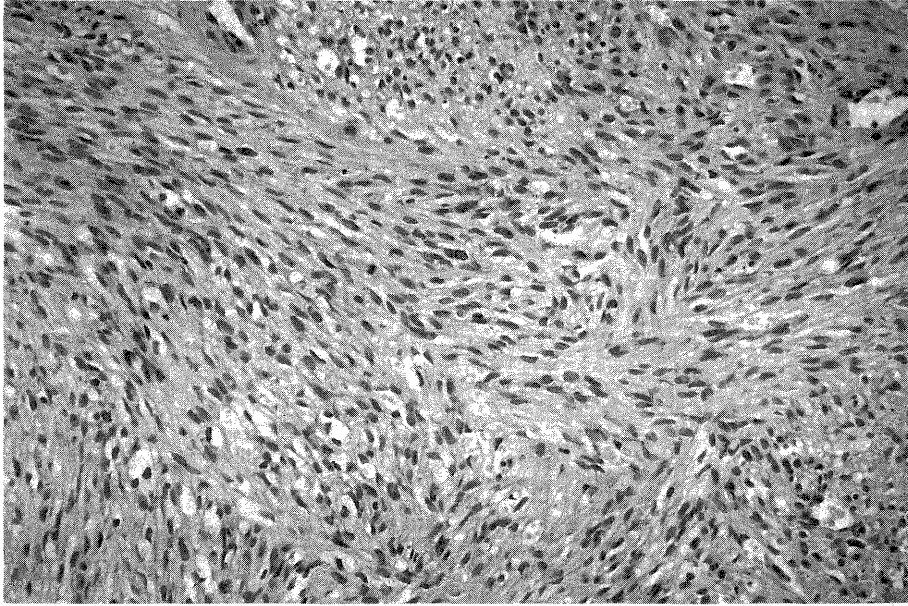


Figure 2 Case 2. Spindle cell/fibrosarcoma type of KS. The lesion is formed by interlacing bundles of spindle-shaped cells. (H.E. $\times 100$)

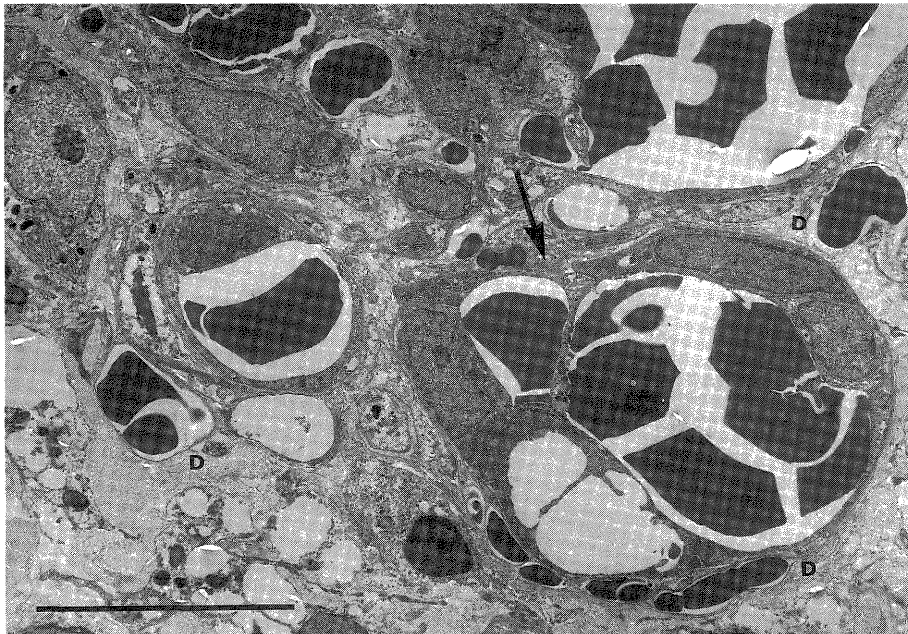


Figure 3 Case 1. Granulation tissue type of KS. Endothelial cells are arranged with no continuity (arrow). Diapedeses of erythrocytes are prominent (D). ($\times 3800$, Bar: $10\mu\text{m}$)

