# KAPOSI'S SARCOMA IN TANZANIA AND SWITZERLAND: A RETROSPECTIVE AND COMPARATIVE STUDY

BY

DR. EPHATA ELIKANA KAAYA, MD
UNIVERSITY OF DAR ES SALAAM - 1981

A THESIS SUBMITTED IN FULFILMENT FOR THE DEGREE OF MASTER OF SCIENCE IN ANATOMICAL PATHOLOGY OF THE UNIVERSITY OF DAR ES SALAAM, 1991

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## ABSTRACT

A retrospective and comparative study was carried out on 605 cases from Tanzania and 33 cases from Switzerland over an 11 year period. Cases from Tanzania were 461 males, 112 females and 11 of unknown gender. In Switzerland 32 were males and 1 was a female. Kaposi's sarcoma (KS) constituted 3.54% of all malignant neoplasms in Tanzania during this period.

The male to female ratio of KS in Tanzania was 4.1:1 and for Switzerland 32:1. Kaposi's sarcoma in Tanzania was seen more commonly in the 4th to 6th decade. There were two peaks in Switzerland, one between 3rd and 4th decade and the second between 6th and 7th decade. There was no significant annual increase in the number of KS in Tanzania during the study period whereas in Switzerland a sharp increase was noted from 1983 which is thought to coincide with the AIDS epidemic.

All age groups were affected in Tanzania but none was seen below the age of 15 years in Switzerland. In children the male to female ratio was 2.3:1 indicating that KS is seen more often in female children than in adult females which may suggest a possible hormonal influence.

The most common epidemiological type of KS was Endemic African (EA-KS) in Tanzania and AIDS-KS in Switzerland. It is concluded that the histological variations seen in KS may reflect the various stages of the lesion.

## LIST OF ABBREVIATIONS

| | | |
|---|---|---|
| AIDS | - | Acquired Immunodeficiency Syndrome |
| $CD_4$ | - | T helper/inducer lymphocyte |
| $CD_8$ | - | T Suppressor/cytotoxic lymphocyte |
| C-KS | - | Classical Kaposi's sarcoma |
| CMV | - | Cytomegalovirus |
| EA-KS | - | Endemic African Kaposi's sarcoma |
| ELISA | - | Enzyme linked immunosorbent assay |
| FVIII-RAg | - | Factor VIII related antigens |
| HIV-I | - | Human immunodeficiency virus-1 |
| HLA | - | Human leucocyte antigens |
| HTLV-III | - | Human lymphotropic virus III |
| I-KS | - | Iatrogenic Kaposi's sarcoma |
| IVDA | - | Intravenous drug addict/abuser |
| KS | - | Kaposi's sarcoma |
| LAV | - | Lymphadenopathy Associated Virus |
| PAS | - | Periodic Acid Schiff |
| PTAH | - | Phosphotungstic Acid Haematoxylin |
| SCC | - | Squamous cell carcinoma |
| UEA-1 | - | Ulex europaeus agglutinin 1 |

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## DECLARATION

I declare that to the best of my knowledge this work has not been submitted for a degree in any other University.

Ephata E. Kaaya

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**Ephata Elikana Kaaya**

# 1. INTRODUCTION AND LITERATURE REVIEW

Kaposi's sarcoma (KS) was first described in 1872 by Moricz Kaposi, a Hungarian dermatologist living in Vienna (14,51). He termed this new condition multiple idiopathic pigmented sarcoma of the skin. Later on it was noted that other sites such as larynx, liver, pylorus and small intestine (36, 51, 81) may be involved. This entity was seen mainly in elderly patients of Eastern European origin, Northern Italy and in Jews (51, 81, 97). It was rarely seen in Great Britain, most parts of Western Europe and the United States of America (66, 97), but was common in Africa (82).

## 1.1 CLASSIFICATION OF KAPOSI'S SARCOMA

Since the description of Kaposi's sarcoma which occurred in elderly men now termed sporadic or classical (C-KS) (43, 51, 81), this entity has further been recognised in three distinct clinopathological syndromes - the endemic African Kaposi's sarcoma (EA-KS), Kaposi's sarcoma occurring in patients with acquired immunodeficiency syndrome (AIDS-KS) and that occurring in transplant recipient patients which has been termed iatrogenic Kaposi's sarcoma (IKS) (28, 43, 65). Harawi (43) has called these the Epidemiological forms and further classified them into clinical patterns and histologic types. Clinically Kaposi's sarcoma can present as a localized skin lesion which can be an early patch lesion, a plaque, a nodule or as aggressive disease. Also it may present as a generalized disease involving the skin, lymphnodes or viscera (43).

## 1.2 EPIDEMIOLOGY OF KAPOSI'S SARCOMA

Kaposi's sarcoma shows a peculiar geographical distribution suggesting an environmental or genetic cause (81,96). The disease was very rare in Western Europe and the United States prior to the occurrence of the AIDS epidemic. It was seen in Jews, Italians and people of East European origin and this was associated with the HLA-DR5 (91). The peak age was 5th-7th decade with a male to female ratio of 10-15:1 and an incidence of 0.06% of all cancers (43). Endemic (EA-KS) is common in Africa and prevalence increases as one approaches the Equator from both North and South (19, 73, 81, 106, 108, 110, 111). In Africa blacks are more affected. The peak age for EA-KS is 4th - 5th decade showing a male to female ratio of up to 13:1 (19, 43, 96, 97) and accounts for up to 10% of all cancers in some parts of Central Africa (43). Templeton (112) reported a male to female ratio of 20:1.

It is generally agreed that in Europe and the United States the disease affects people who are 50 years or older (41), whereas in Africa the affected individuals tend to be younger than the white counterparts (19, 43, 81, 96, 111). A small percentage in Africa consists of children aged 15 years or younger (19, 105). Many authors deny the existence of a racial distribution of the disease except Rothman (81,96) who supports this view. Another piece of evidence in support of this racial theory of distribution is the observation of increased frequency of the disease in Jews both in Europe and North America (33, 81).

Since 1981 an increased incidence of Kaposi's sarcoma has been observed particularly affecting young homo-sexual men with the acquired immunodeficiency syndrome (36, 50, 61, 62, 95). This variant of the disease is rapidly progressive, generalized and often fatal (32, 72, 119). The incidence of KS in the groups at risk for AIDS vary markedly (43).

The data from a 1985 Centre for Disease Control (CDC) study showed KS to occur in 36% of homosexual men, 10.4% of Haitians, 4.3% of intravenous drug addicts (IVDA), 1.9% of transfusion recipients, 1.6% of haemophiliacs (46, 47) and in 12.5% of female drug abusers (43). Reports from the United States and elsewhere of KS in young homosexual men (26, 48), describe an aggressive disease which differs from KS previously seen in elderly Americans (29, 100) and from the disease which was endemic in adult men in Equatorial Africa but similar to KS as seen in African children (82, 105). From 1983 Bayley (7) observed an increased number of KS in Zambia which was similar to that seen in the United States. The most striking features were aggressive tumour behavior and a poor response to chemotherapy.

In Bayley's series 61% of the patients died within six months. Similar cases were seen in Uganda in 1983 (31). Both Zambia and Uganda cases were seropositive for human immunodeficiency virus (HIV) (7, 24, 31). Bigger et al. (12) demonstrated that Zairean KS was not associated with HIV. Similar results were observed by Otu (83) in Nigeria. However, Elirodt et al. (30) isolated a human T-lymphotropic retrovirus (LAV) from a Zairean married couple one with AIDS and the other with prodromes. More confirmation of HIV positive patients in Africa was published by Brun-Vezinet et al. (15). It is now generally agreed that HIV positive KS is found in various parts of the world including Africa (11, 101). This type of KS associated with AIDS showing a reversal of normal CD4/CD8 ratio and other opportunistic infections has been termed AIDS-KS (64, 65, 95).

## 1.3 CLINICAL FORMS OF KAPOSI'S SARCOMA

Prior to AIDS, KS was divided into four clinical patterns: **the nodular type** and **aggressive KS** both cutaneous, **the lymphadenopathic** and **the systemic or generalized KS** (113). With the occurrence of AIDS, a fifth clinical pattern has become apparent and is referred to as **early KS** (43).

**Nodular KS** is the predominant clinical pattern seen both inside and outside Africa (5, 43) as an indolent disease manifesting with nodules or plaque like lesions. **The aggressive** or **florid KS** is a locally destructive disease with skin lesions that often fungate and bone may be involved. **The lymphadenopathic** and **the systemic** forms of KS are most commonly seen in Africa in young children, women and young adults (18, 19, 54, 105, 112). This is a more disseminated and aggressive variety which may also involve viscerae and gastrointestinal tract in addition to lymphnodes. Skin lesions may or may not be present (71, 111, 119). In children the disease is usually rapidly fatal (82). Like in **sporadic KS (CKS)** mucosal involvement in EA-KS is rare and response to therapy is good (119).

In AIDS all clinical patterns of KS are seen. **AIDS-KS** runs an aggressive and fulminant course with widely dispersed skin lesions, mucosal and more commonly lymph-node involvement and has a poor response to therapy (119). In the patch stage of (early) KS, the vascular lesions are predominantly in the upper dermis and in the oropharyngeal and the gastrointestinal sub-mucosa. Grossly the lesions appear as macules, patches or thin plaques. These early lesions have been described in patients with sporadic KS (1), however, they are not a prominent feature of this form of KS, and most often represent a transitory stage towards the nodular disease (43). In AIDS early KS is common, and presents as a mucocutaneous disease without progressing to a nodular stage (35, 41). The

early cutaneous lesions are dark, small, non-blanchable patches and usually less than 1 cm in diameter but may later enlarge. Rarely the whole lesion may mimic an ecchymosis (99). The lesions are elongated, tend to be symmetrical following skin tension lines more often on the neck and back in a pattern resembling pityriasis rosea (43). Most of the lesions involve the trunk, arms, neck and head. Penile and planter involvement is common while palmar lesions are rare (99).

**Nodular KS** is the classical lesion described by Moricz Kaposi in 1872. Up to date its clinical description has remained unalterable (113) and represents the tumour that evolves from the early lesion (76). This commonly manifests as a well defined nodule ranging from a few millimeters up to 3 cm. It may, however, present as large plaques. While the plaques involve the upper dermis and readily ulcerate, the nodule may occur in the upper dermis or lower dermis and ulceration is unusual (80). Both large plaques and the nodules are referred to as nodular KS (43). Although predominantly dermal, nodular KS may involve the viscera but these tend to be asymptomatic and are only incidentally detected. Solitary nodules have been found on the penis or lacrimal gland. In the non-immunosuppressed, simple excision tends to be curative. A solitary nodule on the hand or foot, however, usually heralds progressive disease (113).

**Aggressive KS** presents in two forms of locally aggressive disease (111). One type, **the florid KS** presents as a fungating ulcerating mass that invades the subcutis. The other type infiltrates the deeper tissue and in the majority of cases invades bone. This **infiltrative KS** induces a fibroblastic reaction resulting in diffuse swelling and woody induration of the affected limb making the disease difficult to recognize as KS. This type accounts for 35% of KS in Africans, it is rare in Caucasians and has not been described in AIDS. Sometimes this tumour has a rapid doubling time and a pleomorphic histology (113).

**Lymphadenopathic KS** was commonly seen in children prior to AIDS. Generalized lymphnode involvement accounted for 25-50% of KS in African children. The course is fulminant and death occurs within a year (82). Although it resembles AIDS-KS, the affected African children have no evidence of HIV exposure (43).

In **systemic/generalized KS** there is widespread involvement of the skin, lymphnodes and viscerae. The disease has a rapidly fatal course resulting in death early. This is more common in AIDS and iatrogenic immunodeficiency states. It has been documented that African with systemic KS have profound T-cell dysfunction (113).

Table 1 summarizes the clinical forms and their correlation to the epidemiological forms of KS.

## 1.4 AETIOLOGY AND HISTOGENESIS

The aetiology of KS and its histogenesis remain controversial.

### 1.4.1 Aetiology

Prior to the discovery of HIV, Giraldo et al. (39, 40) provided both serological and pathological data associating cytomegalovirus (CMV) with KS in both sporadic and endemic KS (39, 40, 116). However, with the emergence of HIV a similar association has persisted (25, 38) and therefore such aetiological role has been questioned. Rinaldo et al. (94) have shown that CMV is capable of inducing immunodepression. Malignant neoplasms occur in both congenital and acquired immunodeficiency states (86, 109). KS is commonly seen in patients undergoing immunosuppression for renal transplants (52, 69, 110). Siegel et al. (104) observed a disseminated form occurring after renal transplantation. Doll et al. (22) proposed that the immunosuppressive therapy may have

indirect carcinogenic effect by altering immunological surveillance. Master et al. (67) concluded that the immunological impairment in KS occurs during the malignant tumour stage.

Malignant lymphomas are more often seen in patients who are immunosuppressed (16, 58, 66, 84, 85, 97). Weshler et al. (118) have reported occurrence of Kaposi's sarcoma and chronic lymphatic leukaemia in the same patient affecting the same lymphnode. Hodgkin's disease occurring in association with KS has been reported by Masareli et al. (66) and Slavin et al. (106). Recently KS has been reported in patients with acquired immunodeficiency syndrome (AIDS) (41, 57, 66, 71, 80, 89, 92, 208, 111, 114). The predilection noted for sporadic KS is not environmental since Jews who lived in South Central Europe carried their susceptibility for developing KS to North America and South America (43). Familial KS occurs rarely (33). There is a definite association between KS and HLA-DR5, human histocompatibility anti-gen (91). There is also a strong association between HLA-DR5 and the development of KS in AIDS patients (107). No definite association for any of the HLA antigens have been observed in Africans with EA-KS (43). Harawi (43) proposed that CMV most likely plays a co-factor role in the neoplastic transformation to KS in an immunodeficient, genetically predisposed individual rather than a primary aetiologic agent.

