

Case Report

Widespread and Fungating Kaposi Sarcoma in an HIV Negative Patient

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Abstract: Kaposi sarcoma (KS) is a vascular neoplasm of the endothelial cells that commonly occurs in conditions that may lead to severe immunosuppression, e.g. HIV/AIDS, malignancies or use of immune suppressing medications. The development of KS has been linked to infection with an oncogenic virus, the Human Herpes Virus 8 (HHV-8), also known as KS-associated herpes virus (KSHV). Rarely KS also occurs in individuals with no clinical or pathological evidence of immunosuppression as described in the elderly male population of Mediterranean origin, the Ashkenazi Jews and younger population in parts of Central Africa where the oncogenic virus is endemic. Lesions in non AIDS KS are usually localized and typically involve the lower limbs. Widespread and generalized KS occur more in individuals suffering from HIV/AIDS. We describe a case of a HIV negative 51year old Nigerian male who presented with generalized cutaneous KS. Diagnosis was made by a combination of clinical description, imaging studies and histopathology. Clinical presentation of KS ranges from mild (localized cutaneous) to severe (generalized cutaneous and visceral) features. Treatment modalities are available for KS and use of any particular type of treatment depends largely on the distribution of lesions, visceral organ involvement and the presence or absence of immunosuppression. Treatment of KS, particularly cutaneous presentations does not restore the skin to its premorbid state however early diagnosis and treatment is necessary to achieve a significantly improved outcome.

Keywords: Kaposi sarcoma, Human Herpes Virus 8, AIDS, HIV, KS-associated herpes virus (KSHV), Neoplasm

INTRODUCTION

Kaposi sarcoma is a vascular neoplasm (of endothelial cells) first described in 1872 by Moritz Kaposi (1837-1902). It often manifests with multiple vascular nodules on the skin and other organs. It usually presents as brownish red to purplish patches, plaques or nodules that may enlarge into dome-shaped tumors. The pattern of Kaposi sarcoma is variable, with a course ranging from indolent with only skin manifestations to fulminant with extensive visceral involvement. Cutaneous KS rarely may be infiltrative or exophytic. Exophytic KS may erode downward into bone[1].

The exact nature of the disease is not clear. There is the controversy whether the endothelial cells are of vascular origin, lymphatic origin or both [2]. Current data support the notion that KS is a vascular hyperplasia with a tight link to HHV-8 infection. The virus was first identified in KS cells of a patient with AIDS but later, it had been linked convincingly with all 4 types of KS, an association that is necessary, but not sufficient to develop KS. Other factors seem to be contributory in the development of KS. Immunosuppression appears to be the most significant cofactor[3].

Non AIDS Kaposi sarcoma is a rare disease especially in the absence of demonstrable immunosuppression. Non AIDS KS have been described among elderly male of Mediterranean origin, the Ashkenazi Jews and younger individuals in parts of Central Africa where the oncogenic virus is endemic. Lesions of non AIDS KS have predilection for the lower limbs and are typically localised however widespread distribution have been described in literatures. All forms of Kaposi sarcoma have been linked to infection with human herpes virus (HHV)-8.

CASE REPORT

Mr. O.L.S. is a 51yr old Clergy who presented to the University of Benin Teaching Hospital (UBTH) on the 13th of August 2015 with complaints of generalized skin rashes, leg swelling of 3yrs duration and ulcers on both feet of a year's duration. Rashes increased in size and number over a period of about 18months with development of swelling of the lower and upper limbs, trunk and face. There was associated coalescing of the rashes and progression to development of ulcers on both feet. There was a positive history of weight loss which was observed 6months before presentation to UBTH. There was no history of trauma to the feet or change in body cream or

soaps prior to onset of skin rashes. There was no history of fever, cough, night sweat, diarrhea, abdominal pain, vomiting, chest pain, dysphagia, dysuria or haematuria. There was no history of sexual exposure to person(s) other than the wife. There is no history suggestive of tuberculosis, diabetes mellitus or use of steroids and or other immunosuppressants.