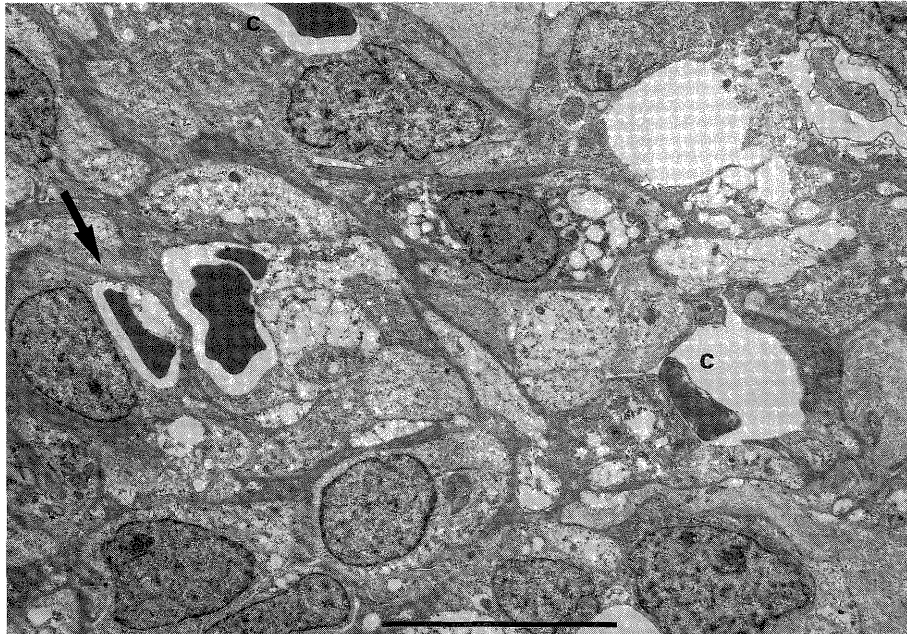


Figure 4 Case 2. Spindle cell/fibrosarcoma type of KS. Incomplete capillary structures (C) covered with enlarged and irregular-shaped cells. Erythrophagia (arrow) is characteristic. ($\times 4000$, Bar: $10\mu\text{m}$)

DISCUSSION

KS shows a wide spectrum of histological changes in the course of the disease. At an early stage, similar lesion to non-specific granulation tissue, with cutaneous edema and perivascular inflammatory cell infiltration, are characteristic. Then spindle-shaped cells appears gradually in the course of the disease. At an advanced stage, slit-like structures with characteristic spindle-shaped cells, similar structure to angiosarcoma and fibrosarcoma, are observed (Itakura *et al.*, 1986; Enzinger and Weiss, 1988). According to McNutt *et al.* (1983), ultrastructural findings of KS at an early stage revealed more prominent irregularity of vascular structure than other vascular proliferative diseases. In this study, the capillaries of KS showed fragmented basal lamina and no continuity of the endothelial arrangement. Diapedeses of erythrocytes were also prominent at an early stage. Some immune factors related to angiogenic activity, such as thymosin, interferon, lymphokines and prostaglandin, are thought to be crucial in the development of KS (Levy and Ziegler, 1983). The lesions mentioned above may be caused by some immune factors. At an advanced stage, incomplete blood capillary structures covered with enlarged and irregular-shaped cells were observed. These cells had abundant cytoplasm with few organelles and no Weibel

-Palade bodies, as occasionally seen in primitive mesenchymal cells. Erythrophagia was frequently seen. Using immunohistochemical methods we have observed that KS cells show a positive reaction for vimentin, which is a marker for mesenchymal cells, and that KS cells are partially positive for factor VIII-related antigen, which is a marker for vascular endothelial cells (Komuro and Toriyama, 1991). These results suggest that KS cells are derived from primitive mesenchymal cells which may differentiate to immature endothelial cells.

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REFERENCES

- 1) Brooks, J.J. (1986): Kaposi's sarcoma: A reversible hyperplasia, *Lancet*, 2, 1309-1310
- 2) Enzinger, F.M. and Weiss, S.W. (eds). (1988): *Soft tissue tumors*. 2nd. ed. pp. 533-544. C.V. Mosby Co. Washington
- 3) Harrison, A.C., and Kahn, L.B. (1978): Myogenic cells in Kaposi's sarcoma: An ultrastructural study, *J. Pathol.*

- ol., 124, 157-171
- 4) Hashimoto, K. and Lever, W.F. (1964): Kaposi's sarcoma: Histochemical and electron microscopic studies, *J. Invest. Dermatol.*, 43, 539-549
 - 5) Itakura, H., Toriyama, K. and Uzuta, F. (1986): Kaposi's sarcoma: Pathology and local epidemiology in Kenya, *Trop. Med.*, 28 (suppl.), 3-8
 - 6) Komuro, S. and Toriyama, K. (1991): Geopathology of endemic pediatric lymph node Kaposi's sarcoma in western Kenya, *Jpn. J. Trop. Med. Hyg.*, 19, 251-263
 - 7) Kostianovsky, M., Lamy, MAJ. Y. and Greco, M.A. (1992): Immunohistochemical and electron microscopic profile of cutaneous Kaposi's sarcoma and bacillary angiomatosis, *Ultrastruct. Pathol.*, 16, 629-640
 - 8) Leu, H.J. and Odermatt, B. (1985): 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, *Virchows. Archiv. A.*, 408, 29-41
 - 9) Levy, J.A. and Ziegler, J.L. (1983): Acquired immunodeficiency syndrome is an opportunistic infection and Kaposi's sarcoma results from secondary immune stimulation, *Lancet.*, 1, 78-80
 - 10) McNutt, N.S., Fletcher, V. and Conant, M.A. (1983): Early lesion of Kaposi's sarcoma in homosexual men: An ultrastructural comparison with other vascular proliferations in skin, *Am. J. Pathol.*, 111, 62-77
 - 11) Pepler, W.J. and Theron, J.J. (1962): An electron microscope study of Kaposi's haemangiosarcoma, *J. Path. Bact.*, 83, 521-525
 - 12) Ramos, C.V., Taylor, H.B., Hernandez, B.A. and Tucker, E.F. (1975): Primary Kaposi's sarcoma of lymph nodes, *Am. J. Clin. Pathol.*, 66, 998-1003
 - 13) Weich, H.A., Salahuddin, S.Z., Gill, P., Nakamura, S., Gallo, R.C. and Folkmann, J. (1991): AIDS-associated Kaposi's sarcoma-derived cells in long-term culture express and synthesize smooth muscle alpha-actin, *Am. J. Pathol.*, 139, 1251-1258