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Case report

Kaposi's sarcoma and malignant lymphoma in AIDS

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Summary. A 48-year-old homosexual with contacts in different countries, including Haiti, presented with multiple pigmented or bluish nodules on both lower legs and upper arms. He had a history of secondary syphilis, hepatitis B and herpes zoster ophthalmicus. Biopsies of the skin tumors revealed a typical Kaposi's sarcoma of low grade malignancy. The endothelial origin of the tumor was indicated by the presence of specific endothelial organelles (Weibel-Palade bodies) in the cytoplasma of the tumor cells. Erythrocytophagocytosis was found in tumor cells within and without the vascular channels. Laboratory tests were compatible with the clinical diagnosis of an acquired immune deficiency syndrome (AIDS) with a helper: suppressor T-lymphocyte ratio of 0.28 and a cutaneous anergy. In the course of the illness tumors of the stomach and duodenum were detected. Histology showed a malignant non-Hodgkin lymphoma of high grade malignancy. Within weeks the patient died in a cachectic state. Autopsy revealed a Kaposi's sarcoma of the skin with metastases in the stomach and a wide-spread malignant lymphoma in the gastrointestinal tract, in several visceral organs and in many lymph nodes.

Key words: AIDS – Kaposi's sarcoma – Malignant lymphoma – Malignant tumors in AIDS

Kaposi's sarcoma, a multicentric haemorrhagic skin tumor, was first described by the Hungarian M. Kaposi (1872). Until recently the tumor was rare in Europe and the United States (Oettle 1962; Rothman 1962) but frequent in some African countries (Lothe and Murray 1963). Safai et al. (1980) reported a 3:1 male-to-female ratio and a mean age of 63 years. The tumor was usually restricted to the lower extremities, its progression was slow and lymph node involvement was late. In African countries, how-

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ever, the tumor comprises up to 9% of all malignancies, children and young adults are frequently involved and early progression into lymph nodes and viscera is common (Finkbeiner et al. 1982).

In the last 3 years multicentric malignant skin tumors have been observed with increasing frequency in connection with the acquired immune deficiency syndrome (AIDS) (Drew et al. 1982; Durack 1981; Finkbeiner et al. 1982; Gottlieb et al. 1981; Hymes et al. 1981; Marmor et al. 1982; Safai and Good 1980; Schwartz et al. 1983). Special risk groups are both homosexuals and bisexuals, occasionally also drug addicts (Gold et al. 1982) and patients with haemophilia. An accumulation of cases has been observed in Haitians (Curran 1983). The histological findings are identical to those found in Kaposi's sarcoma of the Africans (Finkbeiner et al. 1982). Non-specific lymphadenopathy as well as lymph-node involvement by the tumor is frequent in these cases (Guarda et al. 1983). Kaposi's sarcoma alone or in combination with tumors of the reticulo-endothelial system is also known to exist in patients under long-term immunosuppressive therapy (Klepp et al. 1978; Gange and Jones 1978).

Case report

A 48-year-old patient presented in November 1982 with small pigmented skin nodules on the left lower leg. He had a history of secondary syphilis. Laboratory tests revealed liver cirrhosis due to hepatitis B and to chronic alcohol consumption. The man had had homosexual contacts with different partners, among other places also in Haiti. He suffered from intermittent bouts of fever and had an elevated blood sedimentation rate. In April 1983 a necrotizing herpes zoster of the face with ophthalmic involvement developed. During spring and summer of 1983 the skin nodules increased in size and number, became painful and confluent and spread on both legs and both upper arms. Biopsy of one of the skin tumors revealed a Kaposi's sarcoma (see below). The patient was subsequently admitted to the Department of Medicine, Medizinische Poliklinik, University Hospital of Zürich. Upper gastrointestinal endoscopy revealed multiple tumours in the stomach and duodenum. Biopsy of these tumours showed a malignant lymphoma of non-Hodgkin type (findings see below). The laboratory tests confirmed the suspected diagnosis of an AIDS: elevated blood sedimentation rate, anaemia, cutaneous anergy and a helper: suppressor T-lymphocyte ratio of 0.28.