### 1.4.2 Histogenesis

Although the clinicopathological spectrum of all the forms of KS is well defined, the histogenesis of the spindle cell component of the tumour has been the subject of much investigation and debate because of the conflicting results obtained. Histochemical, ultrastructural and immunohistochemical studies have suggested the cell of origin to be the pericyte (61), smooth muscle cell (44, 71), Schwann cell (8, 87), primitive

mesenchymal cell (77), lymphatic capillary endothelial cell (9), vascular capillary endothelial cell (8, 21, 34, 39, 68, 72, 78) and reticuloendothelial cell (20). Some authors have disputed its neoplastic nature (17). Although many authors now favour the endothelial cell origin (42), immunohistochemical studies using factor VIII related antigens (F VIII-RAg) and Ulex europaeus agglutinin I (UEA-1) which are markers for endothelial cells have failed to give consistent results (49, 56). Ultrastructural studies of KS have demonstrated a variety of cells such as fibroblast, endothelial cells, smooth muscle cells, pericytes and histiocytes (45, 76, 79, 88). Basement membrane is often discontinuous or absent (10, 68). Weibel-Palade bodies are seen in the cytoplasm of endothelial cells in vessels with distinct lumens but are nor seen in spindle cells (88). However, the absence of Weibel-Palade bodies does not rule out their endothelial origin as these bodies are often absent in undifferentiated endothelial tumours.

## 1.5 HISTOLOGICAL FEATURES OF KS

It is now well appreciated that skin lesions of Kaposi's sarcoma evolve from an early lesion or patch stage to an older lesion, the nodular stage. Between these two extremes there is the plaque stage. These clinical stages are well correlated histologically. Microscopically KS has been well described, however, a uniform classification is still lacking due to varying designations of the same histological lesions (70, 93, 111).

The skin lesion is usually situated in the mid-dermis and to a lesser extent in the lower dermis (76), except in early (patch stage) KS where the skin lesion is located in the upper half of the dermis (41). The plaques form diffuse lesions while the nodules form more circumscribed lesions. Typically the nodule consist of interlacing and sweeping bundles of spindle cells, proliferating abnormal vascular channels and slits (52, 76, 111,

119). Between the spindle cells run an extensive network of reticulin and collagen fibres and a varying amount of fibrous tissue trabecula (76). Slits containing erythrocytes, plasma cells, lymphocytes and histiocytes are observed between the spindle cells (61, 76, 111).

### 1.5.1 Histological classification

O'Connel (80) and Taylor et al. (111) attempted to classify KS histologically into three histological types as follows:

1. **Spindle cell KS**: In this variety spindle cell predominate the histological picture. Some authors call it **sarcomatous** (43) or **monomorphic KS** (111).
2. **Mixed pattern KS**: This has equal proportions of spindle cells and vascular slits.
3. **Anaplastic (pleomorphic) KS**: This shows more cellular atypia and increased number of mitoses. It is difficult to differentiate it from angiosarcomas. Harawi (43) has added two other histological types to this classification. These are:
4. **Angiomatous KS**: This is a rare variant composed predominantly of well formed usually thin-walled, large and small vascular spaces. It is a difficult pattern to diagnose because of its similarity to angiomas.
5. **Inflammatory KS**: This variant consists of angioproliferative process with arborizing vessels. The vessels may have hyalinized walls resembling those seen in the angioimmunoblastic lymphadenopathy and associated with a prominent lymphoplasmacytic infiltrate.

O'Connel (80) found mixed pattern KS in 80% of the cases reported from Malawi. This seems to be the predominant pattern in all epidemiological forms of KS and the one most easily recognized. The second most common variant is the spindle cell KS (18, 19, 21, 43, 61, 80, 111).

The mixed pattern KS is more commonly seen in the nodular variety, while the spindle cell KS is seen in the florid and infiltrative types (108). The lymphadenopathic disease shows a mixed pattern regardless of the associated skin lesions (80). Dorfell (23) observed bloodless lymphatic channels in the histological picture. Ziegler (119) stresses the presence of extravasated erythrocytes and haemosiderin deposits amidst spindle cells as a common feature in KS. Ultra-structurally the most distinctive feature of KS is phagocytosis of red blood cells by endothelial, pericytic and fibroblastic cells (115).

### 1.5.2 Early KS

The early lesion of Kaposi's sarcoma is subtle and far more difficult to diagnose compared to the tumour stage.

With the epidemic of HIV infection the pathologist is frequently required to rule out early KS (43). Early KS manifests itself in the upper half of the dermis as either a diffuse infiltration by the angioproliferative process or by the formation of small dermal aggregates in close association with sweat glands, pilosebaceous structures and dermal nerves. The dermal aggregates are often composed of a mixture of atypical and apparently normal vessels (41), or dilated thin-walled vascular spaces with jagged outlines and a sparse infiltrate of mononuclear cells, especially lymphocytes and plasma cells surrounding the bizarrely shaped vessels. The endothelial cells of these vessels are not atypical or in mitosis (1).

The early lesion of KS resembles uncontrolled proliferation of granulation tissue indistinguishable from stasis dermatitis (1, 119) or granuloma pyogenicum (119). Francis et al. (35) distinguished the following main architectural pattern to the dermal vessels in early KS:

1. Dissection of the collagen by dilated or compressed vessels giving in some cases a

cracked appearance to the dermis (dermal collagen dissection).

2. Proliferation around apparently normal vessels.

3. Formation of aggregates resembling small capillary haemangiomas.

In the lymphnodes the architecture is preserved in the early lesion but there is a striking follicular hyperplasia (4). The inter and intrafollicular vessels are prominent, ectatic, irregular and increased in number, features that are demonstrated best by reticulin staining. The medullary cords are infiltrated by numerous plasma cells. The picture is similar to that seen in patients with patch lesions of KS (4, 32, 89). The early lesion is later on replaced by interlacing spindle cells with extravasated erythrocytes in vascular slits, haemosiderin deposits and plasma cells. the lymphnode architecture is finally effaced (4, 32, 89), the histological appearance becoming similar to that seen elsewhere (54). The clinically dusky purple plaques have histological feature of both patches and nodules (1).

### 1.5.3 Histology in different clinicoepidemiological types

It is generally accepted by most authors that the histological appearance of KS is similar in all clinicoepidemiological forms. Any variations seen in the histological presentation could reflect differences in age and degree of development of the lesions (23, 76). Lothe (61) observed that differentiated and undifferentiated cell patterns could be recognized and might co-exist in any tumour. Reynolds et al. (93) described histopathological differences which appeared to be related to tumour morphology and behavior. Leu et al. (58) could not find any histological differences between sporadic KS, endemic African KS and Epidemic KS. Francis et al. (35) found that histological appearance of AIDS-KS was different from sporadic KS in that it had a more diffuse pattern with a less inflammatory infiltrate. Histologically lymphangioma like KS has been shown to be more

common in AIDS (108).

## 1.6 THE DIFFERENTIAL DIAGNOSIS OF KS

Certain disease lesions can clinically and histologically be misinterpreted as KS. This is especially so with the emergence of AIDS where early and unusual histological variants of KS are challenging the diagnostic skills of clinicians and pathologists (43).

### 1.6.1 Conditions which mimic KS

These can be either benign or malignant conditions. Scars showing prominent vascular proliferation with plasma cell infiltrate and haemosiderin deposits are wrongly diagnosed as KS. Stasis dermatitis can mimic an early lesion of KS (1). Pyogenic granuloma has been wrongly diagnosed as KS (119). Other tumours such as dermatofibroma, fibrous histiocytoma, haemangioma and squamous cell carcinoma (SCC) have sometimes been wrongly diagnosed as KS (13, 80, 102). Table 2 summarizes conditions which may be misinterpreted as KS.

### 1.6.2 Features important for differential diagnosis

The presence of hyaline bodies in KS is a useful feature in differentiating it from pyogenic granuloma (53, 78). The hyaline bodies are globules of proteinaceous material that stains well by the phloxine tartrazine method of Lendrum (55). They are seen in the cytoplasm of cells or in extracellular spaces. Their nature is not known but is thought to be lysosomal degenerative bodies (79,103). Other features include the uniform occurrence of haemosiderin deposits around lesions of KS (58, 80). Plasma cells, although not a highly sensitive and specific indicator of KS their presence in a borderline

case is more suggestive of KS (1).

## 1.7 DISEASE CONDITIONS ASSOCIATED WITH KS

There is a well established association between sporadic KS and the development of a second malignant neoplasm (86). Such an association is not common in EA-KS (100). In one report, a second primary neoplasm occurred in 37% of 92 cases of sporadic KS (100), and 58% of these were neoplasms of the lymphoreticular system. Hodgkin's lymphoma, non-Hodgkin's lymphoma and leukaemia accounted for 29%, 26% and 18% of the cases respectively, in a review of literature reported early in 1980 whereby 65 cases of KS associated with lymphoreticular tumour were documented (43). These neoplasms may precede, occur simultaneously with or follow KS (100). Approximately 42% of malignancies associated with KS are epithelial. They occur in a variety of organs but commonly involve the skin (100).

## 2. THE PROBLEM

Kaposi's sarcoma is common in East Africa accounting for up to 9% of all malignant tumours in Ugandan males (111). In Tanzania Slavin et al. (106) noted that KS accounted for 4% of all malignancies diagnosed by biopsy in 1964 to 1965. In another report (105) Slavin et al. noted that KS was common in children and was more frequently seen in female children compared to female adults. Schmid (102) found that KS accounted for 17.6% of all skin malignancies in Tanzania and stressed the problem of misdiagnosis.

In Switzerland KS was a rare disease with only few cases of sporadic KS. Recently however, the disease showed an upward trend and this is thought to be associated with the emergence of the AIDS epidemic ( Leu, personal communication). It is thought that AIDS was present in Central Africa as early as in 1975 (43). Lymphadenopathic forms of the disease and childhood Kaposi's sarcoma seem to be on the increase (personal observation). Although it is generally agreed that the histology of all epidemiological forms is uniform (23, 76) there are recent reports against this notion (35, 108).

In the light of the above review and conflicting findings, a decision was made to carry out this study. The study will compare epidemiological factors and morphological feature of **sporadic KS**, **Endemic African, EA-KS** and **Epidemic AIDS-KS** in Tanzania and Switzerland.

## 2.1 THE HYPOTHESIS

Epidemiologically and morphologically there are differences in the various forms of Kaposi's sarcoma.

## 2.2 THE OBJECTIVES

### 2.2.1 Broad objective

To study and compare the epidemiology and morphological features of sporadic (classical), endemic (EA) and epidemic (AIDS) Kaposi's sarcoma in Tanzania and Switzerland from 1975 to 1985.

### 2.2.2 Specific objectives

- Determination and comparison of age, sex, racial distribution of Kaposi's sarcoma.
- Description of the geographical distribution of Kaposi's sarcoma.
- Classification of clinicoepidemiological types of Kaposi's sarcoma.
- To describe histological features for each clinicoepidemiological type.
- To determine other lesions commonly misinterpreted as Kaposi's sarcoma.
- To determine other conditions occurring in association with Kaposi's sarcoma.

## 3. MATERIALS AND METHODS

The material used for this study consisted of 33 cases from the Institute of Pathology, University of Zürich, Switzerland and 605 cases collected from the cancer registry, the Department of Morbid Anatomy and Histopathology, Muhimbili Medical Centre, Dar es Salaam, Tanzania, the Department of Pathology, Kilimanjaro Christian Medical Centre, Moshi, Tanzania, the Department of Pathology, Bugando Medical Centre, Mwanza, Tanzania and the Department of Pathology, Mbeya Referral Hospital, Mbeya, Tanzania. These were mainly biopsies and only a few autopsies, for the time period 1975 - 1985.

3.1 Baseline data for the cases were obtained from re-cord books, request and report forms. Where file numbers were available more data were obtained from patient files. Histological laboratory numbers were recorded to trace old slides and blocks. In Zürich most of the cases had already been separated by Prof. Hans Jörg Leu. Others were retrieved by computerized storage systems.

3.2 For histological studies all slides were examined and morphological features were recorded. New sections were made from old 10% formalin fixed paraffin embedded blocks. Sections were cut at 5 microns, subjected to a battery of different stains and mounted.

3.3 The following stains were used for histological studies:

Haematoxylin and Eosin

Reticulin

Iron stain

Phloxine tartrazine (55)

PTAH (Phosphotungistic Acid Haematoxylin

Periodic Acid Schiff

3.4 Data were analyzed by IBM microcomputer.

3.5 Where appropriate ratios were tested for significance by the Chi-squared test P-values of 0.005 or less were taken as significant.

# 4. RESULTS

A total of 908 cases of KS were collected in Tanzania during the study period. Out of these 605 cases were studied, 584 cases were confirmed to be KS and 21 cases were misdiagnoses. 303 cases were excluded from further studies due to lack of sufficient data and histological material. In Switzerland a total of 33 cases were confirmed to be Kaposi's sarcoma and all were subjected to histological studies. KS accounts for 3.54% of all malignancies in Tanzania. (See Appendix I).

