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MANIFESTATIONS OF AGGRESSIVE ATYPICAL KAPOSI'S SARCOMA [AAKS] IN HIV DISEASE PATIENTS SEEN IN MAIDUGURI, NORTH-EASTERN NIGERIA.

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Infection by the human immunodeficiency virus (HIV) has since the mid-1980's been known to distinguish atypical, aggressive Kaposi's sarcoma (AAKS) from the endemic type in Africa. In our series at the University of Maiduguri Teaching Hospital, we recorded 44 patients with AAKS, 35 of them male and 9 female, giving an M: F ratio approximately 4:1. The peak age groups for the males were 21-30 years, and 31-40 years, while for the females it was 21-30 years. The site distribution of AAKS lesions was predominantly the lower limb (70.5%) followed by the upper limb (9.1%); those with multiple site lesions (nose, face, oral cavity, penis and trunk) also accounted for 9.1% of the cases. The commonest clinical features manifested by the patients were fever (100%), weight loss (86.8%) skin nodules (86.4%), and diarrhoea (55.3%). Virtually, all occupational groups were affected, with students, civil servants and businessmen topping the list.

Key words: Atypical Aggressive Kaposi's sarcoma, HIV infection

INTRODUCTION

From the mid-1980's aggressive, atypical Kaposi's sarcoma (AAKS) has been known to be associated with HIV infection in some African countries (1-3). In a comprehensive review on the AIDS virus, Gallo in 1987 (4) traced the history of evolution of observations that led to the conclusion that KS is associated with HIV infection. According to Gallo's review, KS was the first sign that a new disease was afoot in the USA. This was because KS, in an aggressive form, was appearing in young, middle-class homosexual men in the USA. Hitherto endemic KS, a slowly developing cancer, was only known to occur among the elderly in Europe, the Mediterranean, and parts of Africa. We report here on a series of patients with HIV-associated KS seen

in Maiduguri, North-eastern Nigeria from September 1994 to March 2003, studied prospectively.

SUBJECTS AND METHODS

Study area

Clinical and laboratory investigations were carried out at the University of Maiduguri Teaching Hospital (UMTH) located in Maiduguri. Maiduguri is the capital of Borno State, one of the 36 states, which together with the Federal Capital Territory, make up the Federal Republic of Nigeria. The UMTH is the major referral centre for the six states that constitute the North-eastern geopolitical zone of Nigeria. In addition, patients come to UMTH from Chad and Cameroon Republics, two countries that share borders with Borno State.

HIV serology

Two tests for the presence of antibodies against HIV were carried out on the serum of each study patient. A patient was regarded as HIV-seropositive if he or she tested positive by both tests. About half of the study subjects were tested by a combination of ELISA and Western blot (WB), while the rest were tested by a combination of a latex agglutination test and an immune chromatographic test. Kits for all four types of tests had been evaluated in Nigeria and approved for use by the AIDS Control Programme of tne Federal Ministry of Health. About 5ml of venous blood was drawn from each patient. The blood was allowed to clot at room temperature, and then centrifuged at 1,000xg for 10 minutes. Serum was then aspirated into a cryovial and stored at -20^{0}C until tested.

a. ELISA plus WB

The first 23 patients were tested by this combination. ELISA test was carried out using Wellcozyme HIV 1+2 kits manufactured by Murex Diagnostics Ltd, Dartford, England. Sera found positive by ELISA were subsequently subjected to the Western blot (WB) test. Kits for WB test were Bio-Rad Novapath HIV immunoblot manufactured by Bio-Rad Clinical Division, Hercules, California, U.S.A. for HIV-1, and New Lavblot II from Diagnostics Pasteur, Marnes-la Coquette, France for HIV-2.

b. Agglutination plus immune chromatography

Each serum was initially tested by Capillus HIV-1/HIV-2, which is a latex agglutination test. The kit is a product of Trinity Biotech PLC. Brag Co Wicklow, Ireland. Sera

positive by Capillus were then tested by the Abbott Determine HIV-1/2 test system, a product of ABBOTT laboratories, Diagnostics Division, Abbott Park, Illinois, USA.

Histological examination

The tissue specimens of all patients were fixed in 10% formal saline; several blocks of tissues were embedded in paraffin wax and 5-micron sections were cut. The sections were stained with haematoxylin and eosin (H&E) stains. The diagnosis of Kaposi's sarcoma is based on the 1985 histologic classification system (5), which states the variants as: (a) Granulomatous KS, (b) Angiomatous KS, (c) Sarcomatous KS and (d) Mixed KS.