Histology

Light microscopy (HZ 18905/83 and 20200/83)
(Stains: Haemalaun-Eosin, PAS, van Gieson, Elastin and Gomori's silver stain for reticulin.)

Below the intact epidermal layer lie irregulary shaped nodular areas of a cell-rich tissue without clearly defined borders. Proliferating capillaries, small vessels, singular tumour cells and sprouts of tumour cells are lying between coarse dermal collagen bundles together with haemorrhages, haemosiderin deposits, extravasated erythrocytes and inflammatory infiltrates of lymphocytes and plasma cells. The capillaries and small vessels are lined by proliferating, prominent and occasionally multilayered endothelial cells, but there are also non-endothelialized slits and clefts containing erythrocytes. The tumour cells lining the capillaries as well as most of the cells outside the blood vessels contain pale, large, oval, polymorphic nuclei with prominent nucleoli. Mitotic figures are rarely seen. Reticulin stains show the vascular character of the tumor, the proliferating endothelial tumor cells are situated within the reticulin sheath. The elastin stains show destruction of the elastic fibers of the corium within the tumour area. No mucopolysaccharides are present in the PAS stains (Figs. 1–4).

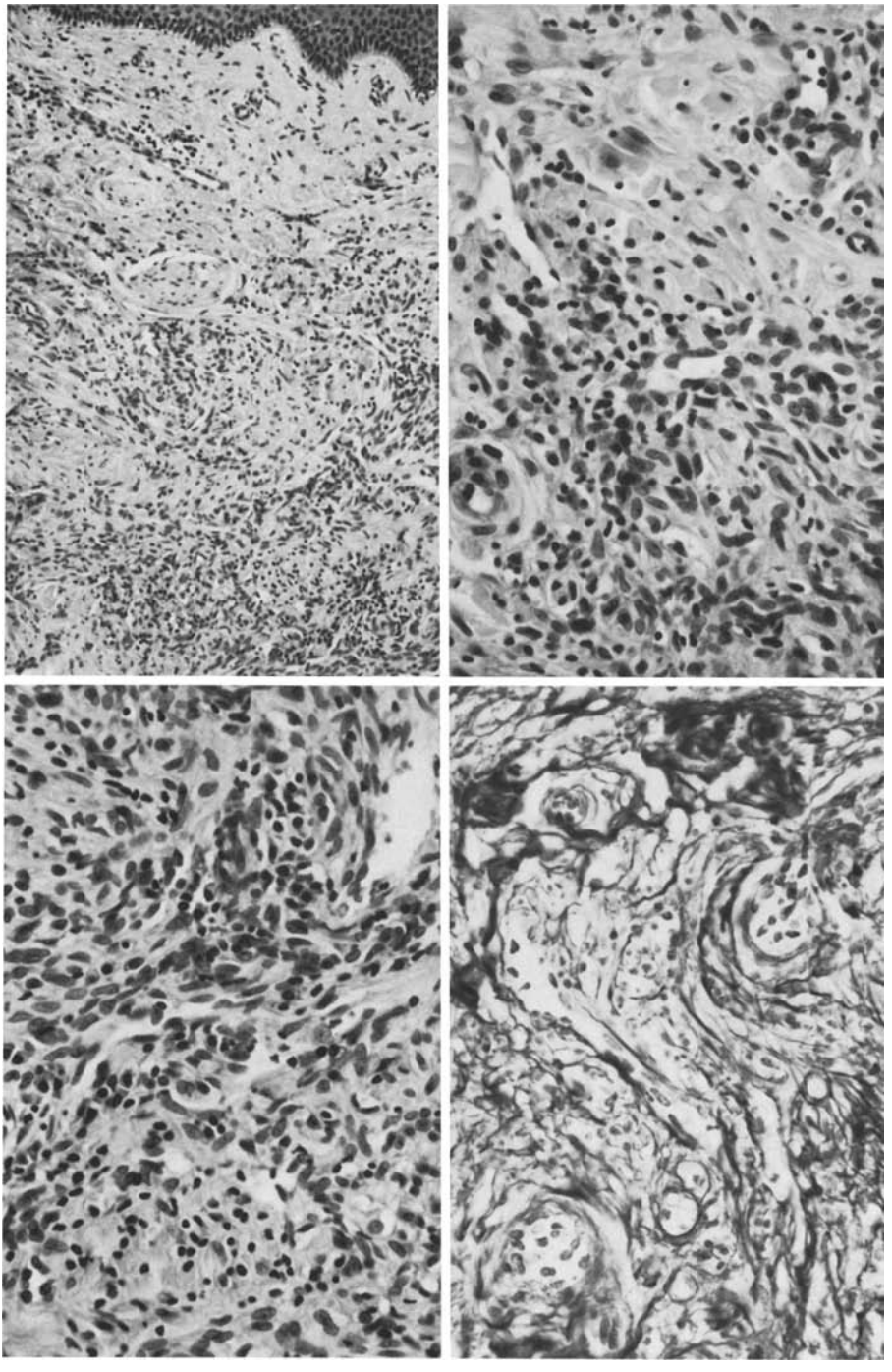

Fig. 1. Infiltrating vascular proliferation with surrounding inflammatory infiltrates in the subcutis. HZ 18905/83. H&E, ×125

Fig. 2. Tumor cells with large pale nuclei and prominent nucleoli lining the capillary channels or lying in the stromal tissue. HZ 18905/83. H&E, ×300

Fig. 3. Tumor tissue consisting of vascular channels and of slits and clefts without endothelial lining. HZ 20200/83. H&E, ×300

Fig. 4. Tumor cells within and without the reticulin sheath of the vascular structures. HZ 20200/83. Gomori's silver stain, ×300

