

CHILDHOOD KAPOSI'S SARCOMA: CLINICAL FEATURES AND THERAPY

C. L. M. OLWENY, A. KADDUMUKASA, I. ATINE, R. OWOR,
I. MAGRATH* AND J. L. ZIEGLER*

*From the Uganda Cancer Institute and Department of Pathology,
Makerere University, Kampala, Uganda*

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Summary.—Twelve cases of childhood Kaposi's sarcoma seen at the Uganda Cancer Institute over the last 7 years are reported. The disease presents mainly as generalized lymphadenopathy, with sparsely and anomalously distributed cutaneous nodules, and has a higher proportion of females with the disease than in the adult form. The histology is usually of mixed cell type. If not treated, childhood Kaposi's sarcoma runs a fulminating course, but disease control with chemotherapy is associated with prolonged survival.

KAPOSI'S sarcoma is rare in childhood. In a review of 1256 cases by Dutz and Stout (1960), only 40 (3.2%) were under 6 years. Eighteen of the 40 cases (45%) were from the African continent alone. The first acceptable case of Kaposi's sarcoma in a child was described in a monograph by de Amics in 1882, and cited in a more recent paper by Ronchese (1958). Features which differentiate childhood disease from the adult form include the clinical presentation with lymphadenopathy, the sparsely and anomalously distributed cutaneous nodules, the high proportion of females and a fulminating course if untreated. In a previous report from this Institute, the varied clinical and pathological features of Kaposi's sarcoma were classified (Taylor *et al.*, 1971a). The lymphadenopathic form was associated with the childhood cases, but this group constituted a very small proportion of the series. In this paper we report in detail 12 cases of Kaposi's sarcoma in children under 15 years of age seen at the Uganda Cancer Institute (UCI) over the last 7 years.

PATIENTS AND METHODS

Details of presentation, clinical course, response to treatment and other associated features were obtained from the case records. Ten children were referred to the Lymphoma Treatment Centre with a provisional diagnosis of malignant lymphoma and two with a histological diagnosis of Kaposi's sarcoma. The histology sections were reviewed by one of us (R.O.) and classified according to the criteria described previously (Taylor *et al.*, 1971a).

We define *complete remission* as disappearance of clinically measurable tumour, *partial response* as a reduction in tumour volume of at least 50% and *no response* as a lesser response, or disease progression.

RESULTS

The clinical details of the 12 patients are given in Table I. The median age at presentation is 8 years (range 1½–15 years). There were 7 males and 5 females, giving a male : female ratio of 1.4 : 1. Ten of the 12 patients presented with lymphadenopathic disease; one had a florid lesion and one had cutaneous nodules. One patient (No. 3) had nodular lesions apart from peripheral lymph-

* Current address: National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20014.

TABLE I.—*Childhood Kaposi's Sarcoma*

Case	Age (yrs) and sex	Clinical features	Histology	Initial treatment	Re-sponse	Re-mission duration	Re-lapse if any	Subsequent therapy	Response to further treatment	Re-mission duration	Fur-ther relapse	Survival	Cur-rent status
1. A.H.	10 F	Lymphadenopathic	MC	Act-D+VCR+DTIC	C	3 mo.	Yes	—	—	—	—	10 mo.+	AWD
2. M.	9 M	Lymphadenopathic	MC	Act-D	P	—	—	Act-D+VCR BCNU RAT	N N P	—	—	—	—
3. K. II	10 F	Lymphadenopathic+nodular	MC	Act-D	N	—	—	Act-D+VCR BCNU RAT DTIC	P N C C	12 mo.	Yes	48 mo.+	AWD
4. M.	2½ F	Lymphadenopathic	MC	Act-D+VCR	N	—	—	Act-D+VCR BCNU RAT DTIC	P N C C	13 mo. 9 mo.	Yes	46 mo.+	AWD
5. N.S.A.	15 M	Florid	MC	Act-D+VCR+DTIC	C	6 mo.	—	—	—	—	—	—	LTFU
6. O.	8 M	Lymphadenopathic	MC	CTX	N	—	—	Act-D	C	8 mo.	Yes	51 mo.	Died
7. W.	1½ M	Lymphadenopathic	MC	Act-D	N	—	—	—	—	—	—	1 mo.	Died
8. S.	1¾ M	Lymphadenopathic	MC	Act-D	C	50 mo.+	—	—	—	—	—	52 mo.+	AFD
9. K.G.	15 F	Lymphadenopathic+visceral	MC	Act-D	P	—	—	—	—	—	—	—	LTFU
10. Z.	4 M	Lymphadenopathic+mandibular	MC	Act-D	C	66 mo.+	—	—	—	—	—	68 mo.+	AFD
11. K.B.	8 M	Nodular	MC	Act-D+VCR	C	24 mo.	—	Act-D+VCR DTIC	—	—	—	—	—
12. N.R.	8 F	Lymphadenopathic	MC	Act-D+VCR+DTIC	C	12 mo.	Yes	—	C	6 mo.+	—	17 mo.+	LTFU AWD

