Classic Kaposi Sarcoma Presenting as Rapidly Growing Nodules

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Classic Kaposi sarcoma (KS) is a sporadic disease that usually affects persons older than 50 years, with a distinct male predominance. Although classic KS has a protracted, indolent course, there appears to be a rare disseminated fulminant type. This report describes a case of classic KS, presenting as a very rapid enlargement and dissemination of skin lesions, without evidence of human immunodeficiency virus (HIV) infection or involvement of other internal organs.

Kaposi sarcoma (KS) is a multicentric vascular neoplasm of the skin and other organs with 4 clinical subtypes.[1,2] Unlike other variants, classic KS traditionally has been considered a slow-growing, vascular, neoplastic disease that usually runs a chronic, mild course and is hardly ever responsible for the death of patients.[3] Rarely, classic KS has rapid courses, with involvement of the lung, spleen, heart, and gastrointestinal tract.[4] This rapid and aggressive form of KS may be characteristic of patients who have acquired immunodeficiency syndrome (AIDS) or other severe immunodeficiency disorders. We describe the case of a 63-year-old man with classic KS presenting with rapidly growing nodules.

Case Report

A 63-year-old man, while being treated for pulmonary tuberculosis, was referred to our department for evaluation of multiple purplish nodules on his left hand. He first noticed the skin lesions one year ago, when they started as bean-sized purplish nodules. During that year, the patient reported that some nodules had slowly enlarged, and others had regressed. The patient presented with multiple pea-sized nodules and a walnut-sized nodule on the dorsal and lateral aspects of his left hand, respectively (Figure 1). On physical examination, the patient was afebrile, with no lymphadenopathy or hepatosplenomegaly.

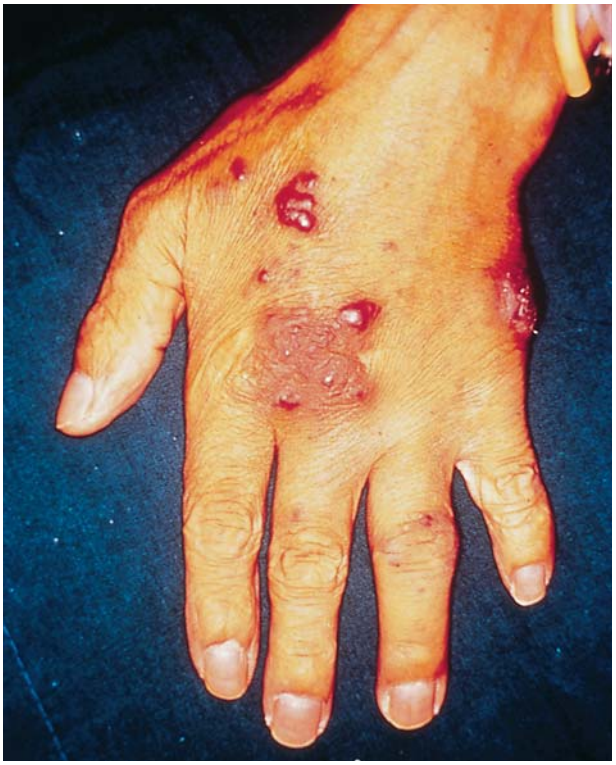

Figure 1. Multiple pea-sized purplish nodules, with violaceous patch on the dorsal aspect of the left hand and a walnut-sized nodule on the lateral aspect of the left hand.

Laboratory studies yielded the following values: white blood cell count, $9.0\times10^3/mm^3$; hemoglobin, 13.8 gm/dL; hematocrit, 41%; platelet count, $1.06\times10^5/mm^3$; antiplatelet antibody, reactive; CD4 cell count, within normal limits; helper T cell to