RESULTS

A total of 44 cases of AAKS were diagnosed within the period of study. There were 35 males and 9 females, giving a male: female ratio 3.9:1. The peak age group is the 3rd and 4th decades of life, which accounted for 40.9% and 36.4% respectively. The lesion is rare before the 1st and after the 5th decades of life. The youngest patient was a 3-year-old boy who presented with inguinal lymph node enlargement (Table-1 and Figure 5). The site distribution of AAKS is predominantly the foot and leg (lower limb), which accounted for 31 cases (70.5% of all cases); 59% (26 cases) were males while 11.4% (5 cases) were females. The upper limb accounted for 4 cases (9.1% of all sites) with no sex bias. Four cases of multiple sites were seen in only males. Three cases of lymph nodes (2-axillary and one cervical lymph nodes) were seen (Table 2).

On the whole, 44 patients were studied, but information on fever, weight loss and diarrhoea is available in respect of only 38 patients. Fever was the most frequent clinical feature in the patients. Weight loss was also a frequent occurrence seen in 86.8% of the patients, and 86.4% of them had skin nodules at various sites. Diarrhoea and oral lesions occurred in 55.3% and 45.5% respectively. Lymphadenopathy was the least common presentation, seen in only 6 patients (13.6%). Table 3 summarizes these observations. All occupational groups were virtually affected, with students, civil servants, and businessmen topping the list as shown in Table 4.

Table 5 shows the various histological patterns of Kaposi's sa-

coma. Mixed patterns accounted for 63.6% of the cases. Spindle cell predominance accounted for 27.3%, while angiomatous and granulomatous variants accounted for 4.5% each.

Figures 1 to 5 show representative sites of manifestations of AAKS in our series. Figures 1 and 2 are the same patient, a 38 yr old man, presenting with multiple-site nodules. Figure 3 is predominantly on the buttocks and trunk. Figure 4 shows a fungating (ulcerated) nodule on the leg of a 30 year old man. Figure 5 is a 3-year-old boy presenting with inguinal lymphadenopathy, biopsy of which revealed KS

Table 1: Age and sex distribution of AAKS cases

Age Group	Male	Female	Total	%
0-10	1	1	2	4.5
11-20	3	1	4	9.1
21-30	12	6	18	40.9
31-40	15	1	16	36.4
41-50	3	0	3	6.8
51>	1	0	1	2.3
Total	35	9	44	100

Table 2: Sex and site distribution of AAKS cases

Site	Male	Female	Total	%
Upper Limb	2	2	4	9.1
Lower limb	26	5	31	70.5
Trunk	2	0	2	4.5
Lymph node	1	2	3	6.8
Multiple	4	0	4	9.1
Total	35	9	44	100

Table 3: Clinical features of the patients

Features	Patients	No manifesting	% manifesting
Fever	38	38	100
Weight Loss	38	33	86.8
Skin nodules	44	38	86.4
Diarrhoea	38	21	55.3
Oral lesions	44	20	45.5
Lymphadenopathy	44	6	13.6

Table 4: Occupational groups of the patients

Occupation	n
Student	8
Civil servant	7
Business	6
Driver	3
Farmer	2
Lawyer	2
Teacher	2
Banker	2
Pupil	2
Military	1
Mechanic	1
Unemployed	2
NA	6
Total	**44**

NA = Not available

Table 5: Histological patterns of 44 biopsies of AAKS

Histologic patterns	Cases	
	n	%
Spindle cell predominant	12	27.3
Angiomatous	2	4.5
Mixed	28	63.6
Granulomatous	2	4.5

Figure 1. A 38-year-old man presenting with nodules on the face (plus oral cavity, chest and legs)

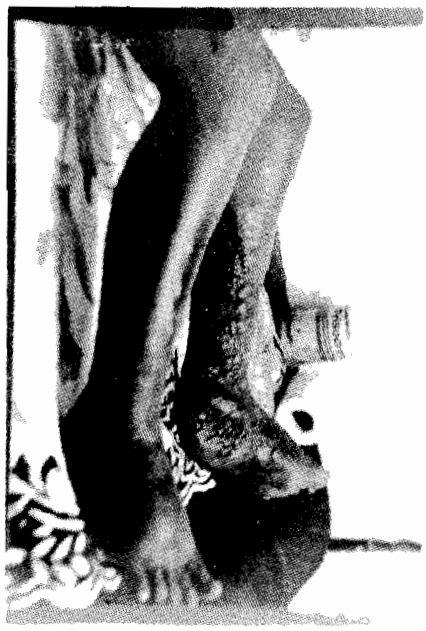

Figure 2. The same patient as in Fig. 1, here showing nodules with severe oedema on the left leg.

