Kaposi's "Sarcoma" — Is It a Sarcoma at All?

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INTRODUCTION

Stimulated by the extraordinary recent changes in our fund of knowledge concerning the disease carrying the eponym Kaposi, we believe it has become imperative to review what has become known about this disease since its original description, and to reexamine Kaposi's original concept that this condition is a genuine sarcoma. An attempt will be made to show that what has become known about this entity since its original description is so contrary or aberrant to that which is known about indubitable sarcomas, that the view that Kaposi's "sarcoma" is a noncancerous condition must not only be seriously considered, but is the probable conclusion which should be drawn. Indeed, it will be the thesis of this paper that the data which has been accumulating is quite supportive of the following view: that Kaposi's disease is a unique, noncancerous, multicentric, atypical, angioblastic hyperplasia, perhaps induced by an angiotropic strain of virus, in immunocompromised hosts.

The importance of accurately defining Kaposi's entity as to whether it is a cancerous versus noncancerous condition cannot be overemphasized. For example, research efforts delving into its etiology, pathogenesis and eventual cure must by necessity be impeded if the very foundation upon which its biologic nature is defined is fallacious. The following quotes from the literature will illustrate the depth of the confusion regarding its fundamental nature:

"Kaposi's sarcoma, a multifocal, metastasizing, malignant reticulosis with features resembling those of angiosarcoma, principally involving the skin..." (1974)1

"Since the name "Kaposi's sarcoma" is generally accepted and understood by the medical profession, it probably should be retained even though only a small percentage of cases progress to the sarcoma stage." (1969)2

"Despite its name Kaposi's sarcoma should not be considered a true sarcoma." (1965)3

"Kaposi's sarcoma is an atypical but true sarcoma which originates in a bluish-red macule." (1966)4

"Now considered to be a multicentric malignant neoplastic process KS manifests as..." (1981)5

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"The epidemic of the generalized form of Kaposi's sarcoma among patients with AIDS is regarded by many as an opportunity to gain insight into the pathogenesis, prophylaxis and treatment of neoplasia. That may well be the case but the idea that Kaposi's sarcoma in its disseminated form is not a neoplasm is seldom considered." (1983)

Since, as it should subsequently become clear that the entity described by Kaposi as a unique sarcoma of the skin is probably not a cancerous condition at all, rather than to continue to promulgate a grave misnomer the entity will herein be referred to as Kaposi's disease (KD) wherever possible.

KAPOSI'S DISEASE-A REVIEW

In 1872, Moriz Kaposi, an Hungarian born, Viennese trained dermatologist, published a paper entitled: "idiopathic multiple pigmented sarcoma of the skin." He described five males ranging in age from 40 to 66 years of age who developed multiple, brown-red to blue-red pigmented macules and nodules of the skin which usually began on the lower extremities. Upon progression of the disease isolated and groupings of similar nodules also appeared on the arms, legs, face and trunk. Occasionally, similar lesions involved the lymph glands and mucous membranes. Some nodules atrophied and regressed while others enlarged and ulcerated. He described the disease as not only incurable, but potentially lethal, although his publication is only clear to the effect that at least one of his patients died at the autopsy. He also had reviewed microscopic observations were those of hemorrhage and large quantities of original article it is apparent that he was reporting as a sarcoma based on the histology of the case. His microscopic observations were those of infiltrating cells associated with hemorrhage and large quantities of pigment. Upon reviewing Kaposi's original article it is apparent that he chose to conceive of the disease he was reporting as a sarcoma based on the following conditions:

1. Its progressive nature
2. Its apparent incurability.
3. Its potentially lethal outcome.
4. Its apparent origin from cells of the connective tissue associated with hemorrhage and pigmentation.
5. His enthusiastic embrace of the term "sarcoma" for any lethal, multiple, nodular conditions of the skin introduced by Kötben, another Viennese dermatologist in 1869. It is interesting to note that it was Kötben who reciprocated his appreciation of Kaposi's paper by coining the eponym " Kaposi's sarcoma" in 1891.

