Kaposi's sarcoma in three HIV-negative, non-immunosuppressed patients

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Over the past two years, three Hong Kong Chinese individuals have presented to the Social Hygiene Service (Department of Health, Hong Kong) with granuloma-like nodules on their lower extremities. Histopathological examination of the lesions revealed that they were Kaposi's sarcoma, two of which were initially misdiagnosed as pyogenic granuloma. All three patients originated from southern China and had previously been in good health, with no evidence of immunosuppression. All ELISA tests for human immunodeficiency virus antibodies were negative. The course of the disease has been favourable. The lesions in the first patient regressed with radiotherapy. Complete surgical excision of the lesion in the second patient was not followed by recurrence. In the third patient, the lesions were static and did not require active intervention. Awareness of the existence of Kaposi's sarcoma among non-risk groups allows for their prompt recognition.

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Key words: Kaposi's sarcoma; HIV seronegativity; Immunocompetence; Hong Kong

Introduction

Kaposi's sarcoma (KS) is characterised by vascular proliferation, and has recently received renewed interest. Four major clinical types are recognised—the classical, endemic, immunosuppressed, and epidemic forms. Reports of KS in Chinese people have been scarce. We report three Hong Kong Chinese with KS who presented to us over the past two years. All three patients tested negative for human immunodeficiency virus (HIV) antibodies and were not immunosuppressed, and thus conform to the classical type. A summary of demographic data and clinical information of the three patients is shown in Table 1.

Case reports

Case 1

A 66-year-old man from Fujian province who had lived in Hong Kong for more than 40 years presented to our clinic in March 1994 with a six-month history of increasing pigmented nodules (number and size) over the right foot. The nodules were neither itchy nor painful. He reported no systemic symptoms or weight loss. He denied a history of homosexuality, sexual promiscuity, receiving a blood transfusion, or drug addiction. Examination showed several bluish papules and nodules on the right ankle, toes, and sole. The biggest lesion measured 1 cm in diameter and one lesion had a crust on the surface. There was no peripheral lymphadenopathy and the systemic examination was normal.

A clinical diagnosis of pyogenic granuloma was made and excisional biopsy of a lesion was performed. This was initially interpreted as a pyogenic granuloma, but on re-examination of the biopsied tissues by a dermatopathologist, the correct diagnosis of KS was made. ELISA tests for HIV types 1 and 2 were negative twice, and human T-cell lymphotropic virus type 1 (HTLV-I) serology was also negative. Other laboratory tests revealed no evidence of immunosuppression. The patient received a course of radiotherapy. The lesions regressed and he remains well.

Case 2

A 70-year-old man from Guangdong province who had been residing in Hong Kong for more than 50

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Fig 1. A solitary, firm, erythematous nodule 1.5 cm in diameter at the lateral edge of the right foot. The surface was abraded with no discernible epidermis.

Fig 2a. Diagnostic low power appearance of Kaposi's sarcoma. In the dermis are multiple nodular aggregates of spindle cells with some vascular slits formation. The overlying epidermis is excoriated and crusted, simulating pyogenic granuloma (H&E, x 20).

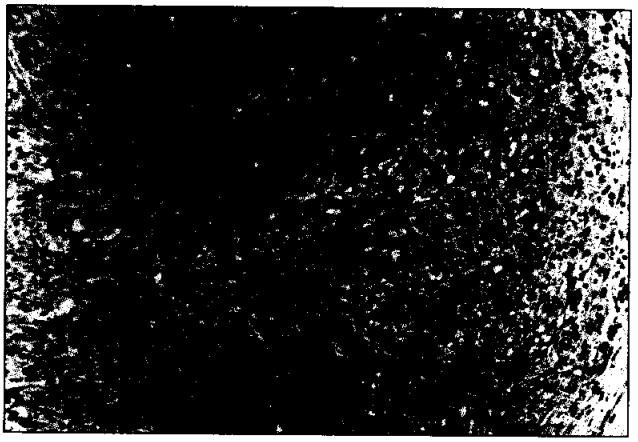

Fig 2b. High power view of one of the nodules shows relatively uniform spindle cells in interlacing short fascicles with formation of intercellular vascular slits, some of which contain red blood cells (H&E, x 400).

years first presented in August 1994 with a two-month history of a red nodule on the lateral edge of his right foot. The lesion had been preceded by a minor abrasion that was induced by friction with his shoe. There was some bleeding but no pain or itch was noted. Before he sought consultation, he had applied some over-the-counter medicament but no improvement was noted. The patient had drunk heavily for the past 15 years and denied any venereal exposure.