MC = Mixed cellularity

Response

C = Complete
P = Partial
N = No response
AFD = Alive and free of disease
AWD = Alive with disease
LTFU = Lost to follow up

Treatment

RAT = Radiotherapy
Act-D = Actinomycin-D (Cosmogen)
VCR = Vincristine (Oncovin) (NSC 67574)
DTIC = Imidazole carboxamide (NSC 45388)
CTX = Cyclophosphamide (Cytosan) (NSC 26271)
BLM = Bleomycin (NSC 125066)
BCNU = 173-Bis (2-chloroethyl)-1-nitrosourea (NSC 409962)

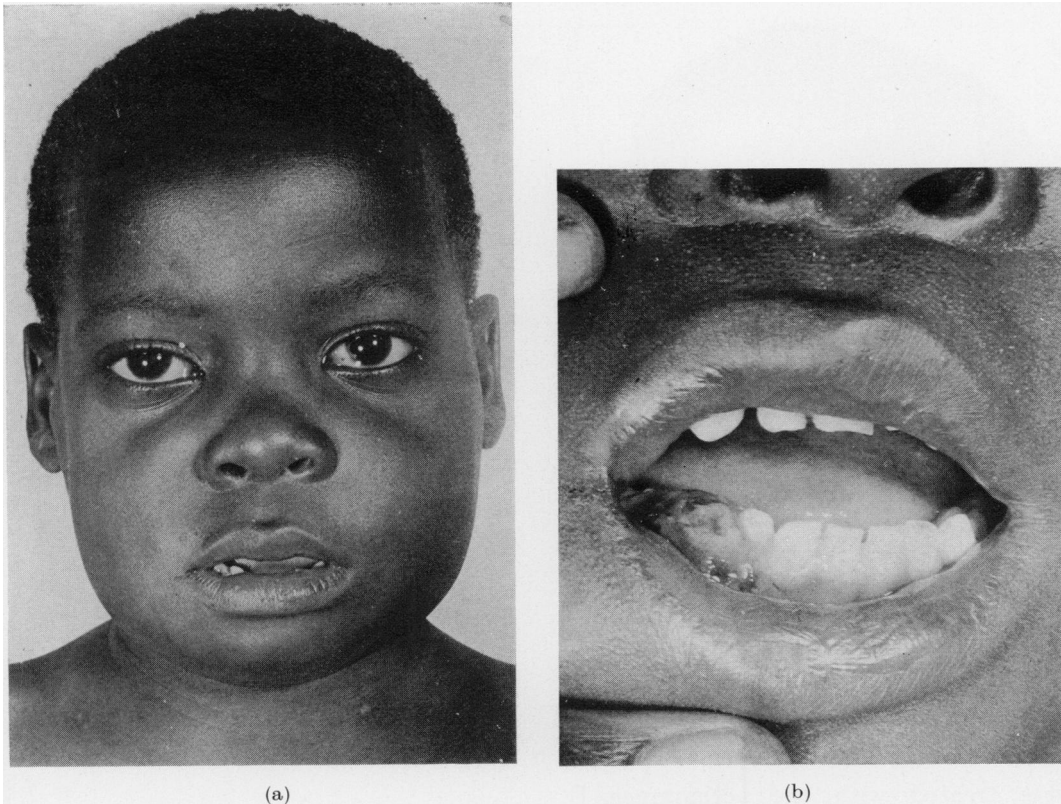


FIG. 1(a).—Patient Z (No. 10) with bilateral mandibular swelling. (b).—Same patient Z (No. 10). Close-up of mouth showing right lower quadrant gingival mass. He also had left upper gingival mass not seen here.

adenopathy. One (No. 9) had visceral disease, while another (No. 10) had mandibular involvement (Fig. 1a and b). The lymphadenopathy was often generalized but particularly marked in the cervical region (Fig. 2) and the groin (Fig. 3). Two had mediastinal widening as shown by the chest roentgenograph (Fig. 4). All 12 children had a mixed cellular histological pattern.