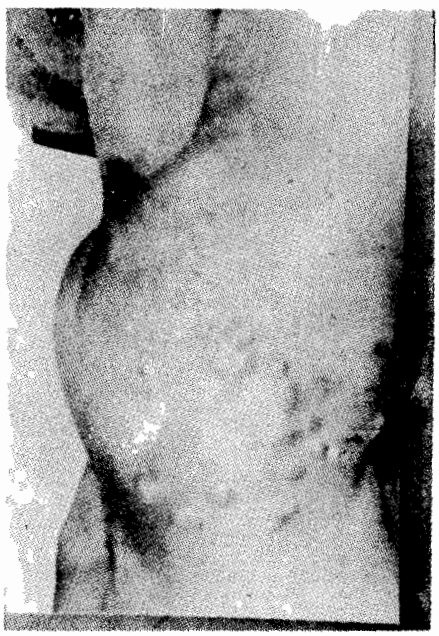

Figure 3. A 36-year- old man presenting with generalized, multiple-site nodules, predominantly on the buttocks and trunk.

Figure 4. A fungating, ulcerated nodule on the leg (popliteal fossa) of a 30-year-old man.

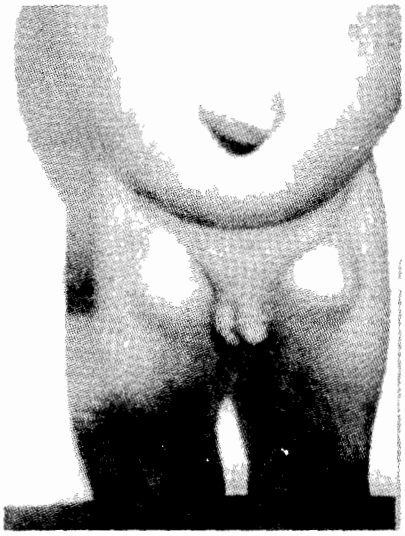

Figure 5. A 3-year-old boy presenting with inguinal lymphadenopathy. Biopsy revealed KS. The boy and both of his parents

DISCUSSION

AIDS-associated KS and other forms of KS have similar histologic features. The clinical history, physical features, and result are the basic parameters possibly suggesting the type of KS. However, KS associated with AIDS commonly presents with variable histologic features based on the stage of the disease and this may have other differential diagnoses. Whether early KS lesions represent a transitional stage of preneoplastic and hyperplastic nodules that will evolve into a true neoplasm is still unresolved and raises interesting issues about the biogenesis of KS. Much evidence has accumulated in favour of the concept that KS begins as a hyperplastic lesion of activated cells that may regress or progress, depending on the host's immune status and the availability of continuous proliferate stimuli. HIV could provide both the mitogenic stimulation through chronic antigenic stimulation and a dysfunction in the host's immune defense mechanisms such as cytotoxic T–Lymphocytes (6). Epidemic KS has been recognized since 1981 in homosexual men and has been associated with HIV infection and was first described in young male homosexuals (7). It affects both sexes with predominance of males over females in Africa, probably due to socioeconomic behaviour in the African society. The pattern of AIDS-associated KS in our study favours the lower extremities that are similar to the classical type. Four of our patients had multiple site involvement, which include the tip of the nose, face, oral cavity, glans penis and trunk. The frequency of large fungating, florid tumour mass with extensive ulceration, haemorrhage and gross oedema of the foot should probably be taken as evidence of aggressive lesion with silent involvement of the deeper tissues. This aggressive lesion is rarely seen in the endemic

KS. When the epidemic KS exclusively involves the lymph nodes, it is more likely that internal organs are also involved and this is probably considered as evidence of aggressive disseminated lesion. In this study we also report three cases with two axillary and one inguinal lymph node KS in adults and a child respectively. However, lymph node involvement has been reported in endemic KS without skin lesion, mainly in children usually with a rapidly fatal course (8,9). It has been reported in association with lymphoreticular tumours and immunosuppressive therapy (10). The behaviour of AAKS ranges from slowly indolent, relatively benign skin nodules, simulating the classic endemic KS, to more commonly aggressive disseminated malignancy, which has been seen in 50% of patients, the average survival of approximately 18 months. KS progresses in an orderly fashion from few nodules in the early stages to innumerable, rapidly progressing nodules, and finally to systemic lesions. HIV infections is associated with generalized aggressive or atypical KS, but not with endemic KS (1-4).

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