Since Kaposi's original paper, considerably more information about the disease has accumulated, which is pertinent to review. At least three distinctive variants are now recognized- the classical, endemic and epidemic forms.

A. Classical KD

This variant is identical to the one originally described by Kaposi. The vast majority of patients are male, between 50 to 70 years of age; primarily of mediterranean extraction. It is rarely familial. Throughout the world (except for Africa), before 1979, this form of KD, although rare, was predominant, if not exclusive.

The lesions begin as one or more red, purple to brown, maculo-papular lesions which over the course of years progress into nodulo-ulcerative lesions. They most commonly begin in the legs and may appear in crops. Complete regression of at least some of the lesions is common. Mucous membranes, lymph nodes, and viscera are occasionally involved. These latter lesions are generally asymptomatic and usually only discovered at autopsy. The disease commonly runs an indolent course for 10-20 years or more, most patient succumbing to other problems such as lymphoproliferative disorders, carcinomas, heart disease, and the like.
The anatomical distribution of the visceral Kaposi's lesions at autopsy are highly peculiar in that within the lungs the lesions spread along the bronchial blood vessels and septae. In the lymph nodes they begin in the capsular sinusoids and in the liver by means of the portal tracts.

**B. Endemic(African) KD**

In the 1950's, KD was recognized as a severe endemic disease amongst the Bantu tribes of South Africa. Approximately 9% of all reported cancers seen in Ugandan males was KD. The geographic distribution of the disease along equatorial Africa was similar to that of Burkitt's lymphoma.

Three distinctive African forms of endemic KD have been reported. The first is essentially identical to classical KD. The second type is a florid, locally aggressive type, in which skin lesions are disseminated and fungating; bone involvement is common, and lymph node involvement is rare. This form is most commonly observed in young, male, black Africans and may progress rapidly, demise often occurring quickly after the onset of symptoms. The third form presents in young black children to young adults (male:female ratio 3:1) as a generalized lymphadenopathy, usually without skin manifestations. Virtually all patients are dead within 3 years.

**C. Epidemic KD and its association with AIDS**

Since 1979 a new, heretofore, undescribed epidemic and fulminant form of KD has followed in the wake of a similarly novel disease process known as the acquired immunodeficiency syndrome (AIDS). By the end of 1985, 16,000 cases of AIDS are expected to occur in the US, and since over 50% of AIDS patients develop KD, this new epidemic of KD totally eclipses the incidence of the classical variant.

Since 1979 the following highly pertinent observations have been made with respect to these two apparently new diseases (AIDS and epidemic KD):

1. 90% of patients with epidemic Kaposi's disease (EKD) are homosexual males who concurrently have the AIDS syndrome.
2. 90% of AIDS patients are male homosexuals. The remainder are parenteral drug users, blood recipients, and heterosexual contacts of AIDS patients. Less than three percent are none of the above.
3. 48% of males with AIDS develop EKD.
4. Most patients also have past histories of multiple, recurrent, sexually transmitted diseases.
5. EKD is characterized by disseminated lesions at the onset of the illness including skin, lymph nodes, gastrointestinal tract, lung, liver and spleen.
6. Patients with EKD either die of opportunistic infections caused by the marked immunosuppression of AIDS or of severe fulminant KD.
7. Most patients with EKD have a high CMV titer.
8. CMV is the only agent which has been consistently identified from the cells of EKD. Identification techniques have included detection of CMV genetic material, CMV related antigens in the nuclei of KD cells, and CMV viral particles in cell lines cultured from KD.
9. AIDS patients are at extremely high risk for developing epidemic KD and one or more severe to fatal opportunistic infections, particularly pneumocystis carinii pneumonia.
10. AIDS patients have an increased risk of developing non-Hodgkins lymphomas and carcinoma of the oropharynx and ano-rectum.
11. AIDS patients demonstrate a severe immunologic dysfunction due to selective destruction of the OKT4+(helper, thymic derived) lymphocytes. The selective destruction of this important arm of the immune system results in a markedly diminished function of monocytes, decreased cellular immunity, susceptibility to numerous infectious agents which depend upon cellular immunity as the major line of defense.
12. The etiological agent of AIDS is now known to be due to a human T-cell leukemia virus (HTLV-III). In order to cultivate large amounts of
the virus for the production of diagnostic antibody test and eventually for the production of a vaccine, it was necessary to grow the virus in cells which did not lyse as easily as did normal OKT4+ cells. For this purpose Popovic et al. in 1984 developed an ingenious solution, namely, by finding an appropriate cancerous human T-cell leukemic cell line. Some of the clones resisted the severe cytolysis of benign OKT4+ cell lines, and HTLV-III could be cultured in a continuous fashion!