The therapeutic approach varied, as the 12 children were admitted when different treatment protocols were under study (Olweny *et al.*, 1974; Vogel *et al.*, 1971). The primary and subsequent treatments given are detailed in Table I. Six received actinomycin-D alone as their primary treatment regimen, two received a combination of actinomycin-D and

vincristine, three received a 3-drug combination consisting of actinomycin-D, vincristine and imidazole carboxamide (DTIC), and one was treated originally with cyclophosphamide. Doses and schedules of chemotherapy are described in detail in previous reports from this centre (Olweny *et al.*, 1974; Vogel *et al.*, 1971). Of the 6 patients treated with actinomycin-D alone, 2 (Nos. 8 and 10) attained complete remissions and remained in remission 50+ and 66+ months, 2 had partial responses and 2 did not respond. Of the 2 patients treated with actinomycin-D and vincristine combination, one (No. 11) achieved complete tumour regression but relapsed after 24 months and the other (No. 4) did not respond. The 3 patients (Nos. 1, 5 and 12), who

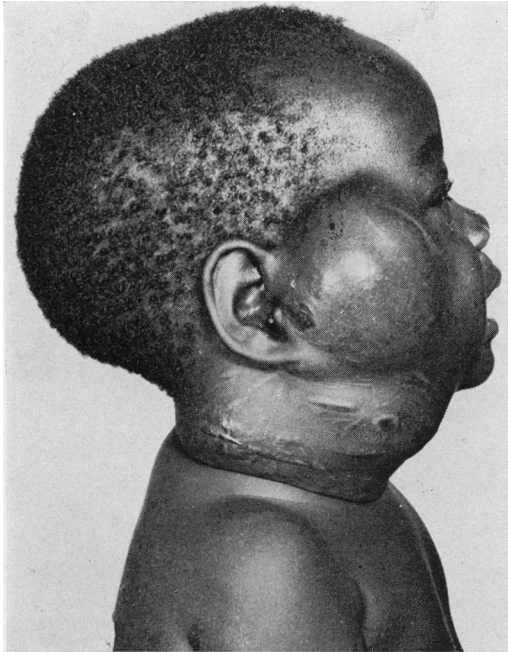


FIG. 2.—Patient M. (No. 4), showing marked cervical lymphadenopathy. Scars are from therapy prior to hospitalization.

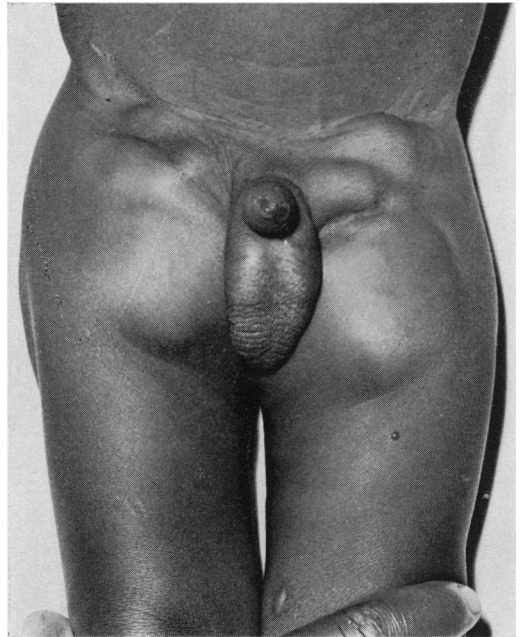


FIG. 3.—Patient W. (No. 7), with prominent bilateral groin lymphadenopathy.

were treated with the actinomycin-D, vincristine and imidazole carboxamide combination all achieved complete tumour regression with remissions lasting 3, 6, and 12 months respectively. The single patient who received cyclophosphamide alone did not respond.

Treatment of relapse included: radiotherapy (3); BCNU (2); actinomycin-D and vincristine (3); actinomycin, vincristine and DTIC (4); and DTIC and bleomycin (1). As can be seen in Table I, the most effective combination in inducing a remission appears to be actinomycin-D, vincristine and DTIC. All 4 patients who later received this combination, having either relapsed or responded incompletely to other forms of treatment, responded with complete tumour regression lasting 6+, 9, 12 and 13 months. In the majority of patients relapse was at the same site as the original tumour suggesting incomplete eradication of tumour.

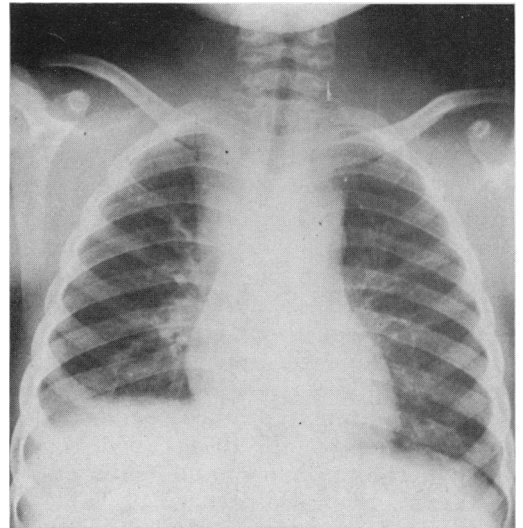


FIG. 4.—Chest roentgenograph of patient A.H. (No. 1) showing the widening of the mediastinum.

