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RESEARCH ARTICLE

CASE REPORT OF AN EPITHELIOID VARIANT OF KAPOSI SARCOMA: A RARE "MIMIC" OF ANGIOSARCOMA

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Abstract

Cutaneous Kaposi sarcoma (KS) is a vascular neoplasm with a broad spectrumclinicopathology. An epithelioid morphology, a rare recent variant of KS, with many variants of KS that may mimic other vascular neoplasms poses a diagnostic challenge. We report on a 75-year-old Saudi man HIV- negative who had been diagnosed with classical KS on the right foot 8 years before the present episode. Histopathological findings of the new lesion included areas showing epithelioid cells with moderate pleomorphism, growing in solid sheets. The epithelioid cells show nuclear enlargement and hyperchromasia mimicking angiosarcoma. Immunohistochemistry shows a strong diffuse nuclear staining pattern for HHV-8 latent nuclear antigen-1 (LNA-1) in the epithelioid as well as the classical spindle cells. A diagnosis of epithelioid Kaposi sarcoma is made, which should be included within the known histological variants of KS. Prior to this case, the epithelioid variant of Kaposi sarcoma has been reported only three times in the literature. Since this variant shares similar clinical and histological features with angiosarcoma, integration of clinical findings and context, histopathologic features and immunohistochemical results is critical in obtaining the correct diagnosis and treatment.

Introduction:-

Moritz Kaposi initially defined Kaposi sarcoma (KS) as "idiopathic numerous pigmented sarcoma of the skin" in a medical literature study in 1872 (1). Herpesvirus-8 (HHV-8)is now proved as the main etiological agent of Kaposi's sarcoma (KS)that is frequently linked to immunocompromised patients. In terms of clinical presentation and histopathologic characteristics, the disease displays a wide range of clinical behavior. Moreover, KS is classified clinically into four subtypes: classic (sporadic), endemic (African), iatrogenic (immunosuppression-related), and epidemic (HIV-associated) (2). On the contrary, different histological patterns of Kaposi sarcoma have been reported in the literature. However, we report a case withan epithelioid variant, a rare histopathological variant that has only been reported three times so far, and which might be a diagnostic challenge for histopathologists.

Case Report

A 75-year-old Saudi male known case of HIV- negative Kaposi sarcoma since 2013 with cutaneous manifestation predominantly over the right foot.He presents to the medical oncology clinic with a painless lesion at the lateral aspect of the right foot (Figure 1 & 2). The patient noticed that the lesion is growing in size.

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On examination, a fungating soft non-tendermass is seen over the lateral aspect of the right foot measuring 5 x 4 cm. The mass is surrounded by erythema and hyperpigmented edematous skin up to the mid-leg level associated with a scant amount of foul-smelling purulent discharge.

The patient received radiation therapy confined to the lower extremities in 2013 as well as he received multiple chemotherapy cycles of Doxorubicin, Vinblastine, and Paclitaxel over the course of four years.

MRI revealed an infiltrating cutaneous soft tissue mass within the lateral aspect of the midfoot with an extension about 0.6 cm deep and abutting the distal base of the fifth metatarsal bone and abductor digiti minimi. The lesion intermediate signals on T1 and fluid sensitive sequences with post-contrast enhancement (Figure 3).The lesion is excised and sent for a histopathology examination. Grossly, the lesion exhibits purple to red nodules with a hemorrhagic cut surface (Figure 4).Histological examination shows nodular proliferation of atypical epithelioid and spindle cells with vascular differentiation (Figures 6). The epithelioid cells exhibit nuclear enlargement and hyperchromasia mimicking angiosarcoma (Figures 5). At the periphery of this tumor, the dermis shows classic features of patch stage Kaposi sarcoma i.e. bland-looking spindle cells and blood vessels dissecting between the collagen bundles in the reticular dermis. Upon immunohistochemistry, both epithelioid and spindled tumor cells components are positive for CD31 and HHV-8 (Figure 5). These histopathologic and Immunohistochemistry findings are consistent with Kaposi sarcoma, epithelioid, and classical variants.

