

Classic Kaposi sarcoma presenting as elephantiasis nostras verrucosa

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Conflict of interest: none to declare

*Received: 10 December 2014
Accepted: 20 January 2015*

Kaposi sarcoma is a malignant disease that originates from the lymphatic system. Different epidemiological, clinical and histopathological variants of this neoplasm have been identified. Classic Kaposi sarcoma is one of the four main clinico-epidemiologic variants. Cutaneous lesions vary from pink patches to dark violet plaques, nodules or polyps, depending on clinical variant and stage. Kaposi sarcoma with elephantiasis is reported in the context of AIDS. An 82-year-old male presented with a 2-year history of progressive verrucous skin changes and non-pitting edema consistent with elephantiasis nostras verrucosa (ENV), secondary to Kaposi's sarcoma. Past medical history, physical examination, lab tests and imaging ruled out common causes of ENV and anti-HIV antibody test was negative. Classic Kaposi sarcoma was confirmed on biopsy. To the best of our knowledge, this study reports the first case of elephantiasis nostras verrucosa in an HIV-negative patient with classic Kaposi sarcoma.

Keywords: elephantiasis nostras verrucosa, Kaposi sarcoma, lymphedema

Iran J Dermatol 2015; 18: 25-28

INTRODUCTION

Kaposi sarcoma (KS) is a tumor mainly affecting the skin, with multifocal presentation and possible lymph node and visceral involvement. Typically, it consists of four clinical variants: Mediterranean (classic) KS, iatrogenic (transplant-associated) KS, African (endemic) KS and AIDS-associated (epidemic) KS¹⁻³. All four variants are associated with human herpes virus-8 (HHV-8), and show a similar histological pattern⁴⁻⁶. KS histopathologic variants reported in older literature include anaplastic KS, lymphedematous KS (comprised of lymphangioma-like, lymphangiectatic and bullous KS) and telangiectatic KS. Other histopathologic variants more recently described consist of hyperkeratotic (verrucous), keloidal, ecchymotic, pyogenic granuloma-like, micronodular, intravascular, glomeruloid and pigmented KS, as well as KS with sarcoid-like granulomas and KS with myoid nodules^{1,2}.

Elephantiasis nostras verrucosa (ENV) is a progressive cutaneous hypertrophy due to chronic lymphedema, following longstanding obstruction of the lymphatic drainage. It usually presents as a non-pitting edema superimposed by hyperkeratotic papules, nodules, and verrucous cobblestone-like plaques^{7,8}. The condition may occur secondary to trauma, radiation, surgery, tumor-obstruction, portal hypertension, congestive heart failure, thyroid dysfunction and AIDS-associated KS⁸⁻¹³. Obesity is a major predisposing factor^{14,15}. AIDS-associated KS with elephantiasis has been previously reported¹⁰. This study reports an 82-year-old male with classic KS presenting with Elephantiasis; a rare manifestation of Kaposi sarcoma.

CASE REPORT

This is the case of an 82-year-old man presented with edema and diffuse, verrucous skin changes on both lower extremities which has been gradually

progressing for the past two years. As a result of feet hypertrophy, the patient was unable to wear shoes. The patient had no history of venous hypertension, trauma, radiation, surgery or soft tissue infections. On physical examination, there was severe woody edema and cobblestone appearance of skin on both lower extremities (Figure 1). Moreover, two violet nodules, one on the right forearm and the other on the plantar aspect of the right foot were obvious. The tibialis posterior, dorsalis pedis and femoral pulses were normal. No lymph adenopathy or organomegaly was detected on physical examination. The patient was not obese, his Body Mass Index (BMI) being 19 kg/m².

All laboratory tests including complete blood count, liver function test, kidney function test and thyroid function test were within normal limits. Anti-HIV antibody was checked twice and the results were negative. Doppler ultrasonography and lymphocintigraphy did not show vascular or lymphatic obstruction.

Skin biopsy from violet nodular lesions of the left foot and verrucous lesions of the right leg and forearm was performed. Histological study of the specimen from verrucous lesions of the right leg showed acanthosis and hyperkeratosis of the epidermis and dilated lymphatic spaces in the dermis, consistent with ENV (Figure 2). A histological study of the specimen from the left leg and right forearm showed proliferation of small vessels lined by inconspicuous endothelial cells and some spindle-shaped cells surrounding slit-like spaces containing erythrocytes, devoid of marked pleomorphism and



Figure 1. Bilateral severe edema and cobblestone appearance of lower limbs.

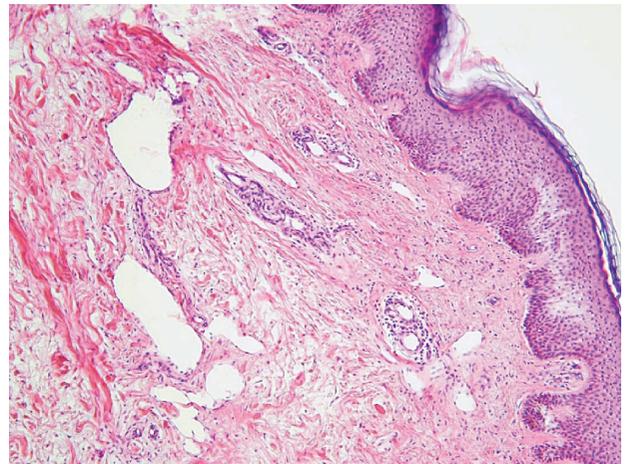


Figure 2. Tissue biopsy of the right leg studied under light microscope shows acanthosis and hyperkeratosis of the epidermis and dilated lymphatic spaces in the dermis (H&E×10).