HIV screening done on at least two occasions were negative, histology of skin biopsy was suggestive of chronic nonspecific dermatitis with no evidence of malignancy while mycological/ bacteriological smear had features suggestive of subcutaneous mycosis for

which he was placed on Amphotericin B and Itraconazole for about 9months without improvement.

On presentation at UBTH, examination revealed an ill looking middle aged man who was pale, anicteric, afebrile, not cyanosed, not dehydrated. There was no peripheral lymph node enlargement. There was bilateral pitting peripheral oedema of the lower limbs, trunk and the upper limbs. There were generalized hyper pigmented/purplish/erythematous papules, plaques and nodules of varying sizes on the trunk, upper and lower limbs with fungating/ulcerated and infected lesions on both feet.



Fig. 1. Image showing widespread distribution of KS lesions on the upper and lower limbs. (At presentation)



Fig. 2. Fungating, infected and ulcerated lesions of KS on both feet



Fig. 3. Fungating and ulcerated lesion on the left foot

Pulse was 106 bpm, regular and of normal volume. Blood pressure was 120/70 mm/Hg. Heart sounds were S₁ and S₂ with no added sounds. There was no significant findings on chest and abdominal examination

Diagnoses made were;

1. Kaposi sarcoma
2. Subcutaneous mycosis

Investigations ordered for include RVS, RBS, FBC/ESR, Urinalysis, E/U/Cr, Histology of skin biopsy, X-ray of the legs/feet.

RVS: Negative
RBS: 179mg/dl.

FBC
WBC: 2.2×10^3
Platelet: 229×10^3
HCT: 26.1%
Hb: 8.7g/dl

E/U/Cr
Urea: 22mg/dl
Creatinine: 0.5mg/dl
Na⁺: 133mmol/l
K⁺: 5.7mmol/l

HCO₃⁻: 19mmol/l
Cl⁻: 104mmol/l

Urinalysis
Colour: Amber, clear
pH: 5
Specific gravity: 1.015
Urobilinogen: +

Wound swab M/C/S
Pus cells ++
Gram -ve bacilli: ++

Culture yielded mixed growth of Klebsiella species & Proteus mirabilis species

X-ray of the legs/feet

There are multiple nodular soft tissue masses involving the posteromedial aspects of the right leg as well as the distal aspects of both legs. There are no calcifications of lucencies within. The bones of both legs appear grossly normal.

There is marked soft tissue swelling of both feet with similar nodular masses noted extending up to the digits, worse on the right. The tarsal bones are osteopenic, with lytic areas involving the heads of the 2nd metatarsal bones bilaterally.



Fig. 5. Radiograph of both feet (AP view)



Fig. 6. Radiograph of the left foot (Lateral view)



Fig. 7. Radiograph of the right foot (Lateral view)



Fig. 8. Radiograph of both legs (AP view)

Conclusion: Considerations are;

1. Kaposi sarcoma
2. Deep soft tissue mycoses.



Fig. 9. Radiology report.

Histology report

Macroscopy: Specimen consists of a negroid skin, firm in consistency and measuring 1x0.5x0.2cm.

Microscopy: Sections show a lesion composed of nodules of spindle shaped cells with plump hyperchromatic nuclei and prominent nucleoli

interspersed with slit-like vascular spaces containing extravasated blood. The overlying stratified squamous epithelium is thinned out and consists of stratified squamous keratinizing epithelium.

Diagnosis: Features are in keeping with Kaposi sarcoma (nodular stage)