Examination showed a solitary, well-defined, round, erythematous nodule that was 1.5 cm in diameter. It was situated on the lateral edge of his right foot at about the level of the base of the fifth metatarsal bone (Fig 1). The surface of the nodule was abraded with no discernible epidermis. The rest of the lower limb was normal in appearance. The systemic examination was normal. A presumptive diagnosis of pyogenic granuloma was made and a shave biopsy was performed. Histopathology of the biopsy revealed an excoriated and crusted epidermis. Spindle cells and vascular slits were evident in the dermis. Red blood cells could be seen in some of the vascular slits. These features are diagnostic of KS.

A complete excision of the residual lesion was subsequently performed. Histopathology of the excised lesion revealed the same features of KS (Figs 2a and 2b). Blood tests showed a normal haemoglobin level and white cell count and his $CD4^+$ cell count was normal. Liver function tests showed mild derangement with the following values: albumin 35 g/L (normal range, 40-60 g/L), alkaline phosphatase 121 U/L (normal range, 30-120 U/L), and alanine aminotransferase 160 U/L (normal range, 0-35 U/L). The test for hepatitis B surface antigen was positive. This picture is compatible with chronic hepatitis. Blood tests for syphilis, HIV infection, and immunoglobulin IgG, IgA, and IgM levels were either negative or normal. A chest X-ray showed no lesions. At his last follow up in January 1995, there was no clinical evidence of recurrence. He has refused further follow up.

Case 3

A 74-year-old woman from Guangdong province presented to us in August 1995 with multiple skin nodules on her left leg and the dorsa of both feet that had developed over the past six months. The nodules were

Table 1. Demographic data of three elderly patients with Kaposi's sarcoma

Features	Patient 1	Patient 2	Patient 3
Sex	Male	Male	Female
Age at presentation (y)	66	70	74
Born	Fujian	Guangdong	Guangdong
Occupation	Messenger	Cashier	Housewife
Resident in Hong Kong (y)	>40	>50	>25
Clinical presentation	Lower limb nodules	Solitary nodule on right foot	Lower limb nodules
Result of systemic examination	N‖	N	N
Concurrent medical illness	Nil	Hepatitis (subclinical)	Diabetes mellitus
HIV status*	Neg¶	Neg	Neg
Results of tests for syphilis (VDRL/FTA-Abs)†	Neg	Neg	Neg
HTLV-1 serology‡	Neg	Neg	Neg
$CD4^+$ count	N	Refused blood test	N
HB_sAg§	Neg	Positive	Neg
Immunoglobulin levels	N	N	N
Chest X-ray result	N	N	N
Treatment given	Two courses	Excision of radiotherapy	Excision
Present condition	Stable	Refused follow up	Stable

* HIV human immunodeficiency virus types 1 and 2
† VDRL Venereal Disease Research Laboratory test/
FTA-Abs Fluorescent treponemal antibody absorption test
‡ HTLV-I human T-lymphotropic virus type 1
§ HB_sAg hepatitis B surface antigen
‖ N normal or within normal range
¶ Neg negative

not itchy or painful but had recently become more numerous and bled easily. The patient had been living in Hong Kong for more than 25 years. Apart from a 20-year history of diabetes mellitus, she enjoyed good general health and had no history of venereal exposure. Her diabetes was well-controlled with oral hypoglycaemic drugs and dietary restriction.

There were multiple, purplish nodules on her left leg and the dorsal aspects of both feet. The size of the lesions varied from 3 to 8 mm in diameter. They were not accompanied by local oedema or varicosities of the limb. The systemic examination was normal with no lymphadenopathy or organomegaly present. The tentative diagnoses were KS or multiple pyogenic

granulomas. Biopsy of the largest lesion from her left foot confirmed the diagnosis of KS. Blood tests for complete blood profile, liver and renal function, $CD4^+$ and $CD8^+$ lymphocyte levels and their ratio, syphilis, and HIV infection yielded either normal or negative results. Her condition did not deteriorate despite no active treatment other than regular observation being given. Recently, she reported regression of some of the some smaller lesions.