## 4.1 SEX DISTRIBUTION

Table 3 shows that 78.9% of the cases in Tanzania were males, and 19.2% were females, giving a sex ratio of 4.1:1. (M:F). In Switzerland 97.0% were males, 3.0% were females and the sex ratio was 32:1.

Figure 1 shows that in Tanzania the number of KS cases was fluctuating up to 1979 and then there was a rise in the number of KS cases in 1980 and 1981 falling again in 1982. Number of KS cases remained relatively higher than 1975 in the subsequent three years. Figure 2 shows that before 1983 KS was rare in Switzerland. No cases were recorded in 1980, 1981 or 1982. Then from 1983 there was an upward trend in the number of cases reaching a peak in 1985.

## 4.2 AGE DISTRIBUTION

Table 4 shows that all age groups were affected by KS in Tanzania, but this was rare before 15 years in Switzerland. Figure 3 shows age stratification of the Tanzania KS cases. A majority of the cases occurs between the 3rd and 6th decade. Figure 4 shows that in Switzerland the distribution was bimodal. Many of the cases occurred between the 3rd and 5th decade with a peak in the third decade and again in the late 6th and 7th decades. Table 5 shows that there was a total of 60 childhood KS cases below the age of 14 years in Tanzania. 70% of these were males and 30% were females. This gives a childhood sex ratio of 2.3:1.

## 4.3 RACIAL AND NATIONALITY DISTRIBUTION OF KS

Tanzania Africans accounted for 99.3% of all cases (Table 6). There was only one Caucasian (an American) and two Asians. Among the Africans there was one Ugandan. All patients from Switzerland were Caucasians.

## 4.4 GEOGRAPHICAL DISTRIBUTION

Figure 5 shows that in Tanzania Kilimanjaro and Mwanza regions had the highest number of KS per 100,000 during the period under study, followed by Mara, Arusha, Iringa and Kagera. Rukwa, Mtwara, Morogoro and Dar es Salaam had the lowest number of cases per 100,000. (See Appendix II). All Switzerland cases were obtained from Zurich.

## 4.5 CLINICOEPIDEMIOLOGICAL FORMS OF KS

**4.5.1** Table 7 shows that the most common clinicoepidemiological form of KS in Tanzania was the Endemic African KS (EA-KS) accounting for 87.3%. Only four cases had previously been confirmed serologically to be AIDS-KS accounting for 0.7%. 12% of the cases could not be classified. In Switzerland the most common type of KS was AIDS-KS, 84.8% of all cases.

**4.5.2** Table 8 shows that in Tanzania KS involving the skin accounted for 86.1% as the most common mode of presentation. Lymphnode involvement was the second most common with 8.7% of all cases. Oral cavity and nose involvement accounted for 0.9% and 0.3% respectively. In 1.2% of the cases location of the lesion was not known.
Table 9 shows that in Switzerland skin involvement by KS accounted for 78.2% of the cases. Lymphnode involvement occurred in 21.8% of the cases. There was no statistical difference when compared to Tanzania.

**4.5.3** Table 10 shows that in Tanzania skin lesions were localized in 98.2% of the cases. 1.8% of the cases showed disseminated skin lesions. In Switzerland 88.5% of skin lesions were localized while 11.5% were disseminated.

## 4.6 HISTOLOGICAL FEATURES

**4.6.1** Table 11 shows that in Tanzania cases, mid-dermis was the most common location of the lesion occurring in 47.1% of the skin lesions. Majority of the lesions were within the upper and mid-dermis 99.2%, while only 0.8% were situated in the lower dermis.

In Switzerland 57.7% were upper dermis lesions followed by mid-dermis lesions (26.9%). Switzerland had more of upper dermal lesions than Tanzania, this was however, of no statistical significance.

**4.6.2** Table 12 shows that 87.1% of Tanzania cases were nodular or tumour stage. Early or patch stage accounted for 5.7% of Tanzania cases. In Switzerland early lesion was the most common accounting for 48.5%. Tumour stage lesions were the least common 15.1%.

**4.6.3** In Table 13 it is seen that the most common histological type of KS in Tanzania was the mixed pattern (52.0%) followed by spindle cell predominant KS (38.0%). Anaplastic KS was seen less frequently. In Switzerland 27.3% of cases were mixed pattern KS, 48.5% angiomatous KS and 24.2% spindle cell predominant.

**4.6.4** Lymphocytic infiltrate was a common finding in nearly all cases. The infiltrate was regarded as minimal if up to five lymphocytes were seen per high power field, as moderate if five to ten lymphocytes were seen per high power field and heavy from ten and above. Since the distribution of lymphocytes was not uniform multiple areas were selected and their averages recorded. Table 14 shows that 72.4% of the cases had minimal lymphocytic infiltrate in Tanzania cases. 20.8% had moderate and 6.8% had heavy infiltrate. Compared to Switzerland 33.3% had minimal, 24.3% moderate and 42.4% heavy infiltrate.

**4.6.5** Plasma cell infiltration was also noted in all cases which were examined as shown on table 15. In Tanzania minimal plasma cell infiltrate was seen in 70.9% of the cases,

moderate in 14.7% and heavy plasma cell infiltrate in 14.4%. In Switzerland plasma cell infiltrate was minimal in 84.8%, moderate in 6.1% and heavy in 9.1% of cases.

**4.6.6** In Tanzania haemosiderin laden macrophages (siderophages) were absent in 14.0% of the studied cases as shown on table 16. Minimal deposits were seen in 66.1% of cases moderate and heavy deposits in 15.6% and 4.3% of cases respectively. Absent and minimal deposits accounted for 80.1% of Tanzania cases. In Switzerland almost every case showed some siderophages. Minimal deposits were seen in 63.7%, moderate in 33.3% and heavy in 3.0%

**4.6.7** Hyaline bodies were not identified in KS lesions both in Tanzania and Switzerland even after using appropriate stains.

**4.6.8** In Tanzania 99.3% of histologically studied cases were EA-KS and 0.7% were AIDS-KS (Table 17). All 4 AIDs cases (100%) had histological features of patch (early) stage KS. 5% of EA-KS had features of early lesion, 7.2% of plaque, stage and 87.7% of nodular or tumour stage.

In Switzerland C-KS accounted for 15.2% of cases whereas AIDS KS constituted 84.8% of studied cases. In Switzerland patch stage was the most common histologically (48.5%).

**4.6.9** Table 18 shows the correlation between the histological class of KS and the epidemiological types. It was found that all 4 Tanzania AIDS cases were histologically angiomatous. 52.4% of EA-KS were mixed pattern and 37.9% monomorphic spindle cell type. In Switzerland 20% of C-KS were monomorphic-spindle cell type and 80% mixed pattern. 57.1% of AIDS-KS were angiomatous, 17.9% mixed pattern and 25.0%

monomorphic-spindle cell type.

**4.6.10** Figure 6 shows that at low magnification the early patch stage of Kaposi's sarcoma shows a sparse lymphocytic infiltrate throughout the dermis and around skin appendages. This closely resembles chronic dermatitis. At higher magnification (Fig. 7), the early lesion shows a proliferation of thin walled blood vessels especially in the upper dermis. Perivascular round cell inflammatory infiltrate is seen. The proliferating blood vessels and slits impart a cracked appearance to the dermis. This is called "the dermal collagen dissection" (35).

In the early lesion of KS (Fig. 8), in addition to blood vessels, slits and inflammatory infiltrate, abnormally dilated thin walled vessels with a thin endothelial lining were seen around normal blood vessels.

Plaques contain features of an early lesion but in addition the beginning of spindle cell proliferation (Fig. 9). The vessels were seen throughout the dermis giving the dermal collagen dissection appearance and also encircling normal dermal capillaries. Initially the spindle cell proliferation is confined in proximity to blood vessels and skin appendages. The tumour stage was characterized by a dermal nodule composed of proliferating interlacing spindle cells with a variable amount of slits and vessels (Fig. 10). Within this background, a varying amount of round cell inflammatory infiltrate was noted (Fig. 11). The nodular lesion was seen to take one of the two patterns, either spindle cell predominant (monomorphic type) as in figure 12 or spindle cell and vascular proliferation (mixed pattern) (Fig. 12).

Haemosiderin was seen as a brown pigment deposited within the proliferating spindle cells or in adjacent collagen fibres around the blood vessels (Fig. 13).

## 4.7 LESIONS MISDIAGNOSED FOR KS

Some lesions were clinically or histologically misinterpreted as KS in Tanzania (Table 19). Squamous cell carcinoma and fibrous histiocytoma were the most frequently misdiagnosed as KS accounting for 23.8% each of all misdiagnoses. Chronic dermatitis was the next accounting for 14.3%. All 33 cases from Switzerland were correctly diagnosed as KS both clinically and by histology.

## 4.8 CONDITIONS OCCURRING IN ASSOCIATION WITH KS

Table 20 shows that there were 4 conditions seen in association with KS in Tanzania. Malignant lymphoma and chronic lymphocytic leukaemia (CLL) each accounted for 33.3%. These were followed by leprosy and tuberculosis each accounting for 16.7%. In Switzerland such conditions were not encountered.

# 5. DISCUSSION

Kaposi's sarcoma (KS) is common in the African, and rare in the Western Europe and United States and in non-Africans living in Africa. However, since 1981 there is an epidemic of KS seen virtually in every race in all continents.

## 5.1 SEX DISTRIBUTION

The ratio between male and female varies widely in most series (Table 21). In most of the reported series the M:F ratio has varied from 9-20:1 (6,43,61,112). However, Murray (76) reported 10 cases in South African whites of whom 6 were females.

The results of the present study compare well with other studies showing a male, female ratio of 4.1:1 and 10:1 for Tanzania and Switzerland respectively, which is lower than that reported by Slavin et al. (105) for Tanzania. Similarly Moshi and Mutta (74), reported a male, female ratio of 11:1. These differences may be due to the fact that the two previous studies were limited to only two years whereas the present study covers a period of 11 years.

There was no significant rise in the number of cases seen annually except for spikes in 1980, 1981 and 1983 in this study (Fig. 1). However, in Switzerland there was a sharp rise in the number of recorded cases from 1983 (Fig. 2). Other studies in East Africa (7,11.31) have shown an increased number of atypical KS from 1983 which is associated with the emergence of AIDS. One would have expected a similar increase in the total number of KS especially for atypical KS in Tanzania. There are unofficial reports of

increased AIDS-like KS, lymphoglandular KS or childhood KS in 1985, but as serological confirmation was not available prior to 1985, this study has failed to demonstrate such an increase. For Switzerland there is a clear cut increase in the number of KS beginning 1983 and these were serologically confirmed as HIV positive. Reasons for the lack of a rise in the number of Tanzania cases are, either the emergency of atypical KS was not recorded clinically or, all cases were not histologically examined from 1982.

## 5.2 AGE DISTRIBUTION

Most studies show that the peak age incidence for EA-KS is in the 4th to 5th decade while that of C-KS is in 5th to 7th decade (19,43,81,96,97,106,110,111). This suggests that in Africa the affected individuals tend to be younger than their white counterparts. The present study shows the same pattern of age distribution with peak age between 4th and 6th decades (Fig. 3) for Tanzania. In Switzerland (Fig. 4) there are two separate groups. One consists of relatively young patients with a peak incidence in the 3rd and 4th decade and another in the 6th and 7th decade. This type of bimodal distribution has not been reported before in literature. The younger age group patients coincides with cases associated with AIDS. The older age group patients show an age structure similar to C-KS (43).

In EA-KS, there is a substantial number of KS patients below the age of 15 years (19,105) as is seen also in figure 3. In children, female cases are relatively more frequent than in adults (105). In Dutz and Stout's review, 25 percent were girls (27). In Moshi and Mutta's study there were five cases under the age of fourteen years of whom two were girls and three boys (74). However, all 10 cases reported by Davies and Lothe (19) were males. In the present study there were 60 cases of KS below the age of 14 years (Table

5). 30% of these were females giving a male to female ratio of 2.3:1. There is no satisfactory explanation as to why in childhood there is more frequent occurrence in females. Hormonal influences after puberty could explain the male predominance. Perhaps female hormones protect women from as yet undiscovered aetiological factors. A majority (99.0%) of the cases were Africans, with only one Caucasian and two Asians. The African forms the majority of the Tanzania population. This cannot be taken as a racial preponderance.

## 5.3 GEOGRAPHICAL DISTRIBUTION

In Tanzania high geographic prevalences are seen in regions of Kilimanjaro and Mwanza, followed by Mara, Arusha, Iringa and Kagera. (Appendix II). This distribution is similar to that of Schmid (102). Moshi and Mutta (74) showed the highest number of KS in Mwanza region. It is interesting to note that the coastal regions and the regions along lake Tanganyika have relatively few cases. This is different from the studies of Schmid and Moshi in which they saw a high number of cases in Kigoma and Dar es Salaam region respectively. If population sizes are not taken into account, Mwanza, Kilimanjaro and Dar es Salaam can falsely show high numbers because it is in these regions where the three consultant hospitals are located. The reason for this regional variation may be explained by the quality of pathology services, readiness of doctors to biopsy lesions and degree of utilization of medical facilities in the various regions. Environmental or genetic factors have also been suggested by some authors (81,95) but don't seem to play a role in Tanzania.