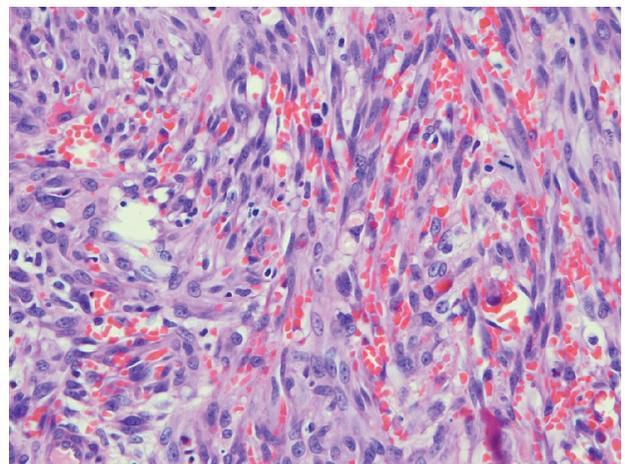


Figure 3. Tissue biopsy of the left leg studied with light microscope shows small vessels lined by inconspicuous endothelial cells and some spindle-shaped cells, slit-like spaces containing erythrocytes, and few pleomorphism and mitotic figures (H&E×40).

mitotic figures (Figure 3), with positive human herpes virus-8 (HHV-8) immunostaining. These findings were diagnostic of KS.

Chest-X-ray, echocardiography, abdominal and pelvic CT scans were normal. Upper endoscopy and colonoscopy were performed which revealed violet lesions consistent with KS in the upper GI tract, but the lower GI tract was intact. After diagnosis of Kaposi sarcoma with skin and GI involvement, the patient was referred to an oncologist.

DISCUSSION

KS is a malignant lesion of vascular endothelial origin with various clinical and epidemiological

forms. Different clinical variants of KS share the same histopathological features including proliferation of new blood vessels, extravasation of erythrocytes, growth of KS spindle cells and formation of slit-like spaces. KS spindle cells are the neoplastic elements of KS, with endothelial origin⁶. KS presents most frequently with cutaneous lesions evolving from patches to plaques and subsequently to nodules. Visceral and nodal involvement is also common, and more frequently seen with AIDS-associated KS^{2,6}.

Human herpes virus-8 (HHV-8) infection is the primary factor in the development of KS; it affects both lymphatic and blood vascular endothelial cells⁵. Upon infection, the blood endothelial cells are reprogrammed to resemble the lymphatic endothelium. Host immune dysfunction is an important cofactor necessary for the eventual progression of the disease¹.

Classic KS is an indolent form of the disease, typically presenting with pink to red-violet macules which may progress to plaques, nodules or polypoid tumors. The primary lesions usually develop on the distal extremities, but may involve upper limb as well as viscera, over a period of years^{1,5}.

Kaposi sarcoma is classified as an AIDS-defining cancer and the HIV-infected individuals with impaired immune function are at increased risk for KS. It is customarily said that AIDS-associated KS most commonly affects HIV-infected patients with CD4 T cell counts, of fewer than 500 cells per cubic millimeter. However, more recent studies show that along with CD4 cell count, there are other factors involved in risk stratification of KS¹⁶. AIDS-associated KS presents as a disseminated mucocutaneous disease consisting of papules and plaques which occasionally form extensive armor-like constricting plaques that may impair the function of extremities and cause lymphedema. Areas such as the trunk and mid-face are common sites of visceral involvement, including the gastrointestinal tract, lymph nodes and lungs.

Here, the case of an 82-year-old male with a classic form of KS presenting with elephantiasis which is a rare manifestation of Kaposi sarcoma, has been reported. Elephantiasis nostras verrucosa (ENV) is a progressive cutaneous hypertrophy characterized by non-pitting edema with superimposed hyperkeratotic papules, nodules, and verrucous cobblestone-like plaques. These cutaneous lesions are a consequence

of chronic lymphedema caused by longstanding lymphatic obstruction. Histological examination of the lesions revealed acanthosis and hyperkeratosis of the epidermis and dilated lymphatic spaces in the dermis^{1,10}. The condition may occur secondary to trauma, radiation, surgery, tumor-obstruction, portal hypertension, congestive heart failure and AIDS-associated KS^{7,9,10,14}. To determine the etiology of ENV in this patient, these conditions were ruled out by means of history, physical examination, lab tests and imaging. Lymphedema associated with KS is most probably due to malignant lymphatic obliteration, nodal obstruction or increased vascular permeability secondary to HHV-8 infection which may lead to impaired lymphatic drainage, lymphedema and rarely elephantiasis nostras verrucosa. ENV with AIDS-associated KS has been reported before but to the best of our knowledge, this study is the first to report ENV with classic KS. In the differential diagnoses of a patient with non-pitting edema and cutaneous lesions suggestive of ENV, Kaposi sarcoma should be considered along with other morbidities.

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