Discussion

This vasoproliferative condition was first recognised by Moricz Kaposi in 1873 as idiopathic, multiple, pigmented sarcoma of the skin. For the first 50 years after KS was described, the neoplasm was said to be most common in southern Europeans and in Ashkenazi Jews, and little was known of KS elsewhere until the beginning of the second half of this century. In 1961, an international symposium was held in Uganda and the high frequency of the tumour in certain areas of Africa was highlighted.[1] In the past decade, there has been renewed interest in KS because of its association with the acquired immunodeficiency syndrome (AIDS). This form of KS affects mostly HIV-positive, homosexual individuals and presents as a disseminated, aggressive disease.[2]

Clinical and epidemiological studies on AIDS-related KS abound, but most are based on data from Western countries. Kaposi's sarcoma in Asians has only been reported anecdotally.[3,4] There is a recent account of the condition occurring in local patients with AIDS.[5] In this article, we attempt to provide additional data on KS not associated with AIDS and in a non-immunosuppressed population.

Our three cases of KS represent the first series of classical type KS reported in Hong Kong. All three patients have lived in Hong Kong for many years, and all originate from southern provinces in China. Two are men, one is a woman, and all are older than 60 years of age. They all enjoy good health, apart from the mild laboratory abnormalities indicative of a subclinical hepatitis found in the second patient and the relatively well-controlled diabetes mellitus of the third patient. All three had negative results for HIV infection and their immunological parameters were normal or within normal ranges.

None of the three patients had any evidence of co-existing haemopoietic neoplasia purported to be associated with classical KS (mostly Ugandan Africans).[6] All three patients had favourable outcomes regarding their skin lesions. The lesions of the first patient showed a very good response to radiotherapy. The second patient had only a single KS lesion on his foot with no evidence of recurrence or occurrence of new lesions on other parts of his body after complete surgical excision. For the third patient, we have adopted a 'wait and see' policy, because her KS lesions were static and did not cause her any discomfort that warranted active intervention.

A search of the English literature showed that cases of KS in HIV-negative, non-immunosuppressed Chinese are rare. In 1992, Lee reported five cases of KS in patients who were born and lived in Tainan, Taiwan.[3] Of these five patients, two enjoyed good health, two were taking steroids for arthralgia, and one was a diabetic. They all denied a history of homosexuality, multiple sex partners, or drug abuse, and their HIV screening tests were negative. In 1993, Shen et al reported 23 cases of classical KS found between 1983 to 1992 in Xinjiang province, China—with particular emphasis on racial traits. Seventeen of these were Uighurs and six were Kazakhs.[4] Thus, it appears that KS unrelated to HIV immunosuppression, may not be so uncommon in ethnic Chinese. Table 2 compares our patients with those reported by Shen.

The first two cases described earlier presented with nodular lesions of the feet that clinically resembled pyogenic granuloma. The initial histopathological assessment in both cases was of pyogenic granuloma. A definitive diagnosis of KS was rendered on review of the histological sections by one of the authors with considerable experience with KS. The initial misdiagnoses were most likely the result of a low index of suspicion and unfamiliarity with the diagnostic histopathological features attributable to this rare sarcoma.

Patients with KS may present to the clinician with lesions at different stages of development—a patch, plaque, or tumorous lesion. The patch and plaque lesions are seen mostly in the context of AIDS, the lesions are often widespread, and involvement of the mucous membranes is characteristic. In contrast, patients with the classical type of KS typically present with nodular lesions on the extremities. Regardless of the clinical types and stages, KS lesions present similar histological features. The nodular lesions of classical KS present

Table 2: Comparison with Shen's 23 cases of Kaposi's sarcoma

Features	Shen et al	Tang et al
Male	22	2
Female	1	1
Ethnicity (no. of patients)	Uighur (17) Kazakh (6)	Native of southern China (3)
Average age at presentation (y)	52	70
Duration before presentation	1-22 y	2-6 mo
Morphology of lesions	Nodules, patches, plaques	Nodules, patches plaques
Site	Predominantly lower limbs	Lower limbs
Regional lymphadenopathy	Groin and axillae	Not detectable

distinct histopathological features. The features include nodular aggregates of intersecting fascicles of spindle cells in the dermis, slits between spindle cells with erythrocytes, and characteristic PAS-positive, diastase-resistant, intracytoplasmic, hyaline globules. This constellation of findings seen under a light microscope allow a specific diagnosis to be made and distinguish KS from other spindle cell proliferations in the dermis.

The aetiology of KS is not entirely known, and both genetic and environmental factors are thought to be involved in its pathogenesis. Pollack et al observed an increased frequency of HLA-DR5 among Italian and Jewish KS patients.[7] Various infectious agents such as cytomegalovirus,[8] human T-cell lymphotropic virus type I and HIV type I have been inconclusively implicated.[9,10] Recently, a human herpesvirus-like agent was reported to have a close association with KS,[11-13] as their DNA material have been demonstrated within the tumour cells in both AIDS and non-AIDS–related KS tissue, implying a possible pathogenetic role for this agent.