## 5.4 CLINICOEPIDEMIOLOGICAL FORMS OF KS

Endemic African KS formed 83.7% of all Tanzania cases in this study. Four cases were positive for HIV so they were classified as AIDS-KS. It is believed that first cases of AIDS occurred in East Africa in 1983 (7), but serological testing for HIV screening was not widely available until 1985. Therefore some AIDS-KS may have escaped detection. The four cases which were confirmed in this study were screened elsewhere (De Witt, personal communication).

In 1983 13 patients (56%) of Bayley's series presented with unusual symptoms of aggressive tumour behavior and poor response to chemotherapy. These adult patients in Zambia had aggressive KS similar to the tumour described in immunosuppressed homosexuals (26,46,47,48). Similar cases were reported in Uganda (31) and Zaire (30). The Zambian and Ugandan cases were positive to HIV 1. These observations in neighbouring countries may indicate that even in Tanzania more AIDS-KS would have been documented if clinical presentation was carefully recorded and serology performed. Switzerland KS was mainly AIDS-KS serologically confirmed. This is strongly supported by the fact that prior to 1983 KS was rare in Switzerland. Only few cases had been reported (15.2%) conforming to the classical variety of KS(C-KS), characterized by an indolent disease affecting extremities and occurring in the 6th to 7th decade (113). Other reports (43) show that in Western Europe and U.S.A. up to 95% of KS cases occurred in HIV infected homosexual men. The present study shows that in Switzerland AIDS-KS accounted for 84.8% of KS cases although the sexual behaviours of these patients is not known.

Slavin et al. (106) noted that the most common manifestation of KS was cutaneous. In the present series (Table 8) cutaneous involvement occurred in 86.1% of the cases.

Extracutaneous sites noted in this study are shown on table 8. This probably is an underestimate because this was a biopsy series. In a biopsy series there is an inevitable distortion of the true distribution of the disease in favour of the skin and other readily accessible biopsy sites. In Switzerland where a majority of the cases were AIDS-KS, a similar cutaneous preponderance (Table 9) was seen. This support previous studies in AIDS patients (35,36,41). However, Bayley (7) stressed that cutaneous lesions are few in AIDS-KS. In Switzerland lymphnode involvement accounted for 21.2%. Other reports have identified AIDS-KS in virtually every organ (59,62,63,92,119). Although extracutaneous KS can occur as an isolated lesion, more often they occur in association with skin lesions (3). The absence of extracutaneous lesions besides lymphnode in the Zurich data again reflects the predominance of biopsy rather than autopsy.

A majority of the skin lesions (98.2%) were localized in Tanzania patients as shown in Table 10. Only 1.8% of the lesions was generalized. There is some difference with Switzerland data which shows localized cutaneous disease in 88.5% and generalized disease in 11.5%. It is generally agreed that AIDS-KS presents as a generalized disease and may involve sites such as the palate (70, 92), oral mucosa, tip of the nose and deep organs (70). The present study (table 8) shows involvement of the tip of nose in 2 cases (0.3%) and oral mucosa involvement in 5 cases (0.9%). In Uganda generalized diseases accounted for 20.5% (31). Before 1983 localized disease in Uganda accounted for over 90% of the cases. This is similar to what is seen in Tanzania in the present study. One can therefore postulate that up to 1985 AIDS-KS was relatively uncommon in Tanzania. Approximately 15% of the cases of KS seen in Europe and North America prior to the onset of AIDS were due to immunosuppressive therapy (IKS) (52). Most of the patients given immunosuppressive therapy are organ transplant recipients especially of kidneys. Approximately 6% of these patients develop a malignancy over an average period of 37

months post-transplantation (range 1-158 months) (84). If non-melanoma skin cancers and in situ carcinomas of the cervix are excluded, malignant lymphomas account for 25% and KS 5% of these cancers. KS is the first neoplasm to occur, next are the malignant lymphomas (85,86). Klepp et al. (52) reports that considering the number of patients on steroids and other immunosuppressive drugs, the overall risk for developing iatrogenic KS is very small. Other factors, probably genetic, are likely to potentiate the oncogenic effect of immunosuppressive drugs. This is supported by the data of Penn (85) where 29 of 60 cases of post-transplant KS occurred in patients of Middle Eastern or Mediterranean origin. Ten of the 29 patients were Jews. In Saudi Arabia out of 11 cases of KS seen in a seven years' period, 4 occurred in renal transplant recipients (2). In the present study there were no I-KS cases reported, probably because organ transplant is not performed in Tanzania.

## 5.5 HISTOLOGICAL FEATURES

The Mid-dermis was the most common location of the skin lesions in the Tanzania series (table 11). In this series mid-dermal and upper dermal lesions accounted for 99.2%. In Switzerland 57.7% were upper dermis lesions. Nodular KS in Tanzania was seen in 87.1% whereas patch stage KS accounted for only 5.7%. In Switzerland the patch stage KS was the most common 48.5% of cases (Table 12). The mixed pattern KS was seen more frequently in Tanzania 52% whereas angiomatous KS was seen more frequently in Switzerland 48.5%. These findings agree with previous reports that the cutaneous lesion of KS is usually situated in the mid-dermis (71,76,119). However, this is not true for early KS. The patch stage or early KS is usually situated in the upper dermis (41). There is some discrepancy in the literature as to how frequently early cutaneous KS presents

as an elevated lesion; that is, whether it is more frequently a patch or a thin plaque. According to Gottlieb and Ackerman (41), the skin lesions tend to persist as small patches without progressing into the nodular stage. Francis et al. comparing cutaneous KS in AIDS and non-AIDS patients (35), found 2 plaques, 1 nodule and 18 patches from twenty-one biopsies of 16 patients with AIDS. Of the biopsies from 9 patients without AIDS, 8 had Nodular KS. The 9th was a renal transplant patient who developed a KS plaque in the operation scar (35). In a study of 40 KS skin biopsies from patients with AIDS in San Francisco, Blumenfeld et al. (13) found the following pattern; 6 patches, 20 plaques and 14 nodules. These discrepancies between series probably relates to the precise definition of "patch lesion". Some Authors have used the term in different ways (43). Alternatively differences can be explained by the fact that AIDS KS lesions are disseminated so they are discovered early, and the patients die early of other opportunistic diseases before the lesions become nodules. Sporadic KS (CKS) is Nodular in 85-90% of cases (93). Like the sporadic KS Endemic KS is predominantly nodular (106). The findings in the present study show that majority of the cases in Tanzania were indeed EA-KS and in Switzerland most of the cases were AIDS-KS (Table 17).

The mixed pattern KS was seen in 80% of O'Connell's study from Malawi (80). This has been seen to be the predominant pattern in all epidemiological forms but more common in the nodular variety (80). The present study supports O'Connell's findings (Table 18). However, angiomatous KS was more often seen in the Switzerland series. This again reflects the predominance of AIDS-KS in this series and supports Smith (108) who reported that lymphangioma like KS is more common in AIDS.

Lymphocyte and plasma cell infiltrates are commonly found in Kaposi's sarcoma. In this series, these were seen in almost every case. The significance of this polymorphic cellular infiltrate is not clear. Reynolds et. al. (93), suggests that it is, in part at least a

reaction to the primary process and perhaps the associated haemorrhage. Thus the presence of histiocytes, lymphocytes plasma cells and other mononuclear cells may be entirely non specific and has no primary role in the origin and development of the disease. In the present study this polymorphic cells/or infiltrates are seen in all stages of the disease supporting the above notion.

Microhaemorrhages and haemosiderin deposition are frequently seen in association with both early and later lesions of KS (1,73,119). These are not constant Findings (93). Haemosiderin deposits in KS could result from the microhaemorrhages and red blood cells extravasation. In the present series haemosiderin deposits were not seen in 14.0% of cases (Table 16) and minimal deposits were seen in 66.1% In Switzerland minimal haemosiderin deposits were seen in 63.7% of cases. These findings suggest that haemosiderin may be absent in a KS lesion and therefore this is not a constant feature to help in the diagnosis of KS.

Hyaline bodies or "eosinophilic" globules are found clustered within the cytoplasm or in the intercellular space of KS lesions (44,103). The nature of these globules is not well understood but it is thought they may represent giant lysosomes, fragments of red cells (43) or glycoprotein (103). The red blood cell origin is supported by the fast that they stain bright red with phloxine tartrazine (55), similar to red blood cells. In a study of 159 cases from Malawi O'Connell (80), identified hyaline bodies in 136 cases in haematoxylin and eosin stained sections whereas Senba et al. (103) saw them in 2 out of 17 cases. They are often seen in AIDS cases, and their presence helps in differentiating KS from the many skin lesions that occur in these patients. Blumenfeld et al. (13), did not identify them in their study. The present study did not show any hyaline bodies in the histological sections despite the use of special stains probably due to technical errors. The value of this needs further studies.

Histological changes in an early (patch) KS are subtle, and are characterized by dilated irregularly shaped, thin-walled, jagged vessels lined by flat endothelial cells mainly in the upper half of the dermis (41). Blumenfeld et al. (13), reported that irregular vessels were often seen adjacent to an apparently morphologically unremarkable small vessels. Ackerman (1), reported that the patch lesion of Kaposi's sarcoma has thin-walled dilated vascular spaces with jagged outlines situated in at least the upper half of the dermis. With scanning magnification, a patch lesion of KS may be misinterpreted merely as a superficial and deep perivascular dermatitis. Francis et al. (35) described the main architectural patterns to the dermal vessel in early KS as dissection of collagen by dilated or compressed vessels giving in some cases a cracked appearance to the dermis, proliferation of thin vessels around apparently normal vessels and formation of aggregates resembling small capillary hemangiomas. These features have been found to be more useful in making the diagnosis. Other authors (1,9,13), have emphasized the first of these features, (dissection of collagen), and this was found in 19 out of 21 biopsy specimens, including peripheral zone of the one case of nodular KS in the study of Francis et al. (35). The present study supports these findings. Figure 6 shows an early lesion of KS. Of particular interest here is the cellular infiltrate around skin appendages and resemblance to chronic dermatitis. Figure 7 of the same lesion at higher magnification shows vascular proliferation situated in the upper dermis. Also seen is a perivascular round cell infiltrate. The proliferating vessels and slits give a cracked appearance to the dermis "dermal collagen dissection". Figure 8 shows abnormally dilated thin walled vessels in proximity to a normal blood vessel, partially encircling it. Patch lesions are more common in AIDS patients and as such pathologists are going to come across histological sections of these lesions more often.

Plaque lesion of KS tends to involve the entire dermis. Vascular changes are similar to

the changes described for the patch lesion. However, there are also increased number of spindle cells between the collagen bundles in the dermis (1,13,35,41). These findings are similar to what was found in this study as seen in figure 9.

In the present study the tumour stage (nodular stage) was characterized by a dermal nodule composed of proliferating, interlacing spindle cells with a variable amount of slits and vessels (Figure 10). The nodular lesion was either monomorphic spindle cell predominant or mixed pattern (Figure 12). These findings are similar to what was reported by other workers (1,76,80,93).

In all stages of Kaposi's sarcoma in the skin especially in the early lesions, the presence of at least some plasma cells around newly formed bizarre blood vessels is a telling clue to the diagnosis (41). Haemosiderin laden macrophages are found in some but not all lesions, and are not necessary or indubitable feature for diagnosis of lesions at any stage. Figure 13 illustrates haemosiderin within the spindle cells and collagen fibres around the blood vessels.

From the foregoing discussion it is evident that C-KS and EA-KS histologically are characterized by nodules commonly of mixed type whereas AIDS-KS is characterized by early lesions. From the evolutionary point of view, these differences do not indicate different histology in different clinicoepidemiological forms. However, they show different ages of the lesions in the different epidemiology forms of KS. Although Gottlieb and Ackerman (4) suggest that the patch stage persists without progressing to nodular stage, given time nodules will

also appear, and have already been described in AIDS-KS (35). It is therefore justified to speculate that nodules are rare in AIDS-KS because patients die early from opportunistic infections or other complications before the evolution of the lesion is complete.

## 5.6 LESIONS MISDIAGNOSED AS KS

The present series shows that SCC (Squamous cell carcinoma) was more frequently misdiagnosed as KS in Tanzania (Table 19). This is similar to Schmid's findings (102). Other studies did not show SCC as a differential diagnosis of KS. However, in San Francisco series of cutaneous lesions suspicious for KS, Blumenfeld et al. (13), dermatofibroma was the lesion most often mistaken for KS in 13 out of 59 cases. This series shows that fibrous histiocytic tumours were equally misdiagnosed (23.8%) to the same extent as SCC. In determatofibroma the spindle cell component tends to be orderly like in a scar or displays stariform pattern. In addition multi-nucleated giant cells are frequently present. In more than 80% of the cases there is hyperplasia of the overlying epidermis (43). Chronic dermatitis (stasis dermatitis) is also commonly misdiagnosed. In this series it accounted for 14.3% of all misdiagnoses. Unlike KS the vessels are orderly, thick walled and associated with fibrosis (43). Pyogenic granuloma histologically shows intervascular oedema, neutrophilic infiltrate and lack the spindle cells. The deep vasoformative part of pyogenic granuloma, however, might resemble KS (53). In this series this lesion formed 19.0% of all misdiagnoses. Angiomatous KS may be difficult to distinguish from benign and malignant vascular tumours. Early KS may resemble the microscopic capillary haemangioma (41) and the tumour stage may resemble lymphangioma (37). Haemangiomas are unifocal with vessels which are uniform in size and shape. In this study haemangioma was misdiagnosed in one case (4.8%). Two cases of leprosy (9.5%) and one malignant melanoma (4.8%) previously not seen as a differential diagnosis of KS from the literature were seen in this series. The absence of abnormal vessels and slits in leprosy and malignant melanoma can help to differentiate these from KS.

