Case Report

Epidemic of Kaposi's sarcoma in the Nuba Mountain: fact or fiction

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Abstract:

Background: Kaposi's sarcoma (KS) is a complex neoplasm characterized by angio-proliferative multifocal tumours of the skin, mucosa and viscera. There are four different epidemiological forms of KS: classic (sporadic) (cKS), African (endemic), AIDS-associated (epidemic), and immunosupression-associated (iatrogenic).

Objectives: In this paper we report for the first time types of Kaposi's sarcoma from the Nuba Mountains as seen in Dermatology Military Hospital.

Patients and methods: Clinical features and confirmative tests were done for six patients. Three, two and one cases were AIDS related, endemic type and iatrogenic type of Kaposi's sarcoma respectively.

Results: We report a series of Kaposi's sarcoma in six Sudanese patients. Mean age 66.7 year, five of them were males and a female. The AIDS associated KS patients showed good response to management and are under follow-up on HAART. The endemic type cases have been improved with chemotherapy. The single case of iatrogenic KS could not be traced.

Conclusion: KS is an important disease that should not be missed and has to be well classified

Keywords: HIV (AIDS), HHV-8, classical KS, Endemic KS, Iatrogenic KS, HAART.

Kaposi sarcoma is a commonly missed disease. Patients present to physicians in general practice but referred to dermatologists to be managed. Delay in diagnosis increases cost of treatment and worsen morbidity of the disease.

Kaposi's sarcoma (KS) is a complex neoplasm characterized by angio-proliferative multifocal tumours of the skin, mucosa and viscera. KS lesions are comprised of both distinctive spindle cells of endothelial origin and a variable inflammatory infiltrate. There are four different epidemiological forms of KS: classic (sporadic) cKS, African (endemic), AIDS-associated (epidemic), and immunosupression-associated (iatrogenic)1.

The racial and geographical distribution of Kaposi's sarcoma is well recognized. Therefore, hereditary and environmental factors are suspected to play a role in its aetiology. Here we describe Kaposi's sarcoma occurring in six patients, presented to Omdurman Military Hospital (OMH).

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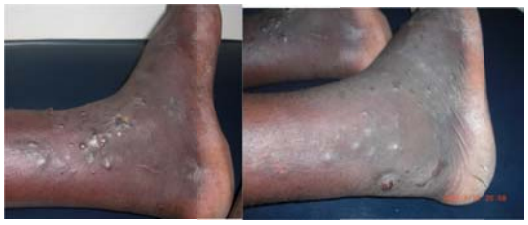
Three of them were HIV related KS, two were endemic type KS and the last one was an iatrogenic type KS2.

Case number 1:

A 30-year old single male, presented with nodules and swellings in both legs for more than a year. The condition is not associated with diarrhoea, loss of weight, fever, cough or any other symptoms. On examination, there were multiple nodules symmetrical, involving both feet and around the ankle, and soles. The nodules were reddish and blue in colour some of them bleed with gross swelling of both legs without lymphadenopathy. Routine investigations were normal regarding full blood count, renal and liver function tests, but HIV screening test was positive.

Fig 1: Skin lesion in case 1.

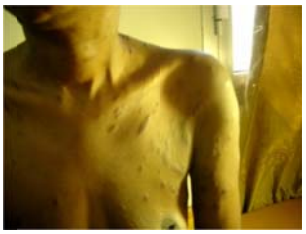


Skin biopsy confirmed the diagnosis of Kaposi's sarcoma. He started Highly Active Antiretroviral Therapy (HAART), on tenth of May 2010. Up to now he is on regular follow-up monthly.

Case number 2:

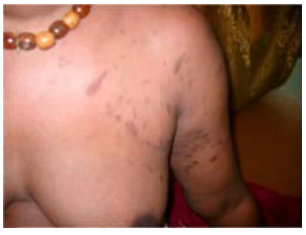
A 37-years old woman, divorced, referred from the surgical department with multiple nodules and swellings for more than a year. Skin lesions were mainly on the trunk, chest, breasts and extremities.

Fig 2a: Skin lesion in case 2 before treatment



The condition is associated with diarrhoea, loss of weight and fever. She became very weak to the extent that she needs to be supported on walking. Repeated episodes of such symptoms were treated as malaria. Investigations were normal regarding full blood count, renal and liver function tests. HIV screening test was positive. Skin biopsy reported as Kaposi's sarcoma.The patient received antiretroviral therapy. After three weeks she showed remarkable clinical improvement. Diarrhoea stopped, her weight improved and she could walk unsupported. She was discharged and followed up regularly. After one year she came back with considerable gaining of weight, with complete resolution of her Kaposi's sarcoma (see Fig 2a and b).