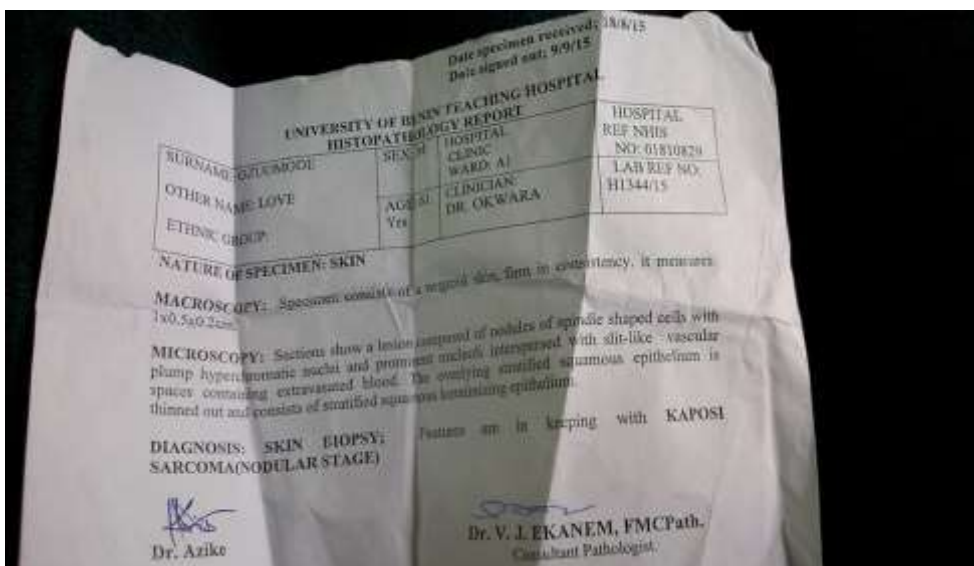


Fig. 10. Histopathology report.

Patient was subsequently worked up for chemotherapy. He was transfused with 3pints of packed cells. Other treatment given include; IV Ceftriaxone 2gm once daily for 1week. Systemic combination

chemotherapy comprising. IV Vincristine 2mg stat IV Bleomycin 15iu stat, IV Doxorubicin 30mg in IVF normal saline. Chemotherapy was administered once every 4weeks. There was significant improvement with

the first 4 courses of chemotherapy however medication was changed to Paclitaxel with a possible use of adjuvant Radiotherapy because of non-response to subsequent courses of combination chemotherapy. He showed significant improvement notably with peripheral oedema subsiding, lesions regressing and healing of the ulcers on both feet.

He has had 4 courses of Paclitaxel and is due for Radiotherapy of residual lesions on the lower limbs after the 6th course of Paclitaxel. He is still being followed up in the clinic.



Fig. 11. Anterior view of both lower legs/feet after 3rd course of Paclitaxel

DISCUSSION

Four clinical variants of Kaposi sarcoma (KS) have been described.

1. Classic KS
2. Endemic (African)
3. Iatrogenic (Transplant, immunosuppression related)
4. Epidemic (AIDS associated)

The classic form is frequently observed in elderly male patients of Mediterranean origin and Ashkenazi Jews, presenting as an indolent disease, with nodular lesions on the skin, and affecting more often the lower limbs and feet and rarely presenting visceral involvement[4]. Endemic KS occurs in people living in Equatorial Africa and comprised approximately 9% of all cancers seen in Ugandan males. It is similar to classic KS however in endemic KS, people generally develop the disease at a younger age. African KS is seen as either an indolent neoplasm identical to the classic disease seen in Europe and North America or as an aggressive disease with fungating and exophytic tumors that may invade the subcutaneous and surrounding tissue including the underlying bone. It can be classified as endemic cutaneous or endemic lymphadenopathic. Endemic KS usually causes skin lesions without any other symptoms however a particularly aggressive form can occur in pre-pubertal children. In these cases, the generalized lymphadenopathy is frequently associated with visceral organ involvement. The prognosis is very poor with a 100% fatality rate within 3 years[5].

Iatrogenic KS

In 1969, the first case of KS in association with immunosuppression in a renal transplant patient was described. Since that time, a number of renal and

other organ allograft recipients who received prednisone and azathioprine developed KS shortly after the onset of immunosuppressive therapy[6]. KS tumor in iatrogenically immunosuppressed patients often remains localized to the skin, widespread dissemination with mucocutaneous or visceral organ involvement is common.