HISTOLOGY OF KAPOSI'S DISEASE

Early Lesions. Virtually all of the variants of KD show basic histologic similarities. The earliest lesion is characterized by an irregular proliferation of dilated, thin walled vessels lined by flattened endothelial cells, and a sparse proliferation of slightly atypical, perivascular, mesenchymal spindle cells. The variable features include: sparse accumulations of plasma cells, extravasated red blood cells, erythrophagocytosis, hemosiderin and pink globules within the cytoplasm of the endothelial and surrounding spindle cells. This latter feature is a useful diagnostic clue, if present, since the remainder of the features are rather non-nondescript and can be simulated by stasis dermatitis, dermatofibroma, and diaper rash.15 Such lesions are extremely difficult for the pathologist to recognize without clinical suspicion due to the innocuous histological appearance and total lack of anaplastic features.

Mid to Late Stages. In these stages the number of spindle cells increases dramatically and are generally arranged in fascicles. The slit-like vascular spaces usually diminish in prominence. The variable features are similar to the early lesions except for increased amounts of each. Again, despite a marked increase in cellularity and nuclear plumpness, the features of unequivocal anaplasia (marked pleomorphism of nuclei, atypical mitoses, and the like) are not seen, with rare exception. These rare anaplastic variants of KD are usually only seen in the classic form of the disease. Many years after the inception of symptoms and signs of Kaposi's disease a single lesion may enlarge much more rapidly than the other lesions, frequently will necrose and develop histologic evidence of a frank spindle cell sarcoma, difficult to distinguish from a high grade angiosarcoma or fibrosarcoma. When this event occurs the patient usually succumbs to classical sarcomatous metastases to lungs and other systems and dies within two years.

DISCUSSION

Given the above considerations and known facts which pertain to Kaposi's disease the discussion will first concentrate on those issues, which in this author's opinion, throw serious doubt on the proposition that the disease is a sarcomatous condition.

A. Inconsistencies in the concept of Kaposi's disease as a sarcoma which date back to over a century ago.

Kaposi began his paper by praising Köbner for his introduction of the concept of sarcomas of the skin. Kaposi then refers to the two cases of skin "sarcomas" which Köbner had published three years before in the following manner:

"In the first case, a large number of sarcomas of the skin had occurred as metastases, probably originating from the lymph glands in the inguinal region; in the second, the general sarcomatosis had originated from a nevus of the left index finger that had existed since childhood and had undergone primary transformation into a pigmented spindle cell sarcoma. Both patients died in three years".

Kaposi then justifies the use of the word sarcoma in relation to his five cases by stating the following:

"I believe that one type of pigmented sarcoma of the skin can be differentiated as a typically clinical form
from those which, under all circumstances, originate as consecutive (metastatic) eruptions and consequently can develop from the most varied primary foci, and of which the cases cited by Köbner are examples. I shall therefore call the form that will be described in this article an idiopathic multiple pigmented sarcoma of the skin.