Fig 2b: Skin lesion in case 2 after treatment



Unfortunately she died many years later with an opportunistic pulmonary infection.

Case number 3:

A 27-year old male, soldier, single was referred from the Chest department after starting antituberculous treatment five months prior to referral. He presented with skin nodules and multiple swellings for less than one year, involving the oral mucosa, nose, face, lower eye lids, head and right side of the neck, with multiple enlarged groups of lymph nodes.

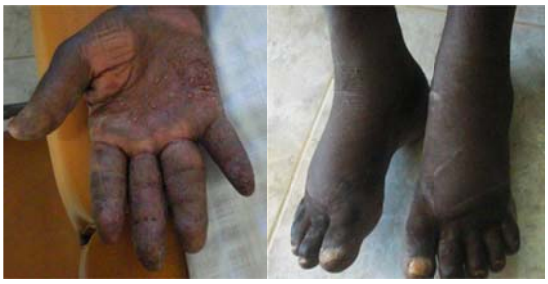
Fig 3: Skin lesion in case 3

The condition was associated with diarrhoea and loss of weight. There was a low grade nocturnal fever and cough, pulmonary tuberculosis was diagnosed previously and managed according to The National Tuberculosis Controlled Program Treatment Protocol. Investigations showed a reactive HIV screening test with skin histopathology diagnostic of Kaposi's sarcoma.The patient received antiretroviral therapy together with antituberculous treatment. Now he is on regular follow up with moderate improvement.

Case number 4:

A 65-year old male, presented with multiple nodular skin lesions for 15 months. Lesions were spread all over the body except the anterior surface of the chest and abdomen. The lesions were itchy but not painful and not associated with fever, cough or diarrhoea, but mild loss of weight. On examination he looks well, not wasted or febrile. Locally, multiple nodular skin lesions with sparing of the anterior aspect of the chest and abdomen. The nodules in the distal limbs were associated with oedema, but are not ulcerated or infected.

Fig 4: Skin lesion in case 4

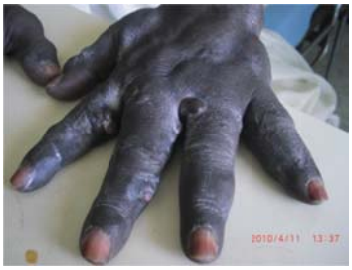


Investigations done on admission showed that liver, renal function tests, serum uric acid and Full Blood Count were within normal values. HIV screening test was negative, Histopathology done for the skin lesion, and confirm the diagnosis of Kaposi's sarcoma. Patient was referred to the Radiotherapy and Isotope Centre Khartoum (RICK), for further management there was remarkable improvement after the second dose of chemotherapy.

Case number 5:

A 75-year old married male, presented with nodules and swellings for more than a year, involving the hands, feet and oral mucosa. The condition was not associated with diarrhoea, loss of weight, fever or cough.

Fig 5: Skin lesion in case 5



Investigations were normal regarding full blood count, renal and liver function tests. HIV screening test was negative. Skin histopathology revealed Kaposi's sarcoma. The patient received sessions of chemo and radiotherapy, now improved and on regular follow-up.

Case number 6:

A 65-year old male, teacher on pension, was referred from the National Renal Centre complaining of skin nodules and swellings for less than one year, mainly in the hands and feet. He had no symptoms related to Kaposi's sarcoma such as diarrhoea, weight loss, fever or cough. He had renal transplantation three years before presentation. He was on immuno-suppressive therapy. HIV screening test was not reactive but, histopathology confirmed the diagnosis of Kaposi's sarcoma. The patient was lost during follow up.

Table1. Summary of all cases:

No	Age in *Years*	Sex	Clinical presentation	Geographic distribution	HIV status
1	37	Female	Nodules all over the body, weight loss, fever, diarrhea.	Darfur	+ve
2	30	Male	Nodules, swellings in lower extremities, mild weight loss.	White Nile	+ve
3	27	Male	Nodules in face, nose, oral mucosa, tongue lower eye lid, cervical and inguinal lymph nodes with pulmonary tuberculosis.	Nuba Mountains	+ve
4	65	Male	Nodules in hands, feet, oral cavity, gross lymph-edema in upper and lower limbs.	Nuba Mountains	-ve
5	75	Male	Nodules in fingers, hands, face, scalp, lymph-edema in upper and lower limbs, sever itching.	Nuba Mountains	-ve
6	65	Male	Nodules in hands and feet, renal transplanted three years ago, on immunosuppressant.	Khartoum	-ve

Discussion:

Kaposi's sarcoma (KS) remains a challenge. Its classic or Mediterranean form tends to be benign, but, in transplant recipients it may be less so. As a part of the AIDS pandemic of which it was an original defining component, it may be life threatening. It is due to human herpes virus 8 (HHV8), which is necessary but not sufficient to produce the disease. KS has a low prevalence in the general population in USA and UK, with intermediate rate in Italy and Greece, and a high one in some parts of Africa3. In Sudan there is no information about this disease. Our report of this case series is a step forward on documenting or trying to identify different types of disease present in Sudan which may be region of high occurrence.