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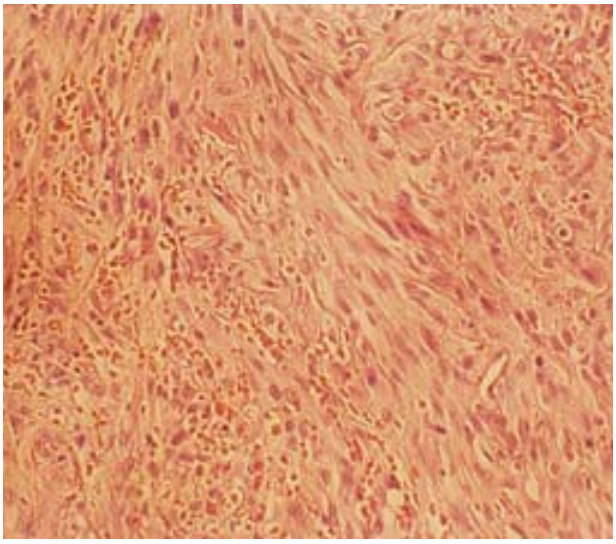

Figure 2. Biopsy shows proliferation of spindle cells and slitlike vascular spaces containing variable numbers of red blood cells (H&E, original magnification ×200).

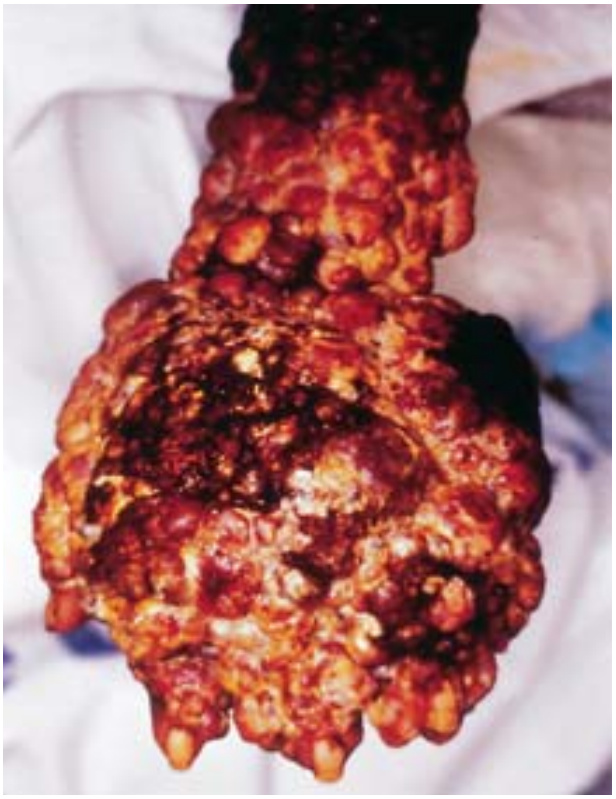

Figure 3. The same lesion as in Figure 2 shown 5 months later. The patient's left hand is covered completely with ulcerated fungating tumors, and extensive spread of numerous warty nodules on his forearm was noted. Necrotic change also was observed.

suppressor T cell ratio, within normal limits; herpes simplex virus (HSV) IgM, negative; HSV IgG, positive; cytomegalovirus (CMV) IgM, negative; CMV IgG, positive; human immunodeficiency virus (HIV) test, negative; multitest cell-mediated immunity, 4-mm tuberculin. A radiography of the chest in posteroanterior view revealed possible active tuberculosis. The findings from gastroscopy, colonoscopy, and bone scan were normal. A skin biopsy specimen showed proliferation of spindle cells and vascular slits containing extravasated red blood cells (Figure 2). Hyalinelike globules were noted with *p*-aminosalicylic staining. Immunohistochemical stain was positive for CD34. The diagnosis of classic KS was made based on clinical, histopathologic, and immunohistochemical findings. Immunohistochemical stain was negative for CMV. In situ hybridization was negative for the Epstein-Barr virus. A DNA band of 233bp, which is specific for human herpesvirus 8 (HHV-8), was detected from tissue specimen by polymerase chain reaction.