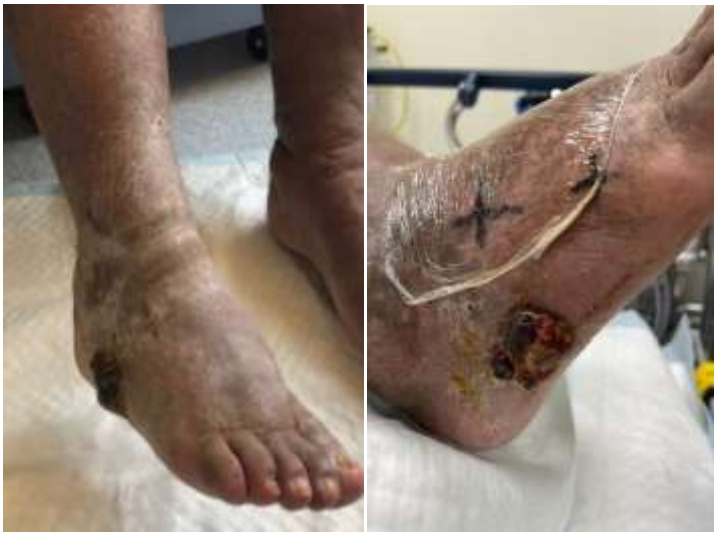


Figure 1 &2:- Right foot fungating mass with ulcer.

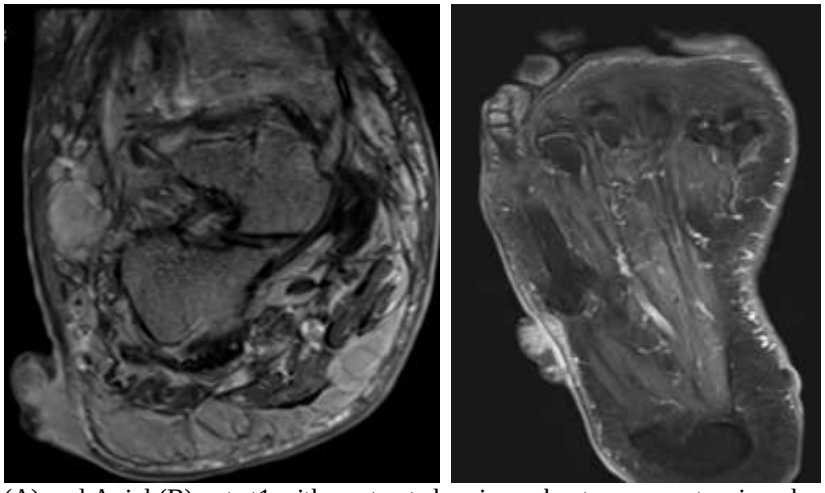
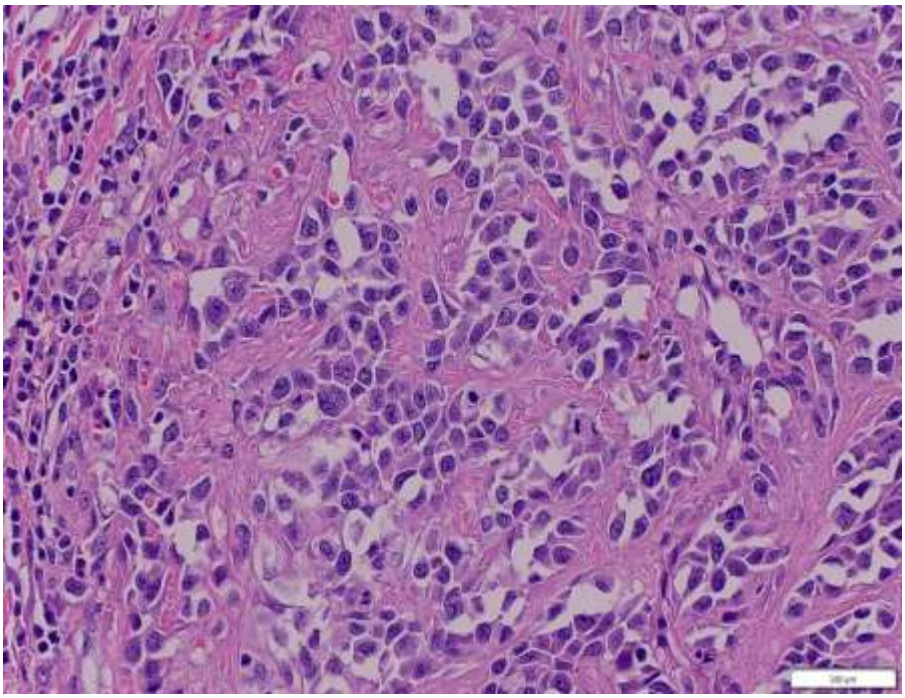


Figure 3:- Coronal (A) and Axial (B) cuts t1 with contrast showing subcutaneous extension about 0.6 cm deep with diffuse interstitial subcutaneous edema.

Figure 4:- Grossly, the lesion has purple nodules with hemorrhagic cut surface.