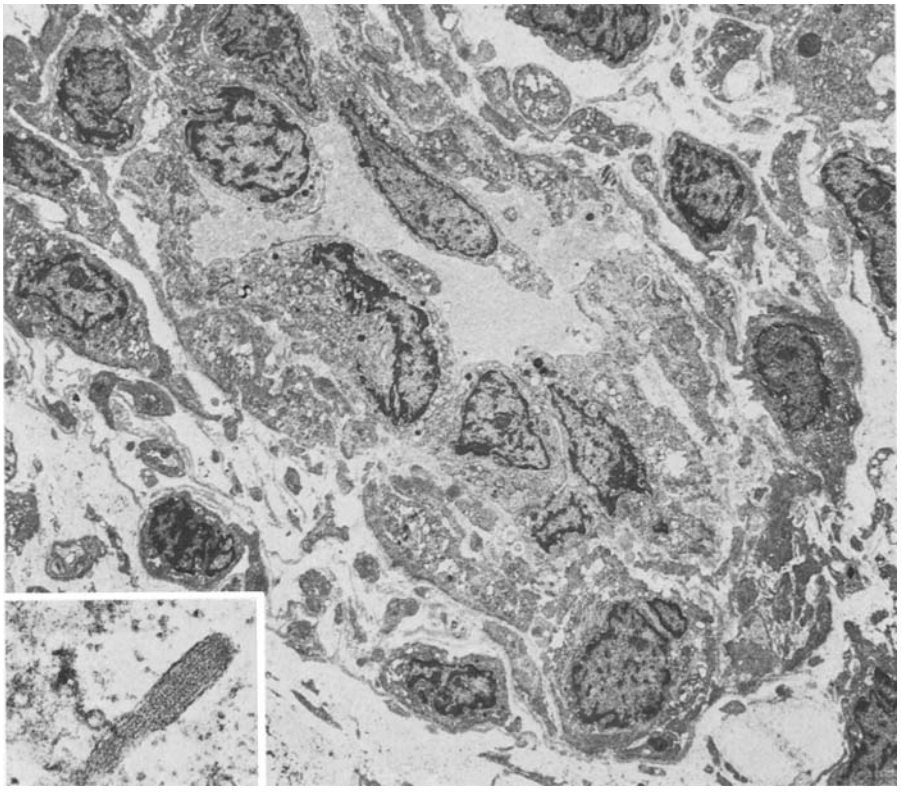

Fig. 5. Capillary with proliferating endothelial cells. The same tumor cells occur outside the vascular channels. Phosphate-buffered glutaraldehyde. Nr. 3554/83, ×2,600. *Inset:* Weibel-Palade body in the cytoplasm of a tumor cell outside of a vascular channel. Phosphate-buffered glutaraldehyde. Nr. 3549/83, × 53,000

Electron microscopic findings

The tumour consists of a network of capillary spaces with proliferating endothelial cells and distinct basement membrane. The endothelial cells are frequently multilayered with tumour cells detaching themselves into the vascular lumen. Similar cells are dispersed in the stromal tissue between the vascular channels, together with fibroblast-like and macrophage-like cells, extravasated erythrocytes and inflammatory cells. Erythrophagocytosis is observed mainly within the stromal tissue. The tumor cells are polymorphic with scarce cytoplasm and large nuclei. The nuclei are polymorphic, frequently of bizarre shape and contain single prominent nucleoli. Mitotic figures are extremely rare. The cytoplasm contains swollen mitochondria, glycogen, polyribosomes, rough