## 5.7 CONDITIONS OCCURRING IN ASSOCIATION WITH KS

There is a well established association between sporadic (CKS) and the development of a second malignant neoplasm. Murray and Lothe (76) observed 3 cases out of 19 autopsy cases. Templeton (112) noted only one case. Safai et al. (100), noted a second primary neoplasm occurring in 37% of 92 cases of sporadic KS, with 58% of these being neoplasms of lymphoreticular system. Approximately 42% of malignancies associated with KS are epithelial, occurring in a variety of organs but most commonly involving the skin (100). Out of 117 cases reported by Slavin et al. SCC was observed in one case and Hodgkin's disease in another (106). It is not clear whether this represents a real association with KS or whether it reflects an accumulated risk for developing neoplasms in an elderly population (113).

The present study shows that in the Tanzania series there were 2 cases of malignant lymphoma, 2 cases of chronic lymphocytic leukaemia and one each of leprosy and tuberculosis in EA-KS (Table 20). There was no epithelial neoplasm seen in these series. Templeton (112), observed one case of leprosy similar to the findings of this study. He stresses that in Uganda many patients died of various infective diseases particularly tuberculosis, which may arise as an opportunistic infection secondary to immunodeficiency in a similar fashion like KS (64).

From the above findings it can be concluded that CKS and EA-KS show more or less the same histological features. Significance testing were, how-ever, jeopardized by sample size. AIDS-KS occurs in a slightly younger age group and show histological features consistent with an early patch lesion. The significance for this was again limited by the small sample of AIDS-KS, otherwise there are no remarkable differences. Further studies involving large sample sizes must be done.

## 6. SUMMARY

This study shows that in Tanzania, Kaposi's sarcoma accounted for 3.54% of all malignancies during the study period. The male to female ratio was 4.1:1 for Tanzania and 32:1 for Switzerland. Although there was a variable annual increase in the number of Kaposi's sarcoma cases in Tanzania up to 1980, there was no significant increase after this year. This picture is different from Switzerland where Kaposi's sarcoma was rare before 1983. From 1983 to 1985 there was a sharp rise in the number of cases coinciding with AIDS epidemic.

In Tanzania Kaposi's sarcoma affects all age groups but the peak was observed in the 3rd to 6th decade. 60 cases of childhood Kaposi's sarcoma were seen in Tanzania 70% of these were males 30% were females. This gives a M:F ratio of 2.3:1 indicating that in childhood KS there are proportionately more females than in adult KS. In Switzerland there were two peaks. One in the 3rd to 5th decade and another in the 6th to 7th decade. The first peak has not been reported before, and is thought to be related to the emergence of AIDS. Kaposi's sarcoma was not seen before the age of 15 years in Switzerland.

In Tanzania the dominant clinicoepidemiological form of KS was the Endemic African (EA-KS) whereas in Switzerland AIDS-KS was more common. Skin involvement was the most common mode of presentation of KS in both countries, and the majority of these skin lesions were localized.

Mid-dermis KS lesions were more frequent in Tanzania whereas upper dermis lesions were more common in Switzerland, and the nodular late stage lesions were seen more

frequently in Tanzania whereas early stage KS was more common in Switzerland reflecting the different epidemiological types of KS in the two countries. In all epidemiological forms of KS, the mixed pattern KS is more commonly seen. However, angiomatous KS seems to be more frequent in AIDS-KS. Lymphocytic and plasma cell infiltrates are common histological finding which may help in the diagnosis. Although haemosiderin deposits may help in reaching a histological diagnosis of KS this is not a constant feature. Eosinophilic globular (hyaline) bodies were not seen in this series.

The patch stage of KS which is more common in Aids is subtle and difficult to diagnose. Features which may help in the diagnosis are the sparse lymphocytic infiltrate especially around skin appendages and upper dermal proliferation of small abnormally dilated vessels with jagged outlines. In addition these vessels have a thin discontinuous endothelial lining. Some of these abnormal vessels occur in close proximity to normal blood vessels and tend to encircle them. The proliferating vessels and slits impart a cracked appearance to the dermis "dermal collagen dissection". Plaques were found to have features of both patch and nodular lesions. Nodular lesions were found to be well circum-scribed consisting of interlacing spindle cells with a variable amount of slits and vessels, assuming either a monomorphic spindle cell or a mixed pattern.

Squamous cell carcinoma and fibrous histiocytoma were commonly misdiagnosed as KS in Tanzania. Only few cases were associated with other conditions.

In this study it has been found that whereas C-KS is a disease of the elderly occurring in the 6th to 7th decade and EA-KS in the 3rd to 6th decade, AIDS-KS occurs in 3rd to 5th decade. Morphologically C-KS and EA-KS are similar but AIDS-KS presents with early lesions. Histologically these show different ages of the same evolutionary process.

## 7. COMMENTS AND RECOMMENDATIONS

This study has compared KS in Tanzania and Switzerland, particularly the various clinicoepidemiological forms. The associations of KS and the emergence of AIDS has well been shown in Switzerland. Such association was not well established in Tanzania, and above all, there was no substantial increase, in the incidence of KS. This type of finding needs careful interpretation, because the general lack of increase in the number of KS cases may reflect the quality of pathology services rendered during the period of the study. Perhaps, due to unavailability of good services, a number of cases were not diagnosed. Likewise this may be the true pictured, that is, there was no increased number of KS cases related to the AIDS epidemic. However, despite the shortcomings this study provides the basis for future studies.

Despite extensive studies on Kaposi's sarcoma, its nature still remains a mystery. A number of studies have shown a peculiar geographical distribution of C-KS and EA-KS. Likewise KS shows a peculiar male preponderance and in children the male to female ratio decreases.

This brings a number of questions. Can environmental, genetic or hormonal factors play part in the aetiology of this lesion? The association of KS and deficient immunological states is well known. How the immunological defect initiates "angiogenesis" is not known. Perhaps the immune defect trigger the release of certain soluble factors (cytokines) which are angiogenic. Furthermore KS shows a rather innocent histological appearance except for few aggressive cases with a pleomorphic picture. The malignant nature of the lesion has therefore been questioned. Retroperitoneal fibromatous lesions have been

seen in monkeys with simian immunodeficiency syndrome (C. Tsai, unpublished data) and also "KS like" lesions have been induced in nude mice (60). Are these lesions "KS" presenting differently in different animal species?

To answer these questions and more future studies on KS must be multidisciplinary in approach including epidemiological studies, genetic and hormonal studies, immunological studies and DNA studies. When facilities allow culture studies and animal models can also be done. Comparison of the different variables will most likely give more clue to the nature of KS and also elucidate its pathogenesis.

**Table 1. CLINICAL AND EPIDEMIOLOGICAL CORRELATIONS OF FORMS OF KS**

| Clinical forms | | Epidemiologic correlation |
|---|---|---|
| **A. Cutaneous KS** | | |
| (i) | Nodular | Sporadic and EA - KS |
| (ii) | Aggressive | EA - KS |
| **B. Lymphnode or visceral KS** | | EA-KS in children and young adults |
| (iii) | Lymphadenopathic | AIDS-KS |
| (iv) | Systemic or generalized | EA-KS in children and young adults<br>AIDS-KS |
| **C. AIDS-KS** | | |
| (v) | Early KS | AIDS and Immunosuppressed states |

Table 2. LESIONS WHICH CAN MIMIC KS CLINICALLY AND MICROSCOPICALLY

| | | | Ref |
|---|---|---|---|
| 1. | **Inflammatory, hyperpalstic and vascular lesions** | | |
| | (i) | Stasis dermatitis | (1) |
| | (ii) | Scars | (80) |
| | (iii) | Pyogenic granuloma | (119) |
| 2. | **Vascular tumours** | | |
| | (1) | Hemangioma | (13) |
| | (ii) | Lymphangioma | (37) |
| | (iii) | Hemangiosarcoma | (73) |
| | (iv) | Lymphangiosarcoma | (43) |
| 3. | **Fibro - histiocytic tumours** | | |
| | (i) | Dermatofibroma | (80) |
| | (ii) | Fibrous histiocytoma | (80) |
| | (iii) | Fibrosarcoma | (73) |
| 4. | **Other tumours** | | |
| | | SCC | (102) |
| | | Leiomyoma | (43) |

**Table 3. DISTRIBUTION OF KS CASES BY YEAR AND SEX**

| Country | Tanzania | | | | | Switzerland | | | |
|---|---|---|---|---|---|---|---|---|---|
| Year | Sex | | | | | Sex | | | |
| | M | F | Unknown | Total | % | M | F | Total | % |
| 1975 | 2 | 0 | 7 | 9 | 1.5 | | | | |
| 1976 | 9 | 4 | - | 13 | 2.2 | | | | |
| 1977 | 44 | 8 | 2 | 54 | 9.2 | | | | |
| 1978 | 36 | 2 | - | 38 | 6.5 | | | | |
| 1979 | 37 | 6 | - | 43 | 7.4 | 1 | 1 | 2 | 6.1 |
| 1980 | 69 | 15 | 1 | 85 | 14.6 | | | | |
| 1981 | 39 | 21 | 1 | 91 | 15.6 | | | | |
| 1982 | 47 | 17 | - | 64 | 11.0 | | | | |
| 1983 | 45 | 14 | - | 29 | 10.1 | 1 | - | 1 | 3.0 |
| 1984 | 61 | 9 | - | 70 | 12.0 | 8 | - | 8 | 24.2 |
| 1985 | 42 | 16 | - | 58 | 9.9 | 22 | - | 22 | 66.7 |
| Total | 461 | 112 | 11 | 584 | 100.0 | 32 | 1 | 33 | 100.0 |
| % | 78.9 | 19.2 | 1.9 | 100.0 | 96.97 | 3.3 | 100.0 | | |

**Table 4. AGE DISTRIBUTION OF KS CASES IN TANZANIA AND SWITZERLAND**

| | Tanzania | | | | | Switzerland | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Sex | | | | | | | | |
| Age | M | F | Unknown | Total | % | M | F | Total | % |
| 0 - 4 | 22 | 5 | - | 27 | 4.6 | - | - | - | - |
| 5 - 9 | 8 | 7 | - | 15 | 2.6 | - | - | - | - |
| 10 - 14 | 12 | 6 | - | 18 | 3.1 | - | - | - | - |
| 15 - 19 | 13 | 7 | - | 20 | 3.4 | 1 | - | 1 | 3.0 |
| 20 - 24 | 22 | 6 | - | 28 | 4.8 | 2 | - | 2 | 6.1 |
| 25 - 29 | 39 | 8 | 1 | 48 | 8.2 | 2 | - | 2 | 6.1 |
| 30 - 34 | 32 | 7 | - | 39 | 6.7 | 5 | - | 5 | 15.2 |
| 35 - 39 | 34 | 11 | 2 | 47 | 8.0 | 8 | - | 8 | 24.2 |
| 40 - 44 | 35 | 5 | 2 | 42 | 7.2 | 4 | - | 4 | 12.1 |
| 45 - 49 | 44 | 5 | 4 | 53 | 9.1 | 3 | - | 3 | 9.1 |
| 50 - 54 | 40 | 9 | 2 | 51 | 9.7 | 1 | - | 1 | 3.0 |
| 55 - 59 | 25 | 9 | - | 31 | 5.3 | 3 | - | 3 | 9.1 |
| 60 - 64 | 33 | 11 | - | 44 | 7.5 | - | - | - | - |
| 65 - 69 | 16 | 1 | - | 17 | 2.7 | 1 | - | 1 | 3.0 |
| 70 - 74 | 7 | - | - | 7 | 1.2 | 1 | - | 1 | 3.0 |
| 75+ | 16 | 1 | - | 7 | 2.9 | 1 | 1 | 1 | 6.1 |
| Unknown | 63 | 17 | - | 80 | 13.8 | - | - | - | - |
| Total | 461 | 112 | 11 | 584 | 100.0 | 32 | 1 | 33 | 100.0 |

**Table 5. SEX DISTRIBUTION OF KS PATIENTS BELOW THE AGE 14 IN TANZANIA**

| Age | Male | Female | Total | Sex ratio (M:F) |
|---|---|---|---|---|
| 0 - 4 | 22 | 5 | 27 | 4.4:1 |
| 5 - 9 | 8 | 7 | 15 | 1.1:1 |
| 10 - 14 | 12 | 6 | 18 | 2:1 |
| Total | 42 | 18 | 60 | 2.3:1 |
| % | 70 | 30 | 100 | |

**Table 6. RACIAL AND NATIONALITY DISTRIBUTION OF TANZANIA KS PATIENTS**

| | Nationality | | | | | |
|---|---|---|---|---|---|---|
| Race | Tanzania | American | Ugand a | Not known | Total | % |
| African | 577 | - | 1 | - | 578 | 99.0 |
| Caucacian | - | 1 | - | - | 1 | 0.2 |
| Asian | - | - | - | 2 | 2 | 0.3 |
| Unknown | 3 | - | - | - | 3 | 0.5 |
| Total | 580 | 1 | 1 | 1 | 584 | 100.0 |
| % | 99.3 | 0.2 | 0.2 | 0.3 | 100.0 | |