Epidemic KS

In 1981, a fulminant and disseminated form of KS in young homosexual or bisexual men was first reported as part of an epidemic now known as AIDS [7]. The etiology of AIDS is a T-cell lymphotropic retrovirus known as HIV. The underlying immunologic deficiency that characterizes HIV disease is an acquired profound disorder of cell-mediated immune functions. This immunologic deficiency and immune dysregulation predisposes the host to a variety of opportunistic infections and unusual neoplasms, especially KS. HIV may play an indirect role in the development of KS[8].

Most patients with epidemic KS eventually develop disseminated disease. The disease often progresses in an orderly fashion from a few localized or widespread mucocutaneous lesions to more numerous lesions and generalized skin disease with lymph node, gastrointestinal tract disease, and other organ involvement. Pleuropulmonary KS is an ominous sign usually occurring late in the course of the disease, especially in those patients whose death is directly attributed to KS [9].

The pathogenesis of KS is uncertain. An association between all types of KS and infection with HHV-8, known as KS-associated herpes virus (KSHV) has been described in several literature. The route of

HHV-8 transmission may be both sexual and nonsexual. High HHV-8 seroprevalence in individuals with high-risk sexual activity represents the sexual route, and the detection of HHV-8 antibodies in children and nuns without sexual activity suggests the nonsexual route. Saliva could be a potential source of spread of HHV-8 in the general population[10].

The differential diagnosis of Kaposi sarcoma, especially non-HIV Kaposi depends on the site involved and these include histiocytoma, bacillary angiomatosis, sarcoidosis, haemangioma, subcutaneous mycosis etc.

Non-AIDS KS is considered a rare disease, but incidence varies according to individual factors such as origin, sex, age and immune status of the patient. Clinically, non-AIDS KS mostly presents itself as multiple bilateral cutaneous lesions of the lower limb[11].

Our patient presented with generalized hyperpigmented/purplish/erythematous papules, plaques and nodules with fungating and infected ulcerated lesions on both feet. He also had tumour associated oedema at presentation.

Biopsy is diagnostic and histopathological findings are the same as KS in other body sites. Those are, blood filled slit like spaces, pleomorphic spindle cells with frequent mitoses, extravasated erythrocytes, hemosiderin laden macrophages and may be cellular infiltrate by lymphocytes and plasma cells[12,13].

KS can be seen as a systemic disease with multilocal occurrence of vascular tumors. Thus the therapeutic administration of KS differs essentially from the management of most other neoplastic diseases. In comparison with other tumors KS therapy comprises growth control rather than elimination without presenting a palliative situation. A standard therapeutic guideline does not exist as the therapeutic options have to be chosen depending on subtype and stage of the disease as well as on the immune status of the patient [14]. Treatment modalities comprise local therapy for example surgery, radiotherapy and local chemotherapy such as injections of vinca alkaloids or local immune therapy by interferon, 9 cis retinoid acid or imiquimod [15,16,17]. Patients with widespread disease may need systemic chemotherapeutic or immunologic medication. Positive results have been found for pegylated liposomal doxorubicin, danaurubicin, paclitaxel and interferon α [18,19]. In patients with iatrogenic KS, immunosuppressive medication may be reduced or modified with the considerate possibility of grafts being rejected with insufficient immunosuppression[20].

Combination systemic treatment with vincristine, doxorubicin and bleomycin was initially used for our patient because he had a widespread distribution of the lesions, with the lower limbs more affected. Treatment was later changed to paclitaxel following non response to subsequent courses of initial combination chemotherapy.

CONCLUSION

Kaposi sarcoma is a neoplasm that typically occurs in the presence of severe immunosuppression. Epidemic (AIDS associated) KS is the commonest variant described. Non AIDS KS has distribution limited to the lower limbs (especially the feet) however findings of widespread distribution of non-AIDS KS have been documented. Our patient who had widespread lesions was HIV negative and had no other finding or history suggestive of immunosuppression. Several treatment options are available for KS and choice of therapy depends largely on distribution of lesions (cutaneous and or visceral) and the presence/absence of immunosuppression.

A high index of suspicion and biopsy of lesion particularly in the absence of demonstrable immunosuppression will facilitate early diagnosis and appropriate treatment in order to achieve an improved prognosis.

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