

## Electron Microscope Observation of Eosinophilic Globules in Kaposi's Sarcoma

Masachika SENBA and Hideyo ITAKURA

*Department of Pathology, Institute for Tropical Medicine,  
Nagasaki University, Nagasaki 852 Japan*

**Abstract:** The authors previously presented two cases of eosinophilic globules in the cutaneous type of Kaposi's sarcoma by light microscope. The globules were stained with periodic acid Schiff (PAS), with periodic acid Schiff (PAS) reagent after diastase digestion, and with phosphotungstic acid hematoxylin (PTAH). Their shapes were very similar to glycoprotein globules of yolk sac tumor (endodermal sinus tumor) in the tissues of the ovary and testis. Further, we developed observation of the globules by electron microscope. The cause of the glycoprotein globule accumulation is not clear. It seems unlikely that they play an important role in the pathogenesis of the Kaposi's sarcoma.

**Key words:** Kaposi's sarcoma, Eosinophilic globules, Glycoprotein globules, Diastase-resistant, Acquired immunodeficiency syndrome (AIDS).

Kaposi's sarcoma (initially called a multiple idiopathic pigmented sarcoma of the skin, later called a multiple idiopathic hemorrhagic sarcoma) was first described by the Hungarian M. Kaposi (1872). The early (patch) stage of Kaposi's sarcoma (KS) is recognized by the presence of increased numbers of vascular spaces that are irregular in shape, and are surrounded by a sparse mononuclear cell infiltrate. The later (plaque) stage is characterized by increasing numbers of abnormally shaped vessels, and the presence of atypical spindle cells within the dermis in close association with reticular dermal collagen. The nodular stage is essentially a spindle cell neoplasm in which irregular vessels with jagged outlines are no longer prominent (Ackerman, 1979; Blumenfeld *et al.*, 1985).

Recently the KS is well known worldwide, for the acquired immunodeficiency syndrome (AIDS) is known to occur among homosexual men, often in association with opportunistic infections, is now well established (Durack, 1981; Fauci, 1982). Black Africans from Central Africa might be another high-risk group (Clumeck *et al.*, 1984;

---

Received for publication, May 7, 1985.

Contribution No. 1648 from the Institute for Tropical Medicine, Nagasaki University.

Downing *et al.*, 1984; Perre *et al.*, 1984). To evaluate AIDS in Equatorial Africa a prospective study was done in Rwanda (Perre *et al.*, 1984), Zaire (Clumeck *et al.*, 1984) and Zambia (Downing *et al.*, 1984), where KS is endemic. The pathogens of AIDS patients infected opportunistically are as follows: candidiasis, cryptococcosis, criptosporidiosis, *Pneumocystis carinii* pneumonia, toxoplasmosis, herpes simplex virus (HSV), cytomegalovirus (CMV), Epstein-Barr virus (EBV), hepatitis B virus (HBV), and human T-cell leukemia virus (HTLV). African KS is associated with immunodeficiency (Taylor and Ziegler 1974), and they decreased T helper/T suppressor and 2 of those were also lymphopenia (Downing *et al.*, 1984).

The authors previously reported two cases of eosinophilic globules in the cutaneous type of Kaposi's sarcoma (Senba *et al.*, 1984) and its materials investigated by light microscopic technique. Further, we have developed observation of the these globules by electron microscopic technique.

Two cases of eosinophilic globule specimens were used for electron microscopic observation. These materials were obtained from resected human subjects at Rift Valley Provincial General Hospital in Kenya. Tissue blocks from the Kaposi's sarcoma including eosinophilic globules were fixed in 10% formalin, and post-fixed in phosphate-buffered 1% osmium tetroxide, serially dehydrated in ethanol, embedded in Poly/Bed-812 (Polyscience, Lot. 00431) and sectioned with glass knives on a LKB 2088 (Bromma) ultramicrotome. Thick sections for light microscopy were stained with alkaline toluidine blue (Toluidine blue: Merck, Art. 1273, Lot. 4101994) and used for histological examination of eosinophilic globule lesions. Ultrathin sections were stained with uranyl acetate and lead citrate and examined with a Nihondenshi 100 CX electron microscope.