**Table 7. COMPARISON OF CLINICOEPIDEMIOLOGICAL FORMS OF KS IN TANZANIA AND SWITZERLAND**

| | Tanzania | | | | | Switzerland | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Sex | | | | | Sex | | | |
| Type | M | F | Unknown | Total | % | M | F | Total | % |
| C-KS | - | - | - | - | - | 4 | 1 | 5 | 15.2 |
| EA-KS | 399 | 100 | 11 | 510 | 87.3 | - | - | - | - |
| AIDS-KS* | 4 | - | - | 4 | 0.7 | 28 | - | 18 | 84.4 |
| Unknown | 58 | 12 | - | 70 | 12.0 | - | - | - | - |
| Total | 461 | 112 | 11 | 584 | 100.0 | 31 | 1 | 33 | 100.0 |

* HIV-testing in Tanzania was done only at KCMC before 1986

**Table 8. DISTRIBUTION OF TANZANIA KS LESIONS BY SITE**

| | Sex | | | | |
|---|---|---|---|---|---|
| Site | Males | Females | Unknown | Total | % |
| Skin | 409 | 85 | 9 | 503 | 86.1 |
| Lymphnode | 32 | 17 | 2 | 51 | 8.7 |
| Visceral (NOS) | 7 | 1 | - | 8 | 1.4 |
| Oral Cavity | 3 | 2 | - | 5 | 0.9 |
| Nose | 1 | 1 | - | 2 | 0.3 |
| Other Sites | 6 | 2 | - | 7 | 1.2 |
| Unknown | 3 | 4 | - | 7 | 1.2 |
| Total | 461 | 112 | 11 | 584 | 100.0 |
| % | 78.9 | 19.2 | 1.9 | 100.0 | |

**Table 9. DISTRIBUTION OF SWITZERLAND KS LESIONS BY SITE**

| | Sex | | | |
|---|---|---|---|---|
| Site | Males | Females | Total | % |
| Skin | 25 | 1 | 26 | 78.2 |
| Lymphnode | 7 | - | 9 | 21.8 |
| Total | 26 | 1 | 35 | 100.0 |
| % | 96.97 | 3.03 | 100.0 | |

**Table 10. DISTRIBUTION PATTERN OF KS SKIN LESIONS IN TANZANIA AND SWITZERLAND**

| Distribution | Tanzania | | | | | Switzerland | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Sex | | | | | | | | |
| | M | F | Unknown | Total | % | M | F | Total | % |
| Localized (one site) | 402 | 83 | 9 | 494 | 98.2 | 22 | 1 | 23 | 88.5 |
| Disseminated | 7 | 2 | - | 9 | 1.8 | 3 | - | 3 | 11.5 |
| Total | 409 | 85 | 9 | 503 | 100.0 | 25 | 1 | 26 | 100.0 |

**Table 11. LOCATION OF KS LESION WITHIN THE SKIN**

| Part of Dermis | Tanzania | | | | | Switzerland | | | |
|---|---|---|---|---|---|---|---|---|---|
| | M | F | Unknown | Total | % | M | F | Total | % |
| Upper only | 146 | 30 | 4 | 180 | 35.8 | 15 | - | 15 | 57.7 |
| Mid only | 188 | 46 | 3 | 237 | 47.1 | 6 | 1 | 7 | 26.9 |
| Upper & Mid | 72 | 8 | 2 | 82 | 16.3 | 2 | - | 2 | 7.7 |
| Lower | 3 | 1 | - | 4 | 0.8 | 2 | - | 2 | 7.7 |
| Total | 409 | 85 | 9 | 503 | 100.0 | 25 | 1 | 26 | 100.0 |

NB. All upper and mid-termis involvement in Tanzania = 99.2%.

**Table 12. DISTRIBUTION OF CASES ACCORDING TO AGE OF THE LESION**

| | Tanzania | | | | | Switzerland | | | |
|---|---|---|---|---|---|---|---|---|---|
| Age of Lesion | M | F | Unknown | Total | % | M | F | Total | % |
| Early (Patch) | 26 | 5 | 2 | 33 | 5.7 | 16 | - | 16 | 48.5 |
| Plaque | 28 | 12 | 2 | 42 | 7.2 | 12 | - | 12 | 36.4 |
| Nodule | 407 | 95 | 7 | 509 | 87.1 | 4 | - | 1 | 15.1 |
| Total | 461 | 112 | 11 | 584 | 100.0 | 32 | 1 | 33 | 100.0 |

**Table 13. HISTOLOGICAL CLASSIFICATION OF KS LESIONS**

| | Tanzania | | | | | Switzerland | | | |
|---|---|---|---|---|---|---|---|---|---|
| Type of Lesion | M | F | Unknown | Total | % | M | F | Total | % |
| Spindle cell pattern KS (Monomorphic) | 178 | 40 | 4 | 222 | 38.0 | 8 | - | 8 | 24.2 |
| Mixed pattern KS | 237 | 64 | 2 | 303 | 52.0 | 8 | 1 | 9 | 27.3 |
| Anaplastic KS (Pleomorphic) | 3 | - | - | 3 | 0.5 | - | - | - | - |
| Angio-matous KS | 43 | 8 | 5 | 56 | 9.5 | 16 | - | 16 | 48.5 |
| Total | 461 | 11 | 11 | 584 | 100.0 | 32 | 1 | 33 | 100.0 |

**Table 14. DEGREE OF LYMPHOCYTIC INFILTRATE IN KS LESIONS**

| Amount | Tanzania | | | | | Switzerland | | | |
|---|---|---|---|---|---|---|---|---|---|
| | M | F | Unknown | Total | % | M | F | Total | % |
| Minimal | 327 | 89 | 7 | 423 | 72.4 | 10 | 1 | 11 | 33.3 |
| Moderate | 105 | 15 | 2 | 122 | 20.8 | 8 | - | 8 | 24.3 |
| Heavy | 29 | 8 | 2 | 39 | 6.8 | 14 | - | 14 | 42.4 |
| Total | 461 | 112 | 11 | 584 | 100.0 | 32 | 1 | 33 | 100.0 |

**Table 15. DEGREE OF PLASMA CELL INFILTRATE IN KS LESIONS**

| Amount | Tanzania | | | | | Switzerland | | | |
|---|---|---|---|---|---|---|---|---|---|
| | M | F | Unknown | Total | % | M | F | Total | % |
| Minimal | 329 | 81 | 4 | 414 | 70.9 | 27 | 1 | 28 | 84.8 |
| Moderate | 68 | 13 | 5 | 86 | 14.7 | 2 | - | 2 | 6.1 |
| Heavy | 64 | 18 | - | 84 | 14.4 | 3 | - | 3 | 9.1 |
| Total | 461 | 112 | 11 | 584 | 100.0 | 32 | 1 | 33 | 100.0 |

**Table 16. AMOUNT OF SIDEROPHAGES IN KS LESIONS**

| Amount | Tanzania | | | | | Switzerland | | | |
|---|---|---|---|---|---|---|---|---|---|
| | M | F | Unknow | Total | % | M | F | Total | % |
| Absent | 69 | 13 | - | 82 | 14.0 | - | - | - | - |
| Minimal | 302 | 79 | 5 | 386 | 66.1 | 20 | 1 | 21 | 63.7 |
| Moderate | 70 | 17 | 4 | 91 | 15.6 | 11 | - | 11 | 33.3 |
| Heavy | 20 | 3 | 2 | 25 | 4.3 | 1 | - | 1 | 3.0 |
| Total | 461 | 112 | 11 | 584 | 100.0 | 32 | 1 | 33 | 100.0 |

**Table 17. CORRELATION BETWEEN AGE OF KS LESION AND EPIDEMIOLOGICAL TYPES OF KS**

| Age of Lesion | Tanzania | | | | Switzerland | | | |
|---|---|---|---|---|---|---|---|---|
| | EA-KS | Aids-KS | Total | % | C-KS | AIDS-KS | Total | % |
| Patch | 29 | 4 | 33 | 5.7 | - | 16 | 16 | 48.5 |
| Plaque | 42 | - | 42 | 7.2 | 1 | 11 | 12 | 36.4 |
| Nodular | 509 | - | 509 | 87.1 | 4 | 1 | 5 | 15.1 |
| Total | 580 | 4 | 548 | 100.0 | 5 | 28 | 33 | 100.0 |
| % | 99.3 | 0.7 | 100.0 | | 15.2 | 84.8 | 100.0 | |

**Table 18. CORRELATION BETWEEN HISTOLOGICAL CLASS OF KS AND EPIDEMIOLOGICAL FORMS**

| | Tanzania | | | | Switzerland | | | |
|---|---|---|---|---|---|---|---|---|
| Class | EA-KS | Aids-KS | Total | % | C-KS | AIDS-KS | Total | % |
| Monomorphic (Spindle pattern) | 220 | - | 220 | 37.6 | 1 | 7 | 8 | 24.2 |
| Mixed pattern | 304 | - | 304 | 52.1 | 4 | 5 | 9 | 27.3 |
| Angio-matous | 53 | 4 | 57 | 9.8 | - | 16 | 16 | 48.5 |
| Ana-plastic | 3 | - | 3 | 0.5 | - | - | - | - |
| Total | 580 | 4 | 584 | 100.0 | 5 | 28 | 33 | 100.0 |

**Table 19. LESIONS COMMONLY MISTAKEN FOR KS IN TANZANIA**

| Condition | Males | Females | Total | % |
|---|---|---|---|---|
| SCC | 3 | 2 | 5 | 23.8 |
| Fibrous histocytoma | 2 | 3 | 5 | 23.8 |
| Chronic dermatitis | 2 | 1 | 3 | 14.3 |
| Granuloma pyogenicum | 4 | - | 4 | 19.0 |
| Leprosy | 2 | - | 2 | 9.5 |
| Haemangioma | - | 1 | 1 | 4.8 |
| Malignant melanoma | 1 | - | 1 | 4.8 |
| Total | 14 | 7 | 21 | 100.0 |

**Table 20. CONDITIONS OCCURRING IN ASSOCIATION WITH KS IN TANZANIA**

| Condition | Males | Females | Total | % |
|---|---|---|---|---|
| Malignant lymphoma | 2 | - | 2 | 33.3 |
| Chronic lymphocytic Leukaemia | 1 | 2 | 2 | 33.3 |
| Leprosy | 1 | - | 1 | 16.7 |
| Tuberculosis | 1 | - | 1 | 16.7 |
| Total | 4 | 2 | 6 | 100.0 |

NB. All these were not associated with AIDS.

**Table 21. PROPORTION OF FEMALE CASES IN LARGE SERIES**

| Coutry | No of cases | Sex ratio | Reference | |
|---|---|---|---|---|
| Uganda | 211 | 2.9 | Lothe | (60) |
| Uganda | 624 | 5.4 | templeton | (11) |
| Tanzania | 117 | 7.5 | Slavin et al. | (105) |
| USA | 70 | 8.5 | Reymolds et al | (92) |
| Tanzania | 584 | 19.2 | Present series | |
| Switzerland | 33 | 3.0 | Present series | |

