Kaposi’s Sarcoma Associated with Gastric Involvement

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We report a case of classic Kaposi’s sarcoma (KS) in a 67-year-old man, who had multiple cutaneous lesions of the feet and left hand as well as an internal involvement of the stomach. The histopathologic findings showed typical features of KS as a mid-dermal tumor composed of vascular proliferations, vascular slits, spindle cells, extravasated erythrocytes and deposits of hemosiderin. Analysis of T-cell subpopulations showed decreased T4 lymphocytes and increased T8 lymphocytes; the ratio of T4/T8 lymphocytes was decreased. Natural killer cell activity was also decreased. These findings suggest a possible relationship between immunological abnormalities and the pathogenesis of this disease. The patient’s serum was negative for antibodies to the human immunodeficiency virus (HIV).

This report describes a case of classic KS with immunological abnormalities and internal involvement and possible pathogenetic mechanisms are discussed.


Key Words: Immunological abnormalities, Internal involvement, Kaposi’s sarcoma

Kaposi’s sarcoma has been thought of as a comparatively rare neoplasm that affected primarily men between their fifth and seventh decades of life until an epidemic outbreak of acquired immunodeficiency syndrome (AIDS) occurred.1 KS is generally believed to be multifocal in origin, sometimes manifesting itself as a solitary cutaneous lesion but, more commonly, as multiple red to purple nodules, plaques, or macules. The lesions are most commonly found on the lower extremities, usually the foot and ankle, but may appear on the mucous membranes or in internal organs.2,3 Internal involvement is encountered in about 10% of the patients, but it would appear that the incidence of clinically silent systemic involvement is probably higher.4

The incidence of KS in our country is relatively rare; there are only 11 cases reported in the Korean literature. Furthermore, there are no reports of cutaneous KS associated with gastric involvement.

We report a case of classic KS with involvement of the stomach.

REPORT OF A CASE

A 67-year-old man presented at the Kyung Hee University Hospital with multiple dark brown nodules and plaques on his left hand and both feet. About 10 years ago, the patient developed a brownish patch on the dorsum of his left foot which was asymptomatic. The lesions progressed to the dermal nodules and plaques and then spread to the ankles and soles. Two years ago, similar lesions developed on the dorsum of the left second finger. He had no systemic symptoms, was taking no medication, and had no significant past medical history.

Physical examination revealed a healthy man with more than 15 dermal nodules and plaques, 1 to 3 cm in diameter, on the left second finger and on his feet (Fig. 1, 2, 3). The skin lesions were sharply demarcated, firm in consistency, and brownish in hue. There was no lymphadenopathy or hepatosplenomegaly. The remainder of the physical examination was unremarkable.

Laboratory tests consisting of a complete blood cell count, urinalysis, serum glucose, liver function tests, blood urea nitrogen, and creatinine were normal. The serum VDRL was non-reactive and the enzyme-
linked immunosorbent assay (ELISA) for the HIV antibody was negative. Serum immunoglobulins and complement (C3, C4) levels were normal. T lymphocyte subpopulations of peripheral blood measured using monoclonal antibodies showed following values: OKT3 = 76.2%, OKT4 = 35.3% and OKT8 = 39.1%; the ratio of OKT4/OKT8 was decreased to 0.89. Natural killer cell activity measured by $^{51}$Cr release assay was decreased to 17.9%. Intradermal skin antigen tests with PPD and trichophyteen were reactive and with candidin and SK/SD were unreactive. A chest radiograph, ultrasonographic examination of the abdomen, and sigmoidoscopic examination were unremarkable. Fiberscopic examination of the stomach showed one large protruding mass which measured 3x4cm on the anterior wall of the lower body of the stomach, the mass had an ulcer on its surface (Fig. 4.)

A biopsy taken from a lesion on the dorsum of the left foot showed nonspecific changes of the epidermis. There was a mid-dermal tumor composed of numerous vascular slits, dilated capillaries with large endothelial cells, and spindle cells (Fig. 5). Extravasated erythrocytes, deposits of hemosiderin, and a cellular infiltration of lymphocytes and histiocytes were also observed (Fig. 6). A biopsy specimen from the stomach mass revealed vascular proliferation, extravasated erythrocytes, spindle cells, and a chronic inflammatory cell infiltration, which were consistent with those of the skin lesion (Fig. 7). When examined with an electron microscope, the dermis showed ill defined proliferations of small vascular spaces with pleomorphic, atypical endothelial cells which had rather abundant cytoplasm and frequently had swollen mitochondria (Fig. 8). Fibroblastic proliferation and scattered macrophages engulfing dark
hemosiderin pigment were also observed.