Periodic acid Schiff (PAS) positive, periodic acid Schiff (PAS) reagent after diastase digestion positive and phosphotungstic acid hematoxylin (PTAH) positive globules in Kaposi's sarcoma were investigated by electron microscope. Blackish globules of different size were observed (Fig. 1).

The glycoprotein globules of yolk sac tumor (endodermal sinus tumor) in the ovary and testicle (Kurman and Norris, 1976 a, b; Shirai *et al.*, 1976; Wold *et al.*, 1984) were very similar to such globules in the tissue of Kaposi's sarcoma. The globules of "marker chemicals" are easily identified in PAS stained sections. However, not all of these globules were stained positively by immunohistochemical techniques for alpha-fetoprotein (AFP), human albumin, beta-subunit of human chorionic gonadotropin, or alpha-l-antitrypsin (Kurman and Norris, 1976a; Shirai *et al.*, 1976; Wold *et al.*, 1984). Another possible explanation for their lack of staining is that the immunologically active sites are masked as a result of "packaging" in the glycoprotein globules (Wold *et al.*, 1984).

Similar globules in the liver have been extensively described in previous reports (Anderson *et al.*, 1961; Aterman, 1958; Bull *et al.*, 1958; Eger *et al.*, 1958; Fisher and Fisher, 1954; Gurd and Vars, 1949; Kettler, 1948; Nairn *et al.*, 1958; Popper *et al.*, 1960; Trowell, 1946; Wold *et al.*, 1941). Evidence that the globules might originate from

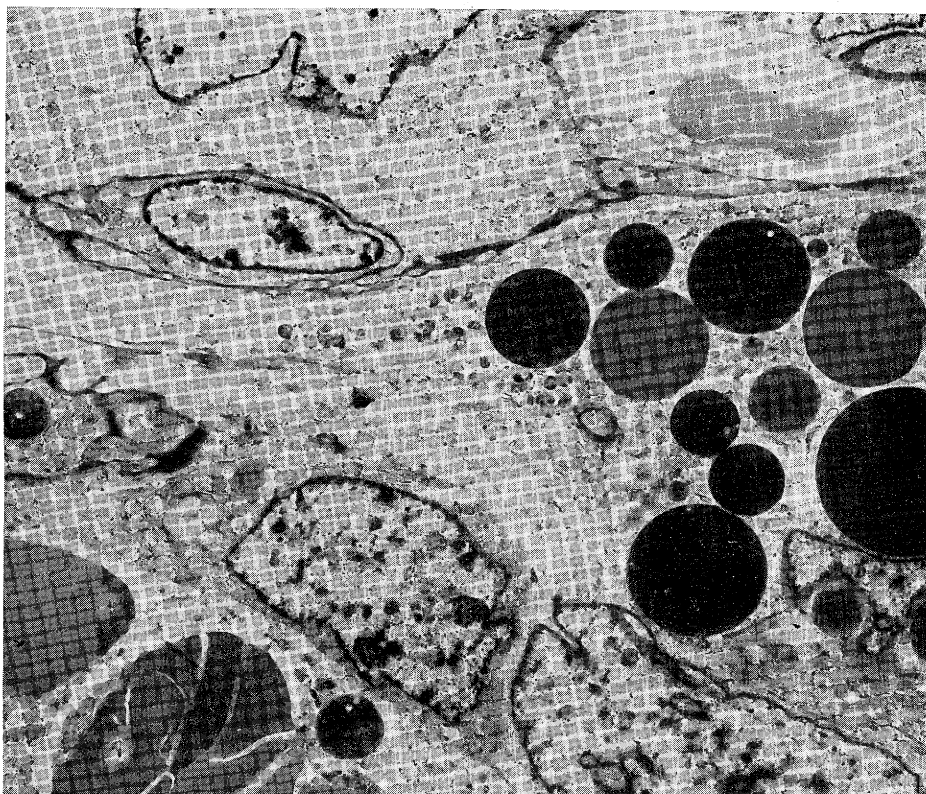


Fig. 1. Ultrastructure of glycoprotein globules are seen in the cutaneous type of Kaposi's sarcoma tissue,  $\times 6,600$ .

