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RESEARCH

Aggressive Classical Kaposi's Sarcoma Mimicking Malignant Lymphoma

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Abstract Classical Kaposi's sarcoma is an unusual multifocal neoplasm of vascular endothelial cell origin, and considered a less malignant, slowly-progressing tumor. Although visceral involvement is occasionally seen in HIV/AIDS patients with KS, tumor dissemination to visceral lymph nodes in classical KS is very rare. A 72-year-old woman without any other relevant past medical history presented with anorexia, weight loss, night sweats, and skin eruptions. As the rapid progression of cytopenias and lymphadenopathy were observed, bone marrow biopsy and imaging were performed. Positron emission tomography showed disseminated lymphadenopathy in the cervical, axillary, mediastinal, inguinal, and abdomino-pelvic nodal areas. Inguinal lymph node biopsy was compatible with KS, positive for CD31, CD34, and human herpesvirus-8 by immunohistochemical stain. We report a case of aggressive classical KS mimicking aggressive malignant lymphoma.

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Introduction

Kaposi's sarcoma (KS) is a low-grade vascular neoplasm first described by Moritz Kaposi, a Hungarian dermatologist, in 1872 [1]. Recently, four variants of KS have been described [2]. Classical KS is usually seen in males of Mediterranean or Eastern European origin. Endemic KS occurs in younger adults and children in Central Africa. Transplantation or acquired immunodeficiency syndrome (AIDS)-associated KS are found in patients who are immunosuppressed due to organ transplant or human immunodeficiency virus (HIV) infection, respectively. Classical KS is considered a less malignant, slowly-progressing tumor [3]. Although visceral involvement by KS is occasionally seen in patients with AIDS, dissemination of classic KS to visceral lymph nodes is very rare [4].

We report a case of an aggressive classical KS mimicking malignant lymphoma with multi-organ failure.

Case Report

The patient was a 72-year-old woman without any other medical problems. She visited our hospital for multiple skin eruptions on the face, abdomen and legs. Three months prior to presentation, she began to suffer from anorexia, experienced weight loss of 10 kg (from 70 mg to 60 kg), and was experiencing night sweats. The skin lesions started as asymptomatic red plaques and first appeared after she began taking medication for the symptoms described above. Blood and urine tests were within the normal range at that time. The rest of the physical examination revealed no significant abnormalities.

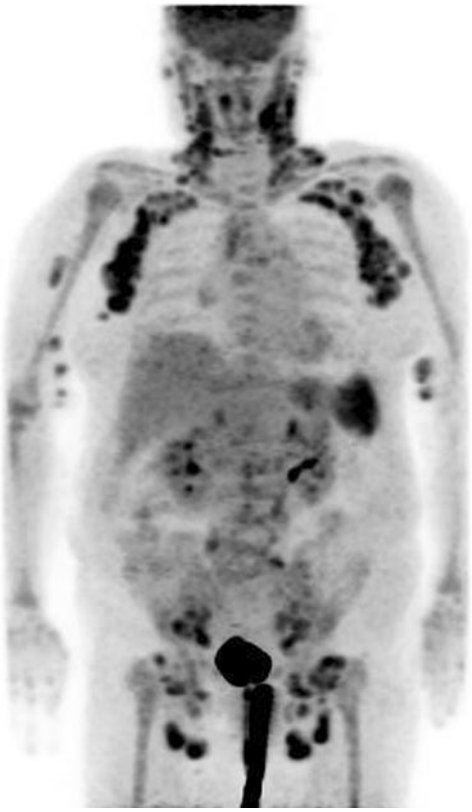

Fig. 1 Positron emission tomography (PET) demonstrates numerous hypermetabolic lymph nodes in the cervical, axillary, mediastinal, abdomino-pelvic, and inguinal areas