FIGURE.1: GRAPH SHOWING ANNUAL DISTRIBUTION OF KAPOSI'S SARCOMA IN TANZANIA

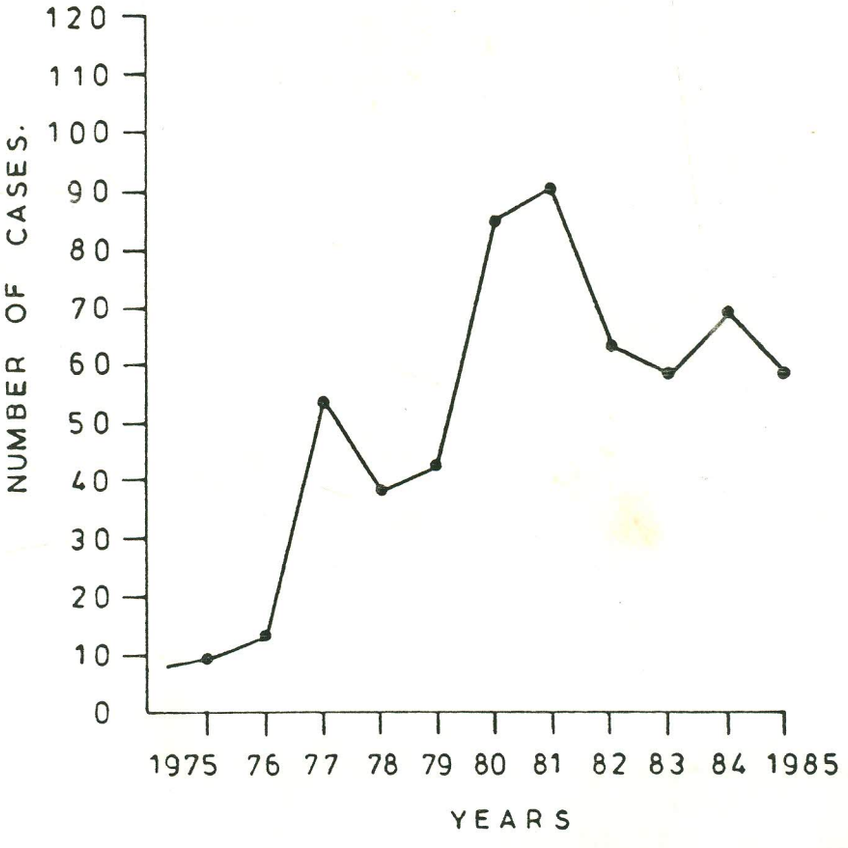


FIGURE 2: GRAPH SHOWING ANNUAL DISTRIBUTION OF KAPOSI'S SARCOMA IN SWITZERLAND

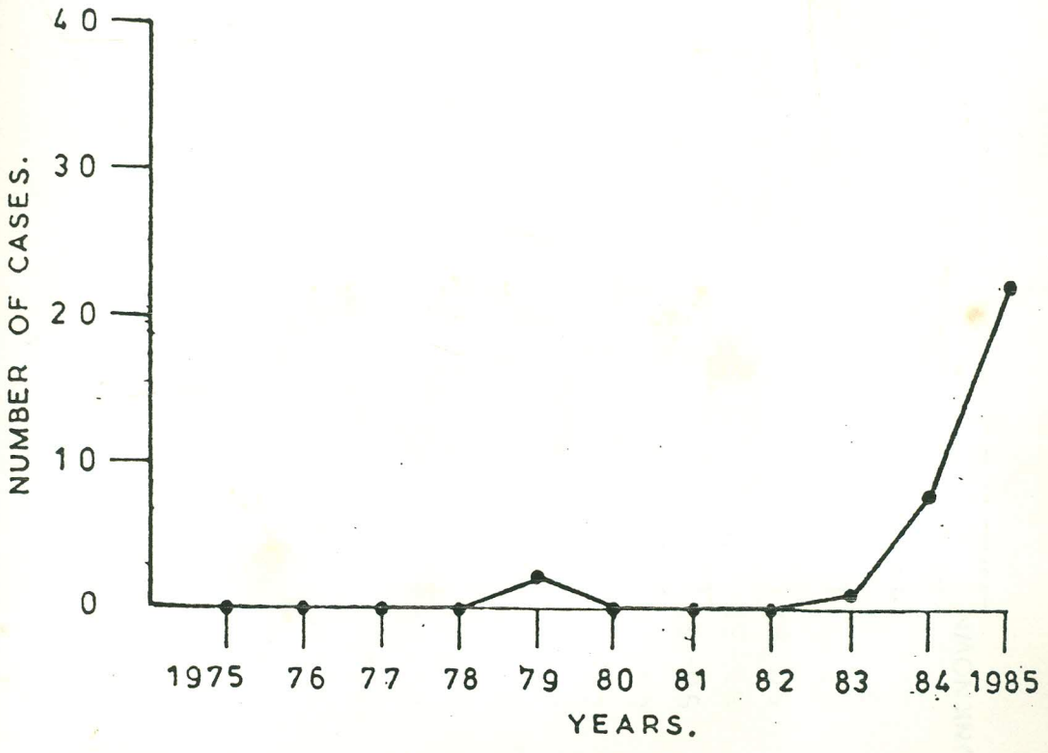


FIGURE.3: AGE AND SEX STRUCTURE OF KAPOSI'S SARCOMA IN TANZANIA

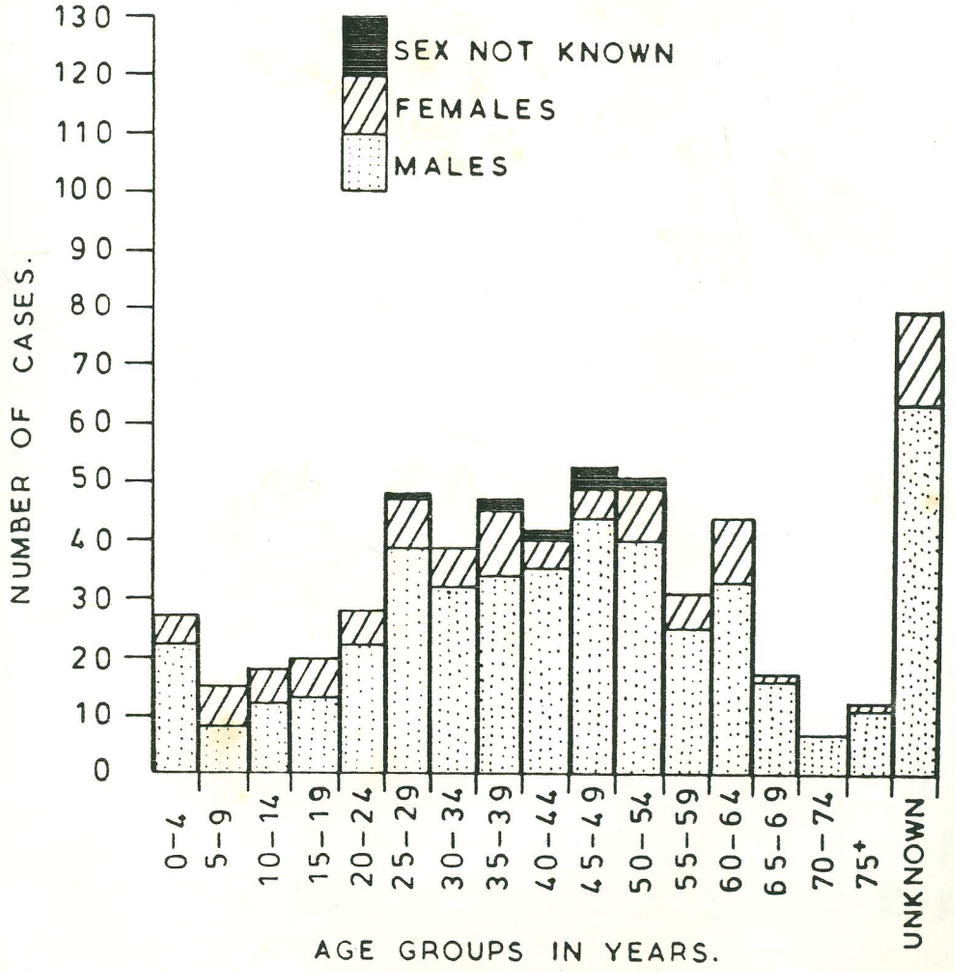


FIGURE.4: AGE AND SEX STRUCTURE OF KAPOSI'S SARCOMA IN ZURICH SWITZERLAND

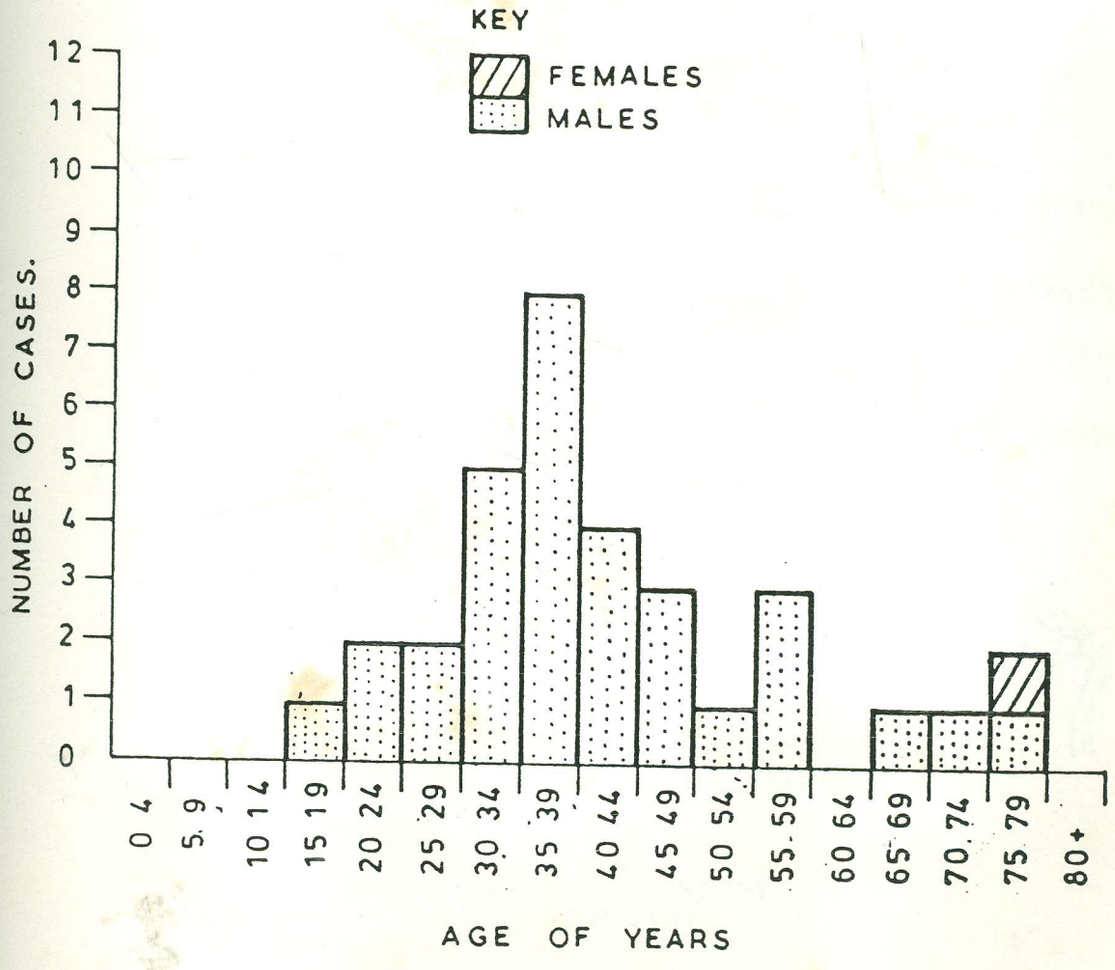
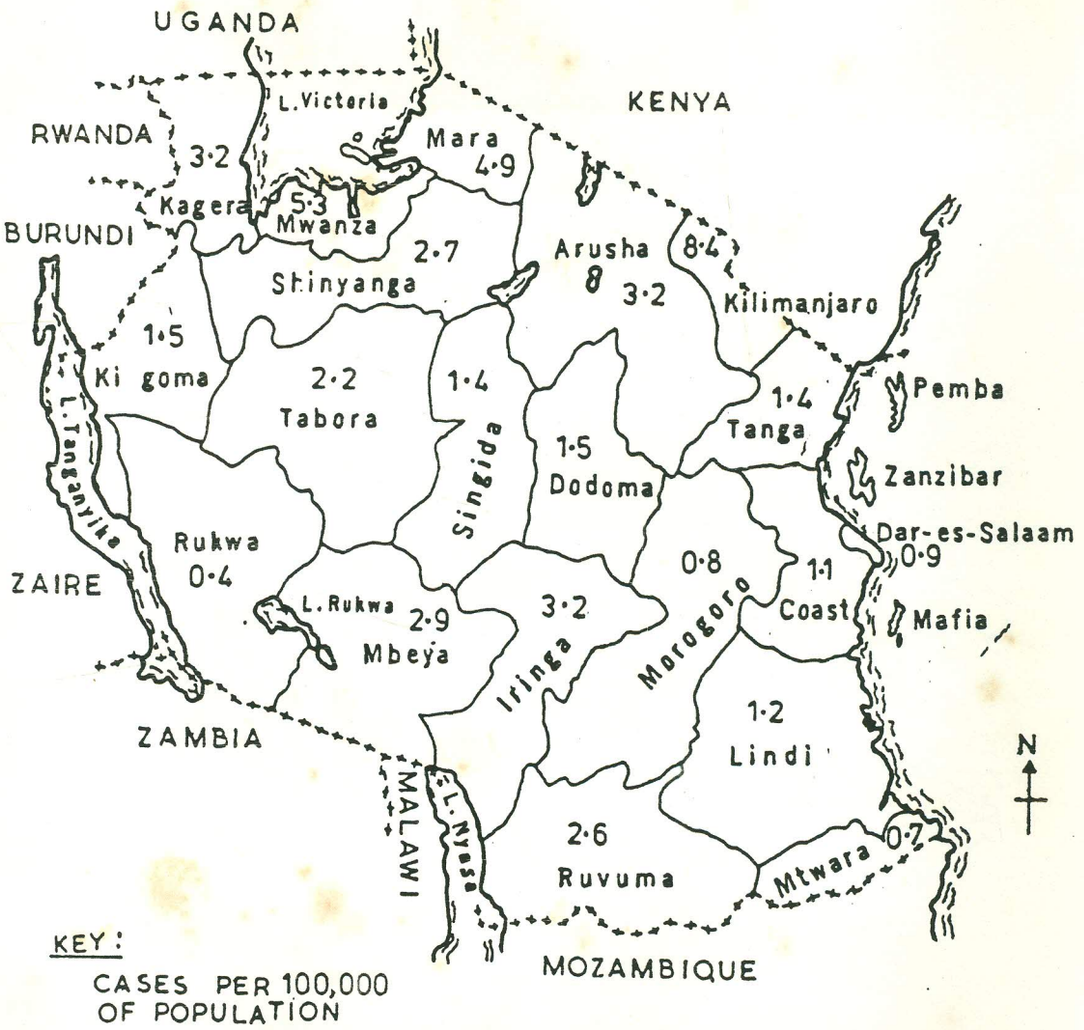