imbibition of serum proteins has been presented (Nairn *et al.*, 1958; Pfeifer and Bannasch, 1968). Condensation of serum proteins in the globules and lysosomal activity of hepatocytes, may determine the intensity of PAS positive and also of eosinophilia (Pfeifer and Bannasch, 1968).

#### ACKNOWLEDGEMENTS

The authors thank Professor Takao Setoguti, Department of Anatomy, Nagasaki University School of Medicine, Professor Masahiko Koike, Department of Pathological Biochemistry, Atomic Disease Institute, Nagasaki University School of Medicine, and Associate Professor Yutaka Okumura, Department of Radiation Biophysics, Atomic Disease Institute, Nagasaki University School of Medicine, for helpful advice.

## REFERENCES

- 1) Ackerman, A. B. (1979): Subtle clues to diagnosis by conventional microscopy: The patch stage of Kaposi's sarcoma. *Am. J. Dermatopathol.*, 1, 165-172.
- 2) Anderson, P. J., Cohen, S. and Barka, T. (1961): Hepatic injury: A histochemical study of intracytoplasmic globules occurring in liver injury. *Arch. Pathol.*, 71, 89-95.
- 3) Aterman, K. (1958): Observations on the nature of "watery vacuolation": The response of the liver cell to the intravenous injection of hypertonic saline, evance blue, dextran, and heparin. *Lab. Invest.*, 7, 577-605.
- 4) Blumenfeld, W., Egbert, B. M. and Sagebiel, R. W. (1985): Differential diagnosis of Kaposi's sarcoma. *Arch. Pathol. Lab. Med.*, 109, 123-127.
- 5) Bull, L. B., Dic, A. T. and McKenzie, J. S. (1958): The acute toxic effects of heliotrine and lasiocarpine, and their N-oxides, on the rat. *J. Pathol. Bacteriol.*, 75, 17-25.
- 6) Clumeck, N., Sonnet, J., Taelman, H., Mascart-Lemone, F., Bruyere, M. D., Vandeperre, P., Dasnoy, J., Marcelis, L., Lamy, M., Jonas, C., Eyckmans, L., Noel, H., Vanhaeverbeek, M. and Butzler, J. (1984): Acquired immunodeficiency syndrome in African patients. *N. Engl. J. Med.*, 310, 492-497.
- 7) Downing, R. C., Eglin, R. P. and Bayley, A. C. (1984): African Kaposi's sarcoma and AIDS. *Lancet I*, 478-480.
- 8) Durack, D. C. (1981): Opportunistic infections and Kaposi's sarcoma in homosexual men. *N. Engl. J. Med.*, 305, 1465-1467.
- 9) Eger, W., Jungmichel, H. and Kordon, G. (1958): Untersuchungen über den Einfluss des Lipopolysaccharid Pyrexal auf die Allylkoholschädigung der Leber als Ausdruck einer Resistenzänderung des Organismus. *Arch. Pathol. Anat.*, 331, 154-164.
- 10) Fauci, A. S. (1982): The syndrome of Kaposi's sarcoma and opportunistic infections: An epidemiologically restricted disorder of immunoregulation. *Ann. Intern. Med.*, 96, 777-779.
- 11) Fisher, E. R. and Fisher, B. (1954): Cytoplasmic liver cell inclusions following arterialization in the dog. *Am. J. Pathol.*, 30, 987-1001.
- 12) Gurd, F. N. and Vars, H.M. (1949): Pathological changes after partial hepatectomy with special reference to hepatic necrosis in protein-depleted rat. *Arch. Pathol.*, 48, 140-149.
- 13) Kaposi, M. (1872): Idiopathisches multiples pigmentsarcoma der Haut. *Arch. Dermatol. Syph.*, 4, 265-273.
- 14) Kettler, L.H. (1948): Ueber die vakuoliger Degeneration der Leberzellen. *Virchows Arch. Pathol. Anat.*, 315, 587-640.
- 15) Kurman, R. J. and Norris, H. J. (1976a): Endodermal sinus tumor of ovary. *Cancer*, 38, 2404-2419.
- 16) Kurman, R.J. and Norris, H. J. (1976b): Embryonal carcinoma of the ovary: A clinicopathologic entity distinct from endodermal sinus tumor resembling embryonal carcinoma of the adult testis. *Cancer*, 38, 2420-2433.
- 17) Nairn, R. C., Chadwick, C. S. and McEntegart, M. G. (1958): Fluorescent protein tracers in the study of experimental liver damage. *J. Pathol. Bacteriol.*, 76, 143-153.
- 18) Perre, P. V., Rouvroy, D., Lepage, P., Bogaerts, J., Kestelyn, P., Kayihigi, J., Hekker, A., Butzler, J. and Clumeck, N. (1984): Acquired immunodeficiency syndrome in Rwanda. *Lancet II*, 62-69.