endoplasmatic reticulum, secondary lysosomes, siderosomes, occasionally micropinocytotic vesicles, multivesicular bodies, tonofilaments and phagocytosed fibrin. A basement membrane occurs in some of the tumour cells. Specific endothelial organelles (Weibel-Palade bodies) are found in the cytoplasm of endothelial tumour cells, occasionally also in tumour cells outside the vascular channels (Fig. 5).

Light microscopy of endoscopic biopsies from the stomach and duodenum (PD Dr. R. Maurer) show fragmented mucosa with diffuse infiltration in the lamina propria of lymphoid cells

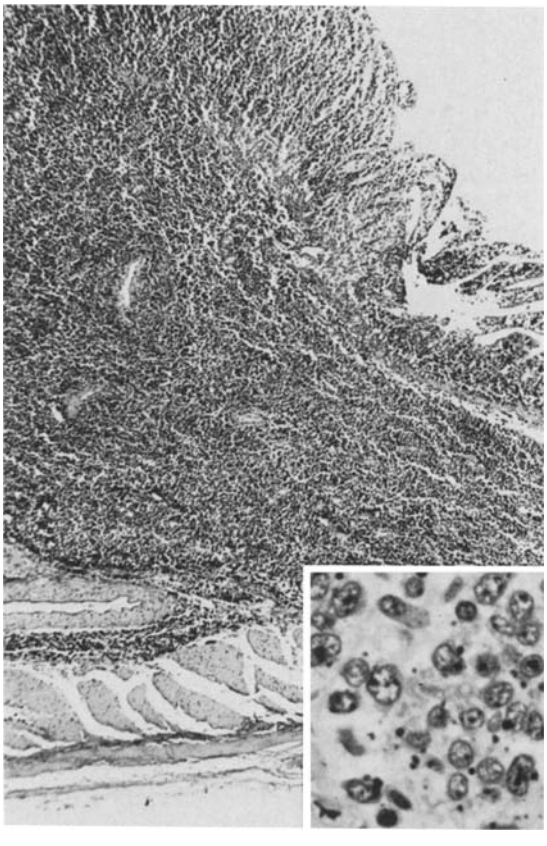

Fig. 6. Malignant non-Hodgkin lymphoma of diffuse centroblastic type in the stomach. AZ 1357/83. Haemalaun-Eosin, ×35. *Inset:* Lymphoid tumor cells with marginated chromatin. AZ 1357/83. H&E, ×500

partly obliterating the glandular structures and also penetrating the lamina muscularis mucosae. The infiltrate is composed of rather uniform cells with round nuclei, vesicular chromatin and multiple sometimes marginated nucleoli. The cytoplasm is distinct but forms only a small rim (Fig. 6).