With above mentioned clinical and histopathologic findings, we could confirm the diagnosis of a nodular form of classic KS associated with gastric involvement. Unfortunately, the patient refused treatment.

**DISCUSSION**

Kaposi's sarcoma (KS) is a rare neoplasm that once was found mainly in elderly patients from eastern European or Mediterranean countries. Three forms of KS showing different biologic behaviors have been
described, the classic, endemic, and epidemic form. The classic form of KS includes cases which are not associated with AIDS. The endemic form has been described in equatorial Africans and the new epidemic form of KS occurring in association with AIDS has been increasing in incidence.

It has been proposed that the etiology of KS is multifactorial, involving genetic predisposition, geographical factor and defects in cellular immunity. The development of KS in immunosuppressed patients and the high incidence of second primary malignancies involving lymphoreticular system in KS patients speaks for a possible role of immune system in the pathogenesis of KS. The reduction of T4 lymphocytes and the increase of T8 lymphocytes in the peripheral blood results in an inversion of the T4/T8 ratio. Also, decreased blastogenic responses to stimulation by mitogens, and skin anergy to a variety of skin-test antigens represent suppression of cell-mediated immunity in KS patients. Natural killer cell activity is decreased in one half of the patients. Decreased T4 lymphocytes, increased T8 lymphocytes and inversion of T4/T8 ratio representing defects in cellular immunity were observed in our patient as in previous reports. Natural killer cell activity was also decreased. Thus it is concluded that the disease is closely associated with defects in immunoregulation in these patients. In all KS patients, the pathogenesis appears to be closely associated with cytomegalovirus (CMV) infection. It has been postulated that genetic factors are important in the etiology of the disease. An increased frequency of HLA-DR 5 has been observed in classic and epidemic KS. Considering all of the various clues, it appears that the main factors in the development of KS are a degree of immune impairment and CMV infection in conjunction with some degree of genetic predisposition. Although the origin of the cells involved in KS is still unclear, it is thought to be vascular. Since the value of factor VIII-related antigen as an immunologic marker for endothelial cells has been established, positive immunologic reaction for this factor in the cells of KS strongly supports an endothelial derivation.

In classic KS, four major forms of the disease are generally accepted: nodular, florid, infiltrative, and lymphohemorrhagic forms. Our case belongs to the nodular variety showing an indolent course and manifesting nodular or plaque-like skin lesions. KS can affect visceral organs, particularly the small intestine and the stomach; it is estimated that the incidence of visceral lesions ranges from 10% to 70%. Lesions in the lungs, liver, pancreas, adrenal glands have also been reported. There is no racial difference in the visceral involvement of classic KS patients, but increased incidence of visceral involvement is noted in endemic KS in Africans and epidemic KS associated with AIDS. Although the precise pathomechanism of the visceral involvement is still unclear, it is thought to be a reflection of a multifocal origin of the lesions. Spread of the lesions is probably not a result of metastases. In most cases of KS with internal involvement there are no systemic complaints, but fever, weight loss, malaise, and anorexia may develop. In our patient there were no systemic signs or symptoms suggesting internal involvement.

Histologically, proliferation of spindle-shaped cells, vascular slits with occasional extravasated erythrocytes and hemosiderin deposits, and the presence of large, protruding endothelial cells as well as lymphocytic infiltrations are characteristics of KS. The blood vessels in the dermis are often dilated and increased in number. Electron microscopic examination discloses large irregular endothelial cells, fibroblasts, a lack of pericytes, and discontinuity of the endothelial lining.

Treatment modalities including radiotherapy, chemotherapy, and immunotherapy have had variable effectiveness. Radiotherapy is the treatment of choice for the localized, nodular form of classic KS. For the treatment of patients with more disseminated disease or with locally invasive tumors chemotherapy, such as vinblastin and actinomycin D, has been used with production of temporary effectiveness. Alpha-interferon is also available as an immunotherapeutic agent. Although many therapeutic modalities are used, recurrences are the rule and at present the disease is incurable. In classic KS, the average survival time is reported to be 8 to 15 years; the patients often dying of concurrent illness rather than KS. However, epidemic KS has a much worse prognosis and an 80% 2-year mortality; the patients dying mostly of opportunistic infection.
REFERENCES