Therefore, the skin lesions were considered to be drug eruptions and she was referred to the department of dermatology. The patient's blood pressure was 110/70 mmHg and her temperature was normal. Complete blood cell count (CBC) revealed anemia (hemoglobin was 9.18 g/dl), thrombocytopenia (platelet count was 26,000/mm^3), and normal white blood cell level (5,600/mm^3; neutrophils 62 %, lymphocytes 20 %, monocytes 12 %, eosinophils 4 %). Erythrocyte sedimentation rate was 78 mm/hr and C-reactive protein was 3.5 mg/dL. Renal function, hepatic function, electrolytes, chest X-ray, electrocardiogram, and urinalysis were within the normal range. A skin biopsy showed focal exocytosis and superficial perivascular lymphocytic infiltration with a few neutrophils. Bone marrow aspiration and biopsy were performed for the evaluation of anemia and thrombocytopenia, and showed 25 % normo-cellularity and reactive proliferation of polyclonal plasma cells. Because there was no malignant cell infiltration or chromosomal abnormality, the patient's thrombocytopenia was thought to be due to peripheral destruction or sequestration. A week later, the patient complained of dyspnea and generalized edema, and multiple palpable lymph nodes were discovered on physical examination. CBC showed further decreases in hemoglobin (6.3 g/dl) and platelet counts (7,000/mm^3). Because clinically-aggressive malignant lymphoma was suspected, computed tomography (CT) scans and positron emission tomography (PET) were performed. There was lymphadenopathy in the cervical, axillary, mediastinal, inguinal, and abdomino-pelvic lymph node areas. There was also diffuse hypermetabolism in the marrow and spleen (Fig. 1). Inguinal lymph node biopsy demonstrated infiltration of atypical epitheloid and spindle cells in the angiomatous components. As the spindle cells were positive for CD31, CD34 and human herpesvirus-8 (HHV-8) and negative for CD3, CD20, CD10, Bcl-2 and Bcl-6 by immunohistochemical stain, a diagnosis of classical KS was reached (Fig. 2). Serologic testing for HIV was negative. The patient was transferred to the intensive care

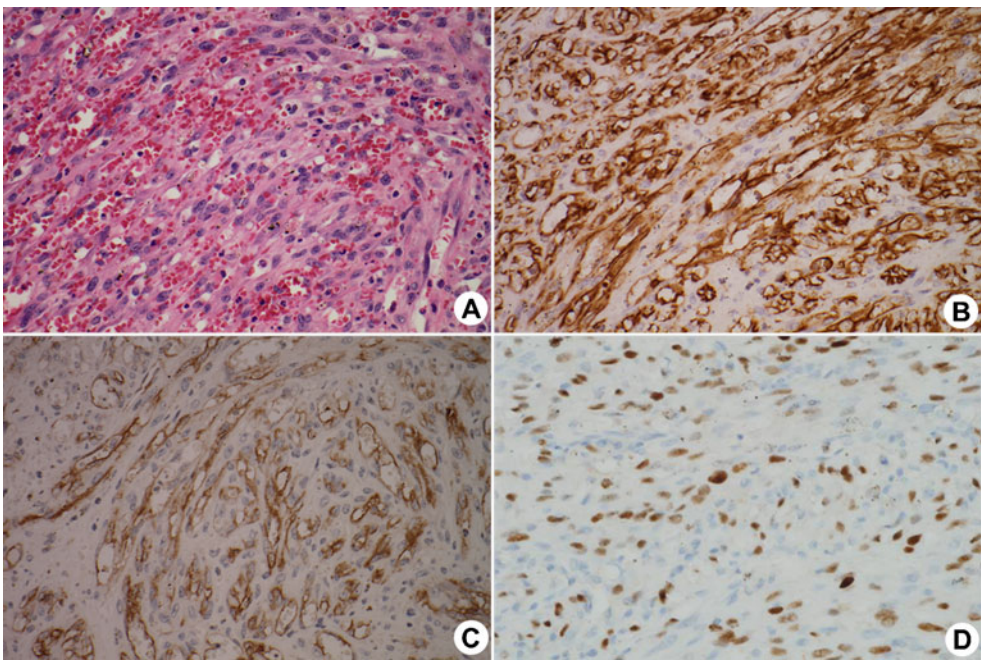

Fig. 2 Inguinal lymph node biopsy. **a** The proliferation of endothelial cells among the spindle-shaped cells and extravasated red blood cells are shown(objective, x400; hematoxylin and eosin); Immunohistochemical stain positive for (**b**) CD 31; (**c**) CD34; (**d**) and HHV-8

unit (ICU), but died due to sepsis and multi-organ failure after 3 weeks.