Histological diagnosis

Multicentric malignant vascular proliferations of low grade malignancy (Kaposi's sarcoma) of the skin.

Malignant non-Hodgkin lymphoma of diffuse centroblastic type and high grade malignancy of the stomach and duodenum.

Further course of the disease

In spite of therapy by interferon infusion the patient died within weeks in a cachectic state. The autopsy findings confirmed the biopsy diagnosis. Infiltration by malignant lymphoma was found in the right and left atrium, pleura, pancreas, stomach, duodenum, ileum, colon, retroperitoneum, thyroid and in lymph nodes (axillar, supraclavicular, inguinal, parapancreatic, parahepatic and paraaortic). Kaposi's sarcoma was detected in the skin, but also in the submucosa of the stomach. In some of the lesions in the stomach both tumours were adjacent without definite separation but with clearly distinctable tumor cell types.

Discussion

The patient's history, clinical course and laboratory tests are compatible with the current definition of AIDS. Histology of the skin tumors shows vascular proliferations with infiltrating growth. The malignant nature of the alterations is indicated by the pleomorphism of cells and nuclei, size of the nuclei in relation to the cytoplasm, prominent nucleoli, occurrence of multilayered endothelia, erythrocytophagocytosis by tumor cells and infiltrative growth of the lesions. Mitotic figures are rare. However, this is not uncommon in Kaposi's sarcoma (Finkbeiner et al. 1982).

The tumour is clearly of vascular origin. Some authors have discussed a possible reticulo-endothelial origin of the tumor, since certain relations to lymphatic malignancies exist (Schmid 1973; Reynolds et al. 1965; Safai and Good 1980; Safai et al. 1980; Scully 1982). The light as well as the electron microscopic findings in this (and in two further cases which we have recently seen) contradict this opinion. The tumor cells line erythrocyte-containing channels and are phagocytic. The cells inside the vascular spaces and some of those in the dermal stroma contain specific endothelial organelles (Weibel-Palade bodies). Furthermore Guarda et al. (1981) have proved the endothelial nature of the tumour cells by demonstration of factor-VIII-related antigen. Erythrocytophagocytosis has also been observed by Schwartz et al. (1983). Tubuloreticular structures in the cytoplasm of tumor cells which have been considered as specific by Sidhu et al. (1983), however, are found in a variety of disorders and lack specificity as markers of disease (Rozman and Feliu 1983; Ewing et al. 1983).

The neoplastic nature of generalized Kaposi's sarcoma has been doubted by Costa and Rabson (1983). Many well documented cases, however, have demonstrated the occurrence of metastases in lymph nodes and viscera (Curran 1982; Curran 1983; Pietra 1983). Also in our case, metastases of Kaposi's sarcoma were detected in the stomach at autopsy. Spontaneous regression of tumor nodes has indeed been observed in the classical Kaposi's sarcoma (Bart and Kopf 1982). To our knowledge spontaneous regression of skin tumors in AIDS has not yet been reported. Remissions under vinblastine therapy have been described (Solan et al. 1981).

Malignant lymphomas are seen with increasing frequency in transplant recipients treated by immunosuppressive drugs and in patients with autoimmune diseases (Lupus erythematodes and Sjögren's syndrome). They have also been reported in relation with the classical Kaposi's sarcoma (Reynolds et al. 1965, Beylot et al. 1977; Weshler et al. 1979; Safai and Good 1980; Safai et al. 1980; Massarelli et al. 1982; Carbone and Volpi 1983). Combination of Kaposi's sarcoma and malignant lymphomas in AIDS have recently been reported by Perlow et al. (1983) and Reichert et al. (1983). Possible interactions between these two distinctly different types of tumors are not yet clarified.

With the increasing fequency of AIDS throughout the world, pathologists will have to be aware of the possibility of Kaposi's sarcoma and/or malignant lymphomas in patients with deficient immune response.

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