Having the advantage of 114 years of hindsight the problems with the thesis that the entity described by Kaposi is indeed a sarcoma from an historical perspective runs into the following problems:

1. The two cases described by Köbner from which Kaposi borrowed the concept of the term sarcoma of skin, by present day terminology, would no longer be designated as such. Köbner's second case is an indisputable example of a malignant melanoma arising from a nevus, which dated back to childhood; while the first case is in all likelihood a disseminated lymphoma to skin beginning in the inguinal lymph nodes. Although both of Köbner's cases were malignant, these examples serve to demonstrate the primitive nature of cancer terminology in Kaposi's day, and the fact that the very foundation of the term sarcoma employed by Kaposi is no longer valid in a strict terminological sense today.

2. It is apparent from a reading of Kaposi's article that the parameters which determined his view that the entity was cancerous (sarcomatous) were based almost exclusively on clinical not histological considerations; the tumorous lesions were progressive, incurable, idiopathic, and could lead to death. Although such clinical features could certainly represent a cancerous process even in the modern sense of the term, by no means are these parameters by themselves pathognomonic of cancer, and therefore cannot serve as proof of Kaposi's thesis. Many entities exist which are progressive, incurable, idiopathic, and can lead to death, yet we do not presume to classify them as cancers. To name just a few: disseminated eosinophilic granuloma (Letterer-Siwe disease); systemic hemangiomatosis, lymphangiomatosis, and congenital fibromatosis with extensive visceral involvement; midline lethal granuloma, etc.

3. Kaposi's histological description of the entity is in parts vague and dated, but more importantly entirely unconvincing, by present day standards, at least, for the diagnosis of a sarcoma:

"In the meantime I had excised two nodules that were evidently of different ages and recognized by microscopic examination that they were parvicular sarcomas whose cell inclusions were present in piles and foci. At some points the symptoms of small hemorrhages in the corium or the papillae could be observed. There were also large quantities of pigment, yellow-brown to black, mostly isolated outside the cells."

4. It is pertinent to be aware that pathology in 1872 was in its very early infancy. The father of pathology, Rudolf Virchow, whose monumental book entitled 'Cellular Pathology had only been published in German in 1858 and in English in 1860.23 Since Kaposi had written his article in 1872, and had received his training in dermatology not pathology, he could only have possessed the most rudimentary notions of a discipline which had just begun to emerge as a science. The tremendously important concept of anaplasia had not as yet even arrived on the scene. According to James Ewing's account of the history of the estimation of malignancy by microscopic endeavors the term anaplasia was first introduced by Hansenmann between 1890 and 1897, at least 18 years after Kaposi's article.

Anaplasia is the pathologists principal method of determining whether a lesion is cancerous or not. Anaplasia can be defined as those cytologic aberrations of nucleus and cytoplasm which enable the pathologist to recognize cancer.
B. Evolution of the word sarcoma since Kaposi's time.

The modern pathologic definition of the word sarcoma is essentially that of a cancer derived from cells of the connective tissues which includes endothelial, fat, nerve, bone, cartilage, fibroblast, histiocytic, and notochordal cells. Thus, if Kaposi's disease were a cancer derived from endothelial cells it would be a variant of angiosarcoma.

The word sarcoma has evolved dramatically in the last 100 years. The word sarcoma is derived from the Greek word sarcos meaning flesh. Before tumors (neoplasms) were classified according to cell of origin (histogenesis), gross morphology or appearance was one of the standards of classification. Thus, a sarcoma originally referred to an exuberant fleshy (connective tissue-like) growth. Virchow believed the word sarcoma should be more specifically applied to benign and malignant growths of connective tissue. Obviously, the meaning of the word has changed considerably since Virchow's early use of the term. Its meaning is now restricted to cancerous growths of the connective tissues. In Virchow's and Kaposi's time the distinction between cancer and fatal noncancerous conditions were unclear, terms and concepts such as anaplasia which we now take for granted had not as yet even been conceived.