FIGURE.5: REGIONAL DISTRIBUTION OF KAPOSI'S SARCOMA IN TANZANIA



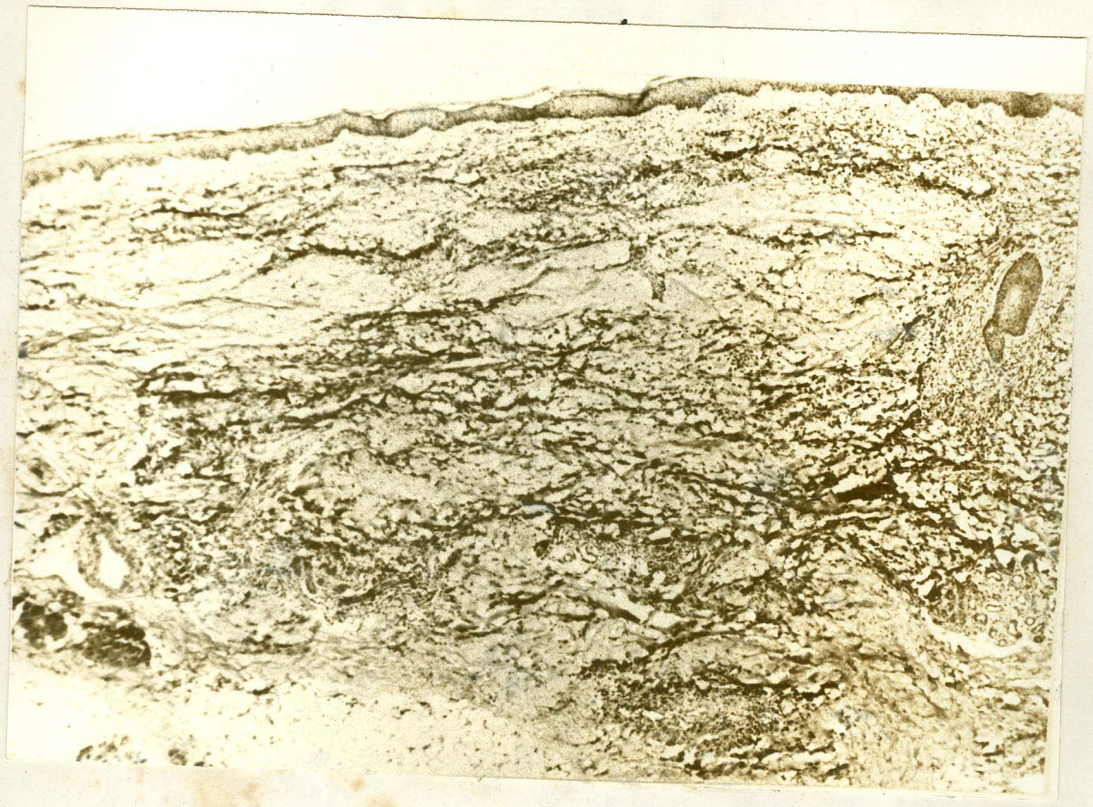


Figure 6. Early lesion of KS. At low magnification it resembles chronic dermatitis involving upper and lower dermis (H & E x 25).




Figure 7. Early lesion showing proliferation of blood vessels (thick arrow) and perivascular round cell infiltrate (open arrow). Dermal collagen dissection is evident in the mid-dermis (DS) (H & E x 88).



Figure 8. A high magnification of an early KS showing a dilated thin walled capillary partially surrounding a normal looking vessel (arrow) (H & E x 63).

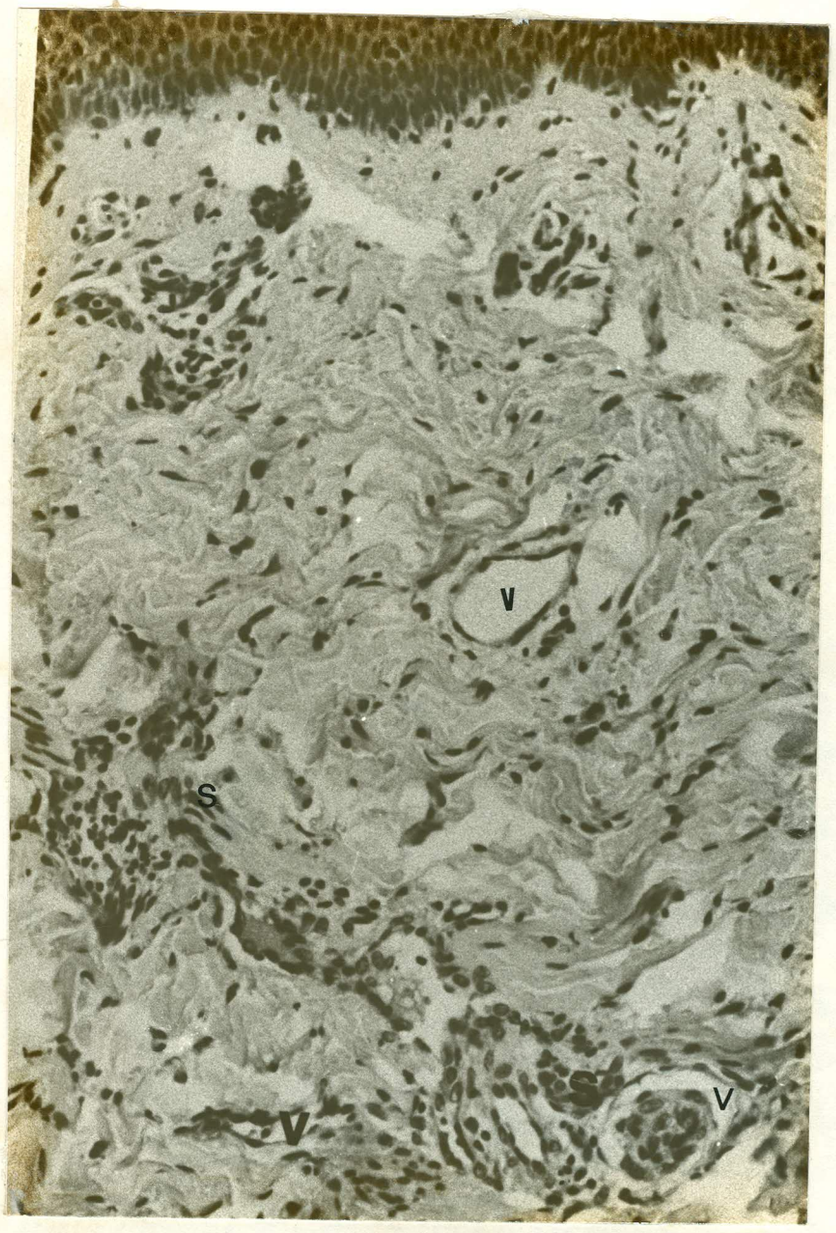



Figure 9. A plaque lesion with dilated blood vessels (v) and also early spindle cells proliferation (s) around the dilated vessels and skin appendages (a) (H & E x 160).




Figure 10. Low power section showing a well formed nodular lesion(N) (H & E x 40).




Figure 11. High power of a nodular lesion showing spindle cell proliferation (spindle cell pattern) (s). Round cell infiltration is noted (rc) (H 6 E x 160).

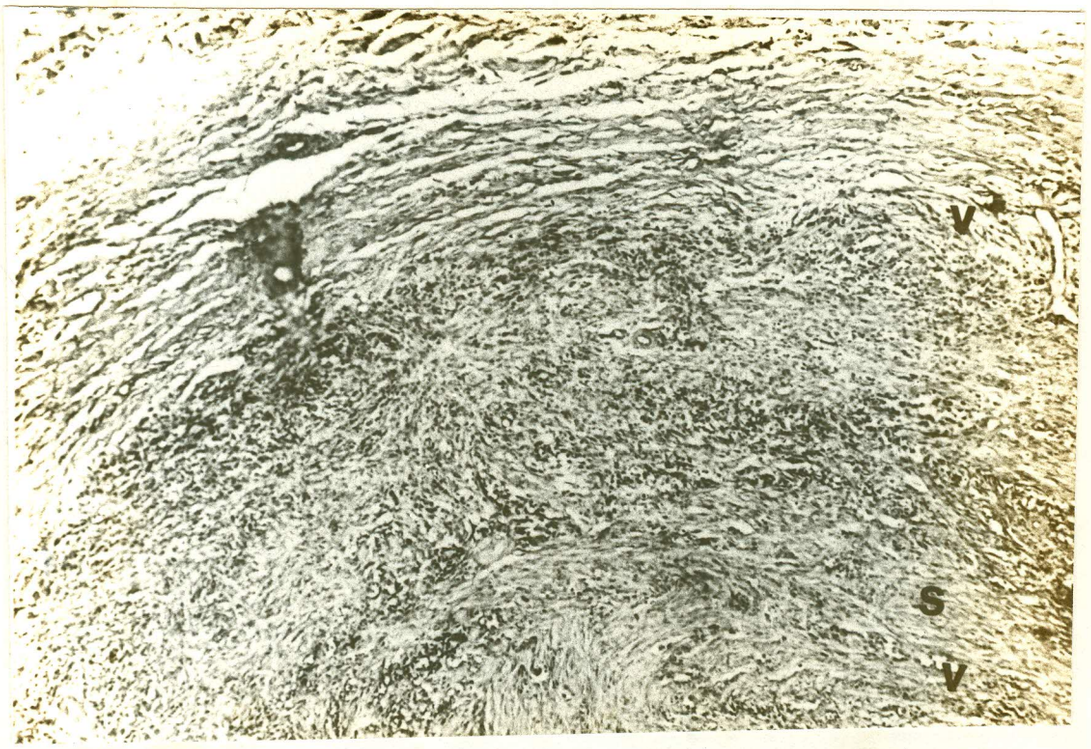



Figure 12. Nodular lesion with both spindle cell (s) proliferation and vascular slits (v) (Mixed pattern) (H & E x 63).

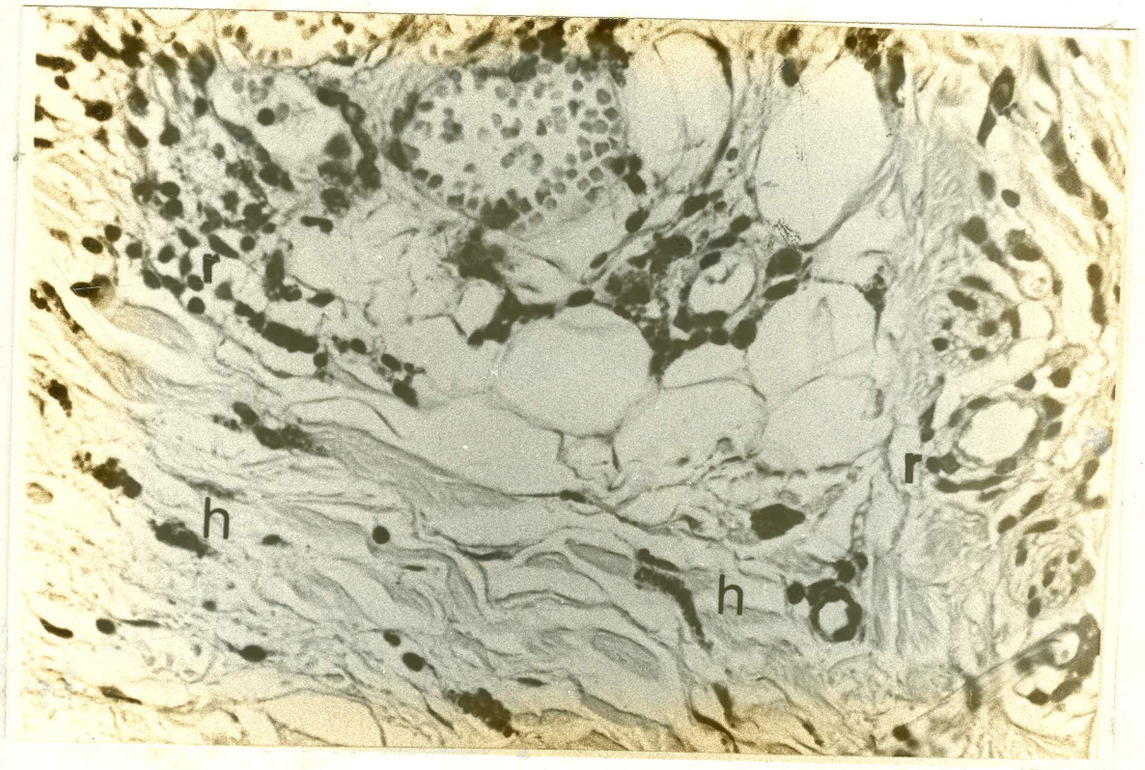



Figure 13. Show Haemosiderine (h) and round cell infiltrate (r) in KS (H & E x 320)

## APPENDIX I

## ANNUAL DISTRIBUTION OF MALIGNANT NEOPLASMS IN TANZANIA 1975 TO 1985

| | YEAR | KS | NEOPLASMS | % KS |
|---|---|---|---|---|
| 1. | 1975 | 9 | 1578 | 0.6 |
| 2. | 1976 | 13 | 1257 | 1.0 |
| 3. | 1977 | 54 | 1945 | 2.8 |
| 4. | 1978 | 38 | 1500 | 2.5 |
| 5. | 1979 | 43 | 1866 | 2.3 |
| 6. | 1980 | 85 | 1286 | 3.9 |
| 7. | 1981 | 91 | 1500 | 6.1 |
| 8. | 1982 | 64 | 906 | 7.1 |
| 9. | 1983 | 59 | 1580 | 3.7 |
| 10. | 1984 | 70 | 1364 | 5.1 |
| 11. | 1985 | 58 | 822 | 7.1 |
| Total | | 484 | 16,504 | |

Total No. of KS cases 1975 to 1985 = 584 = 3.54% of all malignancies

Source: Cancer Registry Data.

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