Of the 12 patients studied, 2 have died, 3 are lost to follow up, 3 are alive and free of disease, and 4 are alive with active disease. The 2 deaths occurred at 1 month and 51 months respectively. Excluding the 3 patients lost to follow-up, the median survival is 46 months (range 1-68).

DISCUSSION

Kaposi's sarcoma though rare in most parts of the world is relatively common in tropical Africa. Childhood cases are particularly uncommon and the majority reported are from the Continent of Africa (Dutz and Stout, 1960). The disease in children has certain atypical features. First, the mode of presentation with generalized lymphadenopathy is almost always confined to childhood cases. Ten out of 12 children in this series presented with moderate to marked lymphadenopathy. The presentation with lymph node enlargement appears to be a feature commoner in Negro children than in Caucasians. In the 40 cases reviewed by Dutz and Stout, 8 out of 18 (44.4%) African children had lymphadenopathy only while only one of the 22 (4.5%) non-Africans presented with similar features (Dutz and Stout, 1960). In a more recent report of 51 autopsies in childhood cases from East Africa, 20 had lymph node enlargement, 5 had skin nodules as well as lymph node enlargement, and 2 had lymph node and ocular involvement as the major clinical features of the disease (Slavin *et al.*, 1970). The skin nodules when present are sparse and distributed over anomalous sites. The eyelids, lacrimal glands, jaw, parotid and salivary glands are areas of predilection and sometimes patients present with Mickulicz syndrome. The reason for propensity to glandular involvement in African children is not clearly understood. Some authors have tended to regard Kaposi's sarcoma as a disease arising in the reticuloendothelial system. This is based on the observation of occasional co-existence of Kaposi's sarcoma and

lymphoproliferative disorders such as Hodgkin's disease, lymphosarcoma, mycosis fungoides and leukaemia (Cox and Helwig, 1959; Moertel, 1966). However, this association is more commonly seen in adult whites than in Africans, while lymph node disease in general is commoner in the Africans than in whites. The presentation with generalized lymphadenopathy may lead to wrong diagnosis. Tuberculosis and/or Hodgkin's disease are the frequent referring diagnoses; both being prevalent in tropical Africa. Ten of the patients reported here were referred with a provisional diagnosis of malignant lymphoma. Kaposi's sarcoma should therefore be included in the differential diagnosis of any child with lymph node enlargement.

A second difference between childhood and adult Kaposi's sarcoma is the greater frequency of females with the disease. Most authors report a male : female ratio of 3 : 1 (Dutz and Stout, 1960; Slavin *et al.*, 1970; Templeton, 1972). This is in marked contrast to the adult series where the ratio is 13 : 1 (Olweny *et al.*, 1974). In the present series the male: female ratio is almost 1 : 1. So far there is no satisfactory explanation for the sex distribution. Sex hormones have been suggested as possibly protecting the post-pubertal females, but treatment with oestrogens has yielded no beneficial results, and some patients have developed the disease while pregnant (Taylor *et al.*, 1971b). However, review of childhood cases in Uganda prior to 1967 revealed that all 9 recorded cases were males (Davies and Lothe, 1962).

The histological features observed in this small series also deserve mention. All 12 patients had the mixed cell type histological picture which is consistent with an earlier report where lymphadenopathic disease was also exclusively of mixed cellular type (Taylor *et al.*, 1971b). This histological appearance occurs overall in some 70% of adult Kaposi sarcoma patients in Uganda (Olweny *et al.*, 1974).

It is generally agreed that lymphadenopathic childhood Kaposi's sarcoma is disseminated and aggressively malignant. If not treated, death will almost certainly ensue within one year. The response to treatment has been varied and difficult to assess as no uniform approach has been used. However, two patients treated only with actinomycin-D are alive and apparently disease free at 52+ and 68+ months respectively, so that there is no doubt that chemotherapy alone can be highly effective therapy. The combination of actinomycin-D, vincristine and DTIC may prove to be even more effective since it has induced complete remission in 3 out of 3 patients when used as primary therapy and 4 out of 4 patients with recurrent tumour. In one of these patients this combination was used after a partial response had been induced by radiotherapy, and the latter form of treatment, although used only for treatment of tumours not responding or responding partially to chemotherapy, has also proved useful in the few patients who received it. In appropriate clinical circumstances radiotherapy may further enhance the efficacy of chemotherapy, and until further data become available, a combination of radiotherapy (where facilities exist) and the three drug combination is probably the treatment of choice.

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