C. Kaposi's disease from a modern perspective.

As should be clear from the prior discussion, great strides have been made over the last 100 years in the evolution of our concepts concerning cancer, sarcoma, neoplasia, and other related terms. Scientific knowledge does not stand still; there is always room for greater in depth understanding, and differing viewpoints from those of our predecessors. Let us, at least momentarily, put aside the dogma that Kaposi's disease is a sarcoma and examine the entity afresh in the light of the last 114 years of discoveries.

We shall begin by comparing most of the present day known features which characterize irrefutable soft tissue sarcomas versus those of Kaposi's "sarcoma" (refer to table 1 including Figures 1-4). After perusing this table and figures it should be evident that there is something quite amiss with the supposition that Kaposi's disease is a sarcoma. The discrepancies between Kaposi's disease and bone fide sarcomas with respect to their clinical, histological, necropsy, and laboratory features are so antithetical, that Kaposi's original thesis suffers from lack of factual support. Those quite rare, chronic forms of classical KD which develop a rapidly growing, solitary mass which demonstrates clear-cut cytologic anaplasia represents transformation of a formerly benign process into a true sarcoma. Such isolated examples should not detract from the view that the majority of Kaposi's lesions are noncancerous.

Cox and Helwig, two prominent experts in dermatopathology, were perhaps the first to realize that Kaposi's entity was not a true sarcoma (refer back to the 1959 quote near the beginning of this paper.) But some 36 years later most investigators still harbor the notion that Kaposi's disease is a sarcoma. Reynolds, also an expert in dermatopathology, and Soule, a World renowned soft tissue tumor pathologist, both Mayo Clinic physicians, declared in 1965, that Kaposi's sarcoma should not be considered a sarcoma. The latest plea, in the form of a letter to the editor of Lancet, that Kaposi's is not a sarcoma, was from two pathologists from the National Cancer Institute, Costa and Rabson. The pattern is consistent, every 5-10 years pathologists of renown are opposed to the view that Kaposi's disease is a sarcoma at all. But, who better than the pathologist, considering his vast experience with cancers of every type, should best know what is or is not a true cancer? Does not the clinician rely on the pathologist for the diagnosis of malignancy in virtually every patient he or she desires to treat? Let us reexamine, from a modern perspective, important
questions which relate to Kaposi’s disease such as:

1. What is the histogenesis of Kaposi’s disease?
2. What is the etiology of the disease?
3. What is its pathogenesis?
4. Is it be possible to develop a specific cure?

1. Histogenesis.

By light microscopy, the earliest lesion is characterized by slit-like vascular spaces, endothelial cells and what appears to be a spindle cell proliferation emanating from the endothelial cell lining, usually in association with minute foci of hemorrhage and hemosiderin pigment. These observations, as numerous observers before have stated, support the view that the basic lesion is one of vascular or endothelial origin. This view is even more strongly supported by electron microscopic and immunohistochemical stains. At least two recent papers dealing with the electron microscopy of KD not only support origin of the cells from endothelium, but more specifically from cells of the lymphatic endothelium.25, 26 In the former paper a number of cases of KD with an aggressive course showed individual endothelial cell necrosis. This finding of individual endothelial cell cytolysis is significant in that it could be an ultramicroscopic clue to an intracellular viral infection. Herpes simplex is, of course, one of the most potent of the cytopathic viruses, but, also is HTLV-III, which is cytopathic to CD4+ helper T-cells. These EM findings also support the observation that if one studies lymph nodes from AIDS patients who have also developed epidemic KD that the earliest changes of KD are identical to the subcutaneous lesion except for its anatomical location. Early lymph node involvement, for example, appears histologically identical to the incipient, cutaneous lesion, except that it begins in the lymphatic pericapsular sinusoids eventually replacing the normal lymphatic sinusoidal system; in the process stimulating a reactive fibrosis and thickening of the capsule. From the capsular sinusoids the process invades the deep lymph node sinusoidal system in advanced stages occasionally leading to total obliteration of lymph node architecture. However, prior to complete obliteration of lymph node architecture, it is possible to diagnose not only Kaposi’s disease but AIDS as well. For if one examines the lymph node under low power examination, the severe depletion of lymphocytes in the parafollicular and paracortical areas reflects the loss of helper T-cells allowing the histologic diagnosis of concomitant AIDS. The combination of Kaposi’s involvement of the lymph node(s) in association with a T-cell depletion is virtually pathognomonic of the epidemic form of KD which, of course, follows in the wake of AIDS.