In addition to the AIDS population, KS in the classical form occurs in the elderly of the non-risk population in Hong Kong. The clinical profile of classical KS seen is comparable to that reported elsewhere, except that we have not seen any associated haemopoietic neoplasms as have been reported elsewhere. It is also apparent that pyogenic granuloma presents a definite diagnostic pitfall for KS, both clinically and histopathologically. Awareness of the existence of KS in Chinese (in particular among those not at risk for AIDS), clinical alertness, and attention to the salient, histological features of KS, will help doctors to recognise the disease, give prompt management of the patient, and improve data collection for further studies.

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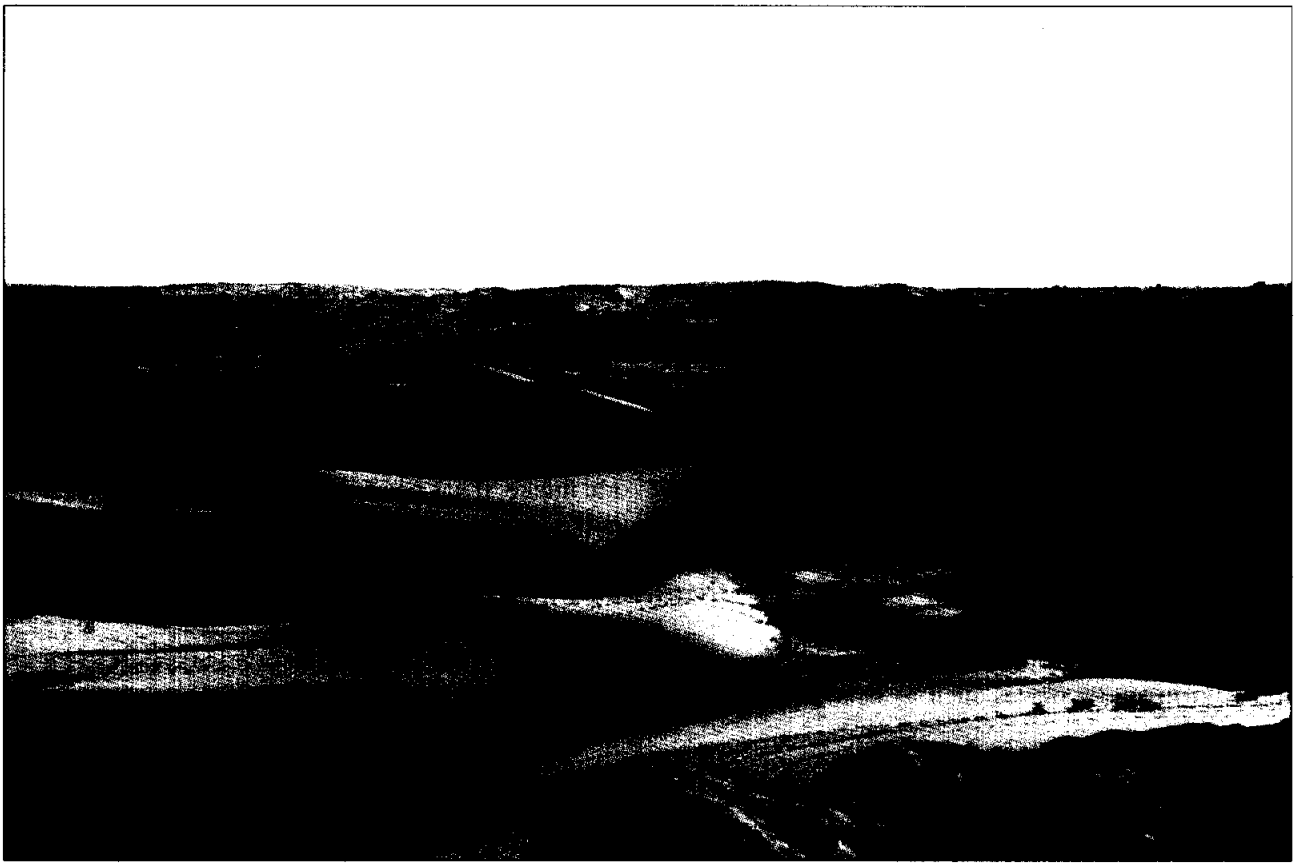

P Smith, Sand dunes in the Rajasthan desert, Rajasthan, India.