Historically in 1872, Moritz Kaposi, a Hungarian dermatologist, in Vienna University first described his series of five patients with enlarged cutaneous nodules and similar internal neoplasm, especially of the larynx, trachea, stomach, liver or colon4. Kaposi's original description of the five patients is more reminiscent of the KS seen in AIDS (KS-AIDS) than Kaposi sarcoma anticipated in elderly men of Italian, Jewish and Mediterranean lineage in whom the disease behavior is usually benign, with all of the original five patients dying within two to three years.

Our series consist of six Sudanese patients' five males and a female with mean age of 66.7 years. In AIDS patients KS account 35% of patients and the incidence that has been declining by the use of HAART, but in our series it accounts for 60%. This percentage declined on HAART when complete remission occurred in one of the patients. Deterioration of his condition was observed when he became poorly adherent to therapy. Opportunistic infection was the leading cause of death.

Another one of our cases was having an advanced disease and the lesions were on the face, nose and even his eyes. His condition was complicated by pulmonary tuberculosis with cervical and inguinal lymphadenopathy. The first AIDS-KS patient had had a limited disease because his lesions were located in the skin around the ankle joint, further so his general condition was well.

In a study done in 2003 the incidence of KS dropped from 30 per 1000 in 1995 to 0.03 per 1000 in 20015. London University found that the current incidence of KS among European HIV patients was less than 10% of that reported in 1994.6The AIDS epidemic has altered KS epidemiology worldwide. An analysis of a group of patients in Sao-Paulo, Brazil, found it mainly to occur in males (94.4%)7. In Zambia KS in infants and young children was found to occur more commonly since the advent of the HIV epidemic. Male to female ratio of 1.76: 1 was observed8. In contrast; because of the absence of Disease Registry in Sudan we cannot determine the frequency of KS but the male to female ratio seems to be in concordance with that in Zambia. On the other hand, African epidemics of KS are 10% of cancers in Central Africa. With a male to female ratio near equal in children but often rising after puberty to 15: 1. (3-4). Most recently in those under 15 year of age with median age of 4 years have a male to female ratio being 1.7 : 1 and 78% of them tested positive for HIV. In Uganda KS has caused one half of cancer in men (48.6%) and (17.6%) in women. The incidence showed more than 10 folds increase in men since 1950s and approximately 3 folds increase in women.

In Sudan there is a suspicion of increased cases of KS since the emergence of HIV epidemic, yet, figure has to be documented after establishing Disease Registry.

In our case study, two cases of endemic African type KS were reported, one of them responded very well to chemotherapy, nodules and oedema regressed. The other one well improved after the 3rd dose of chemotherapy.

Iatrogenic KS lesions vary from chronically to rapidly progression of onset4. Its incidence is 400-500 times greater in tissue recipients than in general population.9 Iatrogenic KS shows ethno-geographic association, occurring in only about 0.4% of transplant

recipient patients in the United States and western Europe to about 4.0% to 5.3% in Saudi Arabia10,11. However, the prevalence of KS in Sudan has to be studied.

Iatrogenic KS may develop after the use of Prednisolone and other immuno-suppressants in settings other than transplant recipients13. KS appears more frequently in patients receiving treatments that include Cyclosporine, a drug that may reactivate HHV-8 from latency to lytic replication in tissues14. Data support that most iatrogenic KS patients are positive for HHV-8 before transplantation, suggesting that the reactivation of the latent viral infection leads to the disease. Nonetheless, less frequently seroconversion following transplantation occurs suggesting infection from the donated organ15. Remission of iatrogenic KS on cessation of immunosupression is the norm12. Concerning our single patient of the iatrogenic type KS, a classical renal transplanted, with a moderate disease features but unfortunately lost trace his fate.

Conclusion:

KS is not uncommon in Sudan. Variant cases need to be recognized, classified and treated as early as possible. Three out of six patients were from the Nuba Mountains. This could be an alarming report for an epidemic of KS in that area which we believe need to have better health service to pick such cases as early as possible for better outcome.

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