2. Etiology.

At present, the only documented source which holds some promise with respect to the etiology of KD is CMV, or more likely, some mutant strain of virus having many of the antigenic determinants of classic or conventional CMV. Several investigators have noted the association of CMV antigens not only within the serum of most patients, but much more significantly within the lesional tissue of the disease.27, 28, 29 No other viral agent has been found with such consistency. As a general axiom, whatever disease is consistently associated with a particular or single agent is often shown, eventually, to be caused by that agent. In AIDS, for example, HTLV-III virus or its antigens was found consistently. Within just a few short years of laboratory investigation, HTLV-III has been conclusively shown to be the etiologic agent of AIDS by the satisfying of Koch’s postulates.30 As was stated earlier in this paper the key to the solution of the problem of etiology was the conception and careful investigation by Popovic, Gallo et al to breed the virus in quantity by finding a malignant T-cell line which the virus found to be an hospitable host in vitro. Obviously, this virus is quite fastidious in that it seems to find helper T-cells, normal and malignant, the most
suitable environment in which to proliferate. This could be referred to as helper T-cell tropism. We will return to the significance of this discovery under potential cure of Kaposi's disease.

3. Pathogenesis.

The pathogenetic scheme which we offer which is consonant with the known phenomena of Kaposi's disease is as follows:

A. The first event is the development of a state of immune deficiency within the host. If the patients develop a relatively moderate state of immune deficiency on the basis of aging, or senescence of the immune system, as can occur in the elderly, or immune deficiency induced by massive steroid therapy and other potent immunosuppressive drugs, they are prone to the classical form of Kaposi's disease. If the immune system is even more gravely damaged, as occurs in the AIDS syndrome due to selective destruction of the OKT4 T-helper cells with its concomitant derangement of the monocyte line of defense, these patients are at tremendously high risk for developing epidemic KD. The endemic form of KD is, perhaps, due to a similar immunosuppressive disorder, induced either on the basis of malnutrition and/or viral or other serious infections indigenous to the regions of Africa in which this form of KD is rampant.

As a result the host is now vulnerable to particular organisms in the environment of formerly low grade pathogenicity, due to the serious depletion of the T-helper-monocyte system which under normal conditions would easily have held such organisms in check.

B. The next step is the invasion of the host by organisms normally handled by the T-helper cell-monocyte arm of the immune system. One of these agents, we believe, is responsible for the development of KD, probably a virus which infects endothelial cells, particularly those of the small lymphatic vessels (lymphangiotropism).

The lymphatic endothelial cell infection can be systemic, but in the classical variant, at least, has a propensity for cutaneous and subcutaneous vessels.

C. The next step is injury and stimulation of endothelial cell growth (hyperplasia). This circumstance results in the development of maculo-papular lesions in examples of cutaneous involvement.

D. The next step is injury to capillaries with hemorrhage. If the local capillary endothelium is also infected, or if the local capillary integrity is disturbed as a secondary phenomenon by the locally aggressive lymphendothelial cell proliferation, the result is the production of minute capillary hemorrhages in the early lesions, and more severe hemorrhagic episodes in more fully developed lesions. The pigmented nature of KD lesions can, as Kaposi realized, thus, be explained on the basis of the vascularity of the lesions, hemorrhage and resultant hemosiderin production.

Continued angioblastic proliferation results in plaques and nodular to nodulo-ulcerative lesions, whatever the organ of involvement.

Involvement of visceral lymphatic endothelium would account for the sinusoidal distribution seen in the lymph nodes which begins in the capsular sinusoids, and, as well the distribution of lesions within the lungs (peribronchiolar lymphatics), liver (lymphatics of the portal triads), etc. The brain does not have a lymphatic system, or at most, a very attenuated one as compared to other organ systems. For this reason the brain is rarely, if ever, involved by the characteristic Kaposi lesion.