- 19) Pfeifer, U. and Bannasch, P. (1968): Zum Problem der "hyalinen EiweiBtropfen" im Cytoplasma der Leberparenchymzellen: Light-und elektronenmikroskopische Untersuchungen nach 3/4-Hepatektomie. Virchows Arch. Abt. B Zellpathol., 1, 365-388.
- 20) Popper, H., Paronetto, F. and Barka, T. (1960): PAS-positive structures of nonglycogenic character in normal and abnormal liver. Arch. Pathol., 70, 300-313.
- 21) Senba, M., Itakura, H., Toriyama, K. and Uzuta, F. (1984): Periodic acid Schiff (PAS) and phosphotungstic acid hematoxylin (PTAH) positive materials in cutaneous type of Kaposi's sarcoma. Trop. Med., 26, 87-91.
- 22) Shirai, T., Itoh, T., Yoshiki, T., Noro, T., Tomino, Y. and Hayasaka, T. (1976): Immunofluorescent demonstration of alpha-fetoprotein and other plasma proteins in yolk sac tumor. Cancer, 38, 1661-1667.
- 23) Taylor, J. F. and Ziegler, J. L. (1974): Delayed cutaneous hypersensitivity reactions in patients with Kaposi's sarcoma. Br. J. Cancer, 30, 312-318.
- 24) Trowell, O. A. (1946): The experimental production of water vacuolation of the liver. J. Physiol., 105, 268-297.
- 25) Weld, J. T., Glahn, W. E. and Mitchell, L. C. (1941): Production of cytoplasmic inclusions in liver cells of rats injected with certain proteins. Proc. Soc. Exp. Biol. Med., 48, 229-233.
- 26) Wold, L. E., Kramer, S. A. and Farrow, G. M. (1984): Testicular yolk sac and embryonal carcinomas in pediatric patients: Comparative immunohistochemical and clinicopathologic study. Am. J. Clin. Pathol., 81, 427-435.

---

#### カボン肉腫の組織内に見られる好酸性球状物質の電子顕微鏡による観察

千馬正敬, 板倉英世 (長崎大学熱帯医学研究所病理学部門)

著者らは、カボン肉腫の組織内に好酸性に染色される球状の物質を2例見出した。この球状物質の組織化学による性質は、PAS (過ヨウ素酸・シッフ)、アミラーゼ消化 PAS および PTAH (リンタングステン酸・ヘマトキシリン) において陽性に染色される。これらの形態は卵巣および睾丸の卵嚢腫瘍に見られる糖タンパクの球状物質によく似ている。電顕標本はホルマリン固定の材料を使用しているため、組織内の詳細な点が観察できないが、糖タンパクの球状物質は電顕による観察では黒色の球状体として組織内に見られる。

熱帯医学 第27巻 第2号, 113-117頁, 1985年6月