The patient refused any therapy for his skin lesions. One month after diagnosis, the skin lesions became coalescing and ulcerating with rapid enlargement, reaching the size of a child's fist. A complete blood count showed marked reduction in platelet count ($0.32\times10^5/mm^3$). Bone marrow biopsy showed consistent findings with idiopathic thrombocytopenic purpura (ITP). Although γ-globulin, oral prednisolone, and splenectomy were tried for correction of platelet count, they had no effect. For the treatment of his skin lesions, interferon alfa was tried without success, worsening the thrombocytopenia, and was discontinued. Subsequently, the patient was treated with vinblastine, which effectively restored the platelet count ($1.61\times10^5/mm^3$) but was not effective for the skin lesions. Furthermore, the preexisting nodules had grown rapidly, and 3 months after diagnosis, the nodule had reached the size of an adult's fist. Two months after discharge, his left hand was covered completely with ulcerated fungating tumors, with necrotic change, and the spread of numerous nodules on his forearm was noted (Figure 3). Furthermore, the patient's general condition worsened, and he had to be readmitted to our hospital for supportive care. The patient progressed to acute respiratory distress syndrome and died.

Comment

In 1872, Moritz Kaposi described 5 patients with blue-red cutaneous tumors that he called *idiopathic, multiple, pigment sarcoma*.[1] Four forms of KS have since been identified: classic (Mediterranean), endemic African, iatrogenic, and KS associated with AIDS.

Classic KS is a sporadic disease that is prevalent in Mediterranean countries.[1,4,5] It is primarily a skin disease of the legs that predominantly affects older men and usually progresses very slowly. Initially, it presents

as a bluish red macule on the distal portion of the lower extremities. However, as the lesion ages, it may coalesce to form large plaques and later change to a more disseminated pattern. Although classic KS is characterized by its slow-growing nature, rapid courses with involvement of other organs have occasionally been reported.[3,4] The rapid and aggressive form of classic KS may be characteristic of patients who have AIDS or other severe immunodeficiency disorders.

There have been many potentially transmissible infectious agents in KS other than HIV, including CMV, hepatitis B virus, human papilloma virus, and *Mycoplasma penetrans*.[1,6] Recent molecular studies suggest that a new human herpesvirus, HHV-8 (KS-associated herpesvirus), is etiologically involved in KS.[5,7-9] Its DNA sequence can be detected not only in tissue specimen but also in peripheral blood mononuclear cells.[10] Recently, HHV-8 DNA has been localized to the nuclei of spindle cells and KS tumor cells.[11-13]

Thrombocytopenia in patients with KS usually is related to malignant disorders of the reticuloendothelial system, such as Hodgkin disease or lymphosarcoma. There is also a suggestion that thrombocytopenia may be due to phagocytosis of platelets by abnormal endothelial cells in KS. Turnbull et al[14] reported a case of KS with ITP in which restoration of the platelet count was achieved after effective treatment of the skin lesions. They suggested the possibility that thrombocytopenia might be related to the skin lesions on the analogy of Kasabach-Merritt syndrome. In our case, the platelet count was normalized after treatment with vinblastine, without improvement of skin lesions. This finding may indicate that the thrombocytopenia in our patient was caused by ITP.

Treatment of KS is based primarily on the extent and localization of the lesions and clinical subtypes.[1,4,6] A solitary lesion usually is treated with excision or laser irradiation. However, patients whose disease is progressing rapidly—as in our patient—need to be treated with chemotherapeutic agents. Recently, Costa da Cunha et al[15] confirmed the efficacy and safety of low-dose recombinant interferon alfa-2b for the long-term treatment of both cutaneous and visceral lesions of KS not related to HIV. Unfortunately, our patient necessitated discontinuing interferon alfa-2b therapy because of severe thrombocytopenia. Instead, we started a vinblastine regimen—an effective treatment in disseminated forms of KS—that resulted in correction of the thrombocytopenia caused by ITP. However, it failed to improve the skin lesions.

Comparing this case with other reported cases of KS, our patient is unique in that his skin lesions showed impressive rapid enlargement and dissemination. This is a very unusual finding in classic KS because, in most instances, the disease runs a slow course, even when extracutaneous sites are involved. We consider that this patient's probable immunosuppressed state due to pulmonary tuberculosis and prolonged steroid therapy for ITP might have accelerated the growth of his skin lesions.

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