In the classical form of the disease death is either from unrelated
causes, or, if related, by massive internal hemorrhage due to the involvement of the vascular system (similar events occur in systemic hemangiomatosis), or from deadly opportunistic infections. Those KD patients who survive for 10 or more years with the disease may develop a single true angiosarcomatous lesion by malignant transformation of the atypical, angioblastic hyperplasia, or they may develop secondary cancers on the basis of a defect in immune surveillance. Patients with AIDS and KD die much more quickly than the majority of those with classical KD due to their much more grave disruption of the immune system. Most die of opportunistic infections; others die of secondary cancers by a similar mechanism to that described above. Endemic KD behaves in an intermediate fashion except in children, implying also a very serious disruption of the immune system by means of factors not well understood.

If this pathogenetic scheme is substantially correct then Kaposi's disease can be essentially defined as follows: Kaposi's disease is a multicentric, atypical, (lymph)angioblastic hyperplasia induced by an (lymph)angiotropic strain of virus within immunocompromised hosts.

4. Is Kaposi's disease curable?

If the above thesis is correct then Kaposi's disease is potentially curable. The vast majority of cases in the US are related to AIDS. This form should disappear when a specific vaccine to HTLV-III virus is obtained. The other forms of KD could be prevented by means of developing vaccines to the culprit strain(s) of virus. This could, perhaps, be achieved by employing a similar approach to that of Popovic et al. by attempting to grow the suspect virus in an appropriate malignant vascular cell line. Perhaps, the best cell line to try obtain would be from the lymphangiosarcoma of Stuart-Treves also known as the postmastectomy lymphangiosarcoma. Angiosarcoma cell lines might also be appropriate to try. If an etiologic agent can be grown in quantity in such a system a vaccine should be possible to produce. Individuals at high risk for the development of KD should be the recipients of such a vaccine including: patients on high chronic high dose steroids or other immunosuppressive drugs; the elderly who have developed signs of immunosuppression; and the endemic African population.

In final summary, we propose that the eponym Kaposi's sarcoma be changed forthwith to Kaposi's disease, and research efforts be redirected to the etiology and cure for a noncancerous, although admittedly, severe affliction, probably caused by a virus, rather than as is now being directed to the study of a cancerous or sarcomatous process.
Table 1. The clinico-pathologic characteristics of Kaposi’s Sarcoma as compared to indubitable sarcomas