Discussion

Classical KS usually has a chronic, indolent clinical course over many years, and is not life-threatening. Brenner and colleagues found that 18 % of patients showed centripetal progression from local to diffuse skin involvement during a median time of 22.4 months (range 2–156 months) in a retrospective analysis of 248 cases [4]. Although visceral involvement of KS is occasionally seen in patients with AIDS, less than 4 % of patients with classical KS had visceral spread during a median duration of 33 months of follow-up (range 2–192 months). Death from KS has been reported to occur in 1.6 %–9.0 % of cases, from 2 to 5.7 years after the onset of the disease [5].

The pathologic characteristics of KS are a proliferation of spindle cells, endothelial cells, extravasation of red blood cells, hemosiderin-laden macrophages, and, in early cases, inflammatory cell infiltrate. Due to overlap of histologic features, distinguishing KS from other benign or malignant vascular tumors as well as other nonvascular spindle cell soft-tissue neoplasms may be difficult [6]. In 1994, Chang and colleagues identified DNA fragments of a previously-unrecognized herpes virus, which has been called KS—associated herpesvirus (KSHV, also known as human herpesvirus-8), in a KS skin lesion from a patient with AIDS [7]. Although most primary KSHV infections appear to be asymptomatic, some patients with AIDS develop KS after the loss of response to KSHV proteins in HLA class I—restricted cytotoxic T-lymphocytes as immunodeficiency worsens [8]. Immunohistochemical staining for human herpesvirus-8 (HHV-8) latent nuclear antigen-1 (LNA-1) is a highly sensitive, specific, and simple technique to aid in the diagnosis of KS and to distinguish it from other diseases [9]. In our case, the spindle cells in the inguinal lymph node biopsy were positive for vascular markers such as CD31, CD34 and HHV-8 on immunohistochemical staining.

With relatively few exceptions, the published literature on the treatment and prognosis of classical KS consists of retrospective series and case reports. There is no consensus on the optimal tumor-directed therapy for different KS manifestations. Once classical KS is diagnosed, observation is appropriate for immunocompetent asymptomatic patients, as there is little progression of disease over a long period [2].In a 39-patient series, 15 (38 %) remained progression-free for 4 months (duration, 1–83 months) [10]. For patients who have a limited volume of disease causing symptoms or cosmetic disfigurement, local treatment such as radiation, excision, cryotherapy, laser ablation or intralesional injection of chemotherapy are thought to be better than observation or systemic chemotherapy [11]. When widespread, bulky, or rapidly progressive, classical KS, particularly when it interferes with function or is associated with moderate to severe symptomatic edema or visceral organ involvement, should be treated with systemic chemotherapy. Some studies have reported the efficacy of pegylated liposomal doxorubicin [12], paclitaxel [13], and gemcitabine [14]. Although recombinant interferon alfa (IFNa) is approved for the treatment of AIDS-associated KS in the US, there is limited experience with this drug in classical KS [15]. Unfortunately in our case, the disease displayed aggressive behavior with multi-organ failure occurring during a short period, such that there was no chance to treat with chemotherapy.

Classical KS is rare and usually has a chronic progression with skin lesions. We report a case of an aggressive form of cutaneous lymphoma-like disease with visceral lymph node involvement and a very poor prognosis. Therefore, Kaposi sarcoma should be considered in the differential diagnosis of patients with skin lesions and lymphadenopathy.

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