AN ULTRASTRUCTURAL STUDY OF AFRICAN ENDEMIC KAPOSI'S SARCOMA

HIDEAKI ETO, KAN TORIYAMA and HIDEYO ITAKURA
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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 diaphoresis 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.

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

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>Site of Location</th>
<th>Histological type</th>
<th>Cellularity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>38</td>
<td>M</td>
<td>skin of leg</td>
<td>G</td>
<td>+</td>
</tr>
<tr>
<td>2</td>
<td>53</td>
<td>M</td>
<td>skin of leg</td>
<td>S</td>
<td>+++</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>M</td>
<td>scrotum</td>
<td>S</td>
<td>++</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>M</td>
<td>axillary lymph nodes</td>
<td>S</td>
<td>+++</td>
</tr>
</tbody>
</table>

G: granulation tissue-like type  
S: spindle cell/fibrosarcoma-like type

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

Figure 3 Case 1. Granulation tissue type of KS. Endothelial cells are arranged with no continuity (arrow). Diapedeses of erythrocytes are prominent D. (×3800, Bar: 10μm)
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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