<table>
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<tr>
<th>CLINICAL FEATURES</th>
<th>KAPOSI’S <em>SARCOMA</em></th>
<th>INDUBITABLE SARCOMAS</th>
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<tbody>
<tr>
<td>1. Usually begins in subcutaneous tissues.</td>
<td>Usual</td>
<td>Rare</td>
</tr>
<tr>
<td>2. Multiplicity of lesions from onset.</td>
<td>Usual</td>
<td>Rare</td>
</tr>
<tr>
<td>3. Begins as flat maculopapular lesions.</td>
<td>Usual (Fig 1)</td>
<td>Rare, if ever</td>
</tr>
<tr>
<td>4. New lesions may develop in crops.</td>
<td>Common</td>
<td>Never</td>
</tr>
<tr>
<td>5. Individual lesions may regress spontaneously.</td>
<td>Common</td>
<td>Rare, if ever</td>
</tr>
<tr>
<td>6. The lesion(s) spread similarly to an angiomatos lesion like a hemangioma or lymphangiomia.</td>
<td>Almost always (Fig 1)</td>
<td>Never</td>
</tr>
<tr>
<td>7. Begins as a solitary lesion which, if near the skin, rapidly becomes nodular-ulcerative.</td>
<td>Never</td>
<td>Usual (Fig 2A)</td>
</tr>
<tr>
<td>8. The lesion(s) destroys all anatomic structures in its path, including bone, in a cancerous fashion.</td>
<td>Rare</td>
<td>Always (Fig 2B)</td>
</tr>
<tr>
<td>9. Can spread in epidemic manner.</td>
<td>Epidemic KD</td>
<td>Never</td>
</tr>
<tr>
<td>11. Associated with immunosuppression.</td>
<td>Usual</td>
<td>Rare, if ever</td>
</tr>
<tr>
<td>12. Lesions can be induced by massive steroid therapy.</td>
<td>Reported association31, 32, 33, 34</td>
<td>No known association</td>
</tr>
<tr>
<td>13. Lesions may regress upon withdrawal of steroid therapy.</td>
<td>Reported association31</td>
<td>No known association</td>
</tr>
<tr>
<td>14. Visceral lesions characterized by minimal clinical symptomatology.</td>
<td>Usual (Fig 4)</td>
<td>Rare</td>
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<tr>
<th>PATHOLOGICAL FEATURES</th>
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<tbody>
<tr>
<td>1. Clear-cut anaplasia (nuclear pleomorphism, atypical mitoses, etc.)</td>
<td>Rare (Fig 3)</td>
<td>Usual (Fig 4)</td>
</tr>
<tr>
<td>3. At autopsy death clearly due to classic “cannonball” metastases.</td>
<td>Rare</td>
<td>Usual</td>
</tr>
<tr>
<td>4. At autopsy death due to opportunistic infection or visceral hemorrhage.</td>
<td>Usual</td>
<td>Rare</td>
</tr>
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<tr>
<th>SPECIAL STUDIES</th>
<th>Common</th>
<th>Rare</th>
</tr>
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<tbody>
<tr>
<td>1. Commonly associated with a specific viral antigen such as CMV within the lesion.</td>
<td>Rare, if ever</td>
<td>Common</td>
</tr>
<tr>
<td>2. Possible to serially culture lesional cells indefinitely.</td>
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Figure 1. Kaposi's disease (KD) of the Foot. This is a typical example of KD of the foot in a patient with AIDS. The lesions are multiple, dark red, maculo-papular, and spread in a benign, angiomata-like manner.

Figure 2. Angiosarcoma of the Foot. A. This example shows the typical features of an angiosarcoma. It is a solitary, large, fleshy, dark red to tan, nodulo-ulcerative mass. B. On cut section the tumor has destroyed all of the structures in its path including the joint cartilages and bones of the foot, as would be expected in a truly cancerous process.

Figure 3. Histology of Kaposi's Disease. A. This view shows the typical features of KD, which consist of thin slits lined by one or more layers of endothelial cells. The cells do not form cohesive clusters nor do they shed into the lumina. The slits most closely resemble those of the lymphatics by light and ultramicroscopy, and as confirmed by immunological studies. (H&E X250) B. High power view showing the bland nature of the nuclear morphology. Chromatin is evenly dispersed, nuclei are regular in size and shape, nucleoli are small to absent, and mitoses are rare to occasional and always typical (mirror images). (H&E X1000).

Figure 4. Histology of Angiosarcoma or Lymphangiosarcoma. A. This field shows the typical moderate power features of a truly malignant vascular lesion, namely, spaces, lined by cells which form cell clusters some of which shed into the lumen. In addition, there is individual cell shedding, another hallmark of cancerous vascular lesions. Note also the general disorganization of the cells as compared to the much more organized features seen in KD (Fig 3A) (H&E X250) B. As important as the above lower power features are to the recognition of a vascular malignancy the cells show the classic features of anaplasia, namely, marked variation in the size and shape of the nuclei, hyperchromatism, abnormal chromatin clumping, prominent nucleoli, and voluminous cytoplasm also quite variable in size and shape. In other fields not displayed here there were numerous mitoses, many of which were atypical or non-mirror images. (H&E X1000)
REFERENCES

25. McNutt NS, Fletcher V, and Conant: Early lesions of Kaposi's sarcoma