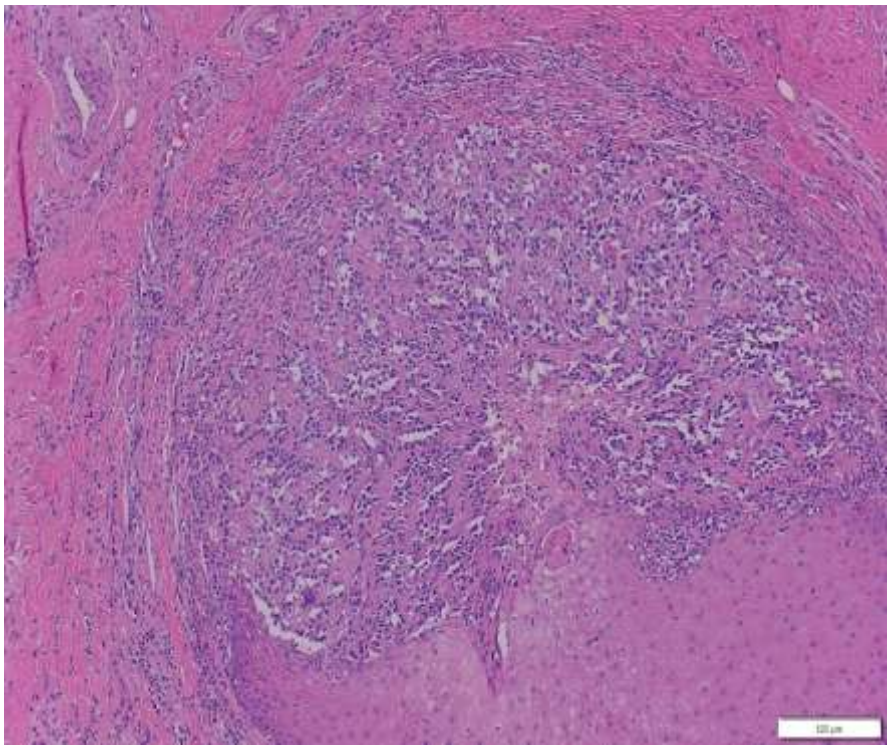
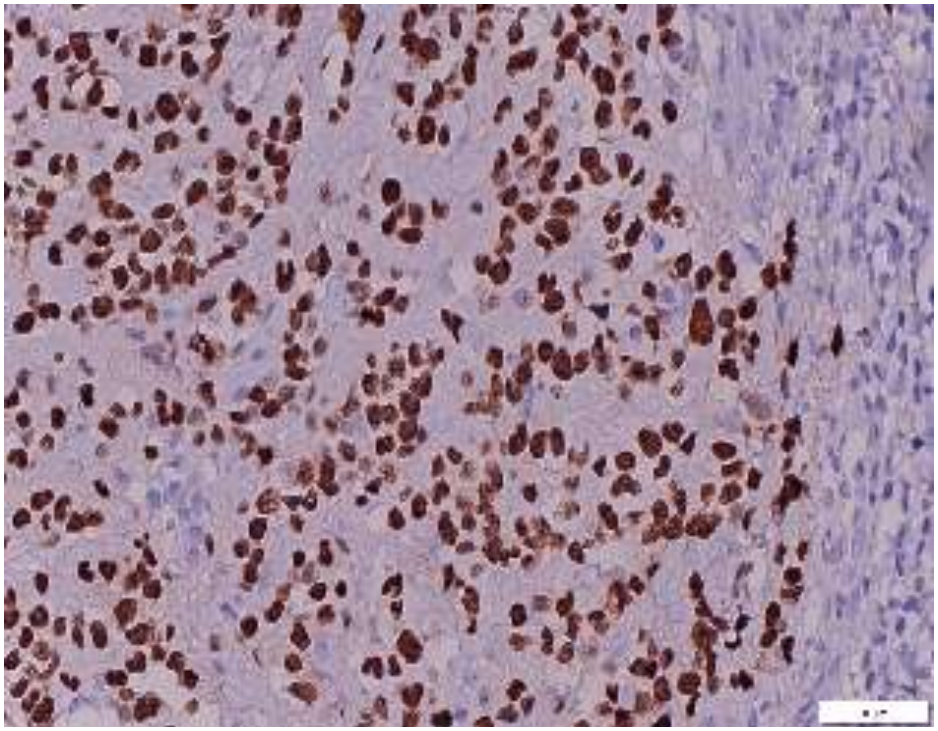


Figure 5:- (A) Epithelioid variant of KS, H&E stain showing a sheets and nests of pleomorphic cells with an epithelioid pattern (X100), (B) Higher power shows highly atypical epithelioid neoplastic cells with numerous mitotic figures, plasma cells and extrvasated RBCs (X400). The histological features are mimic angiosarcoma. IHC shows a diffuse nuclear staining of the neoplastic cells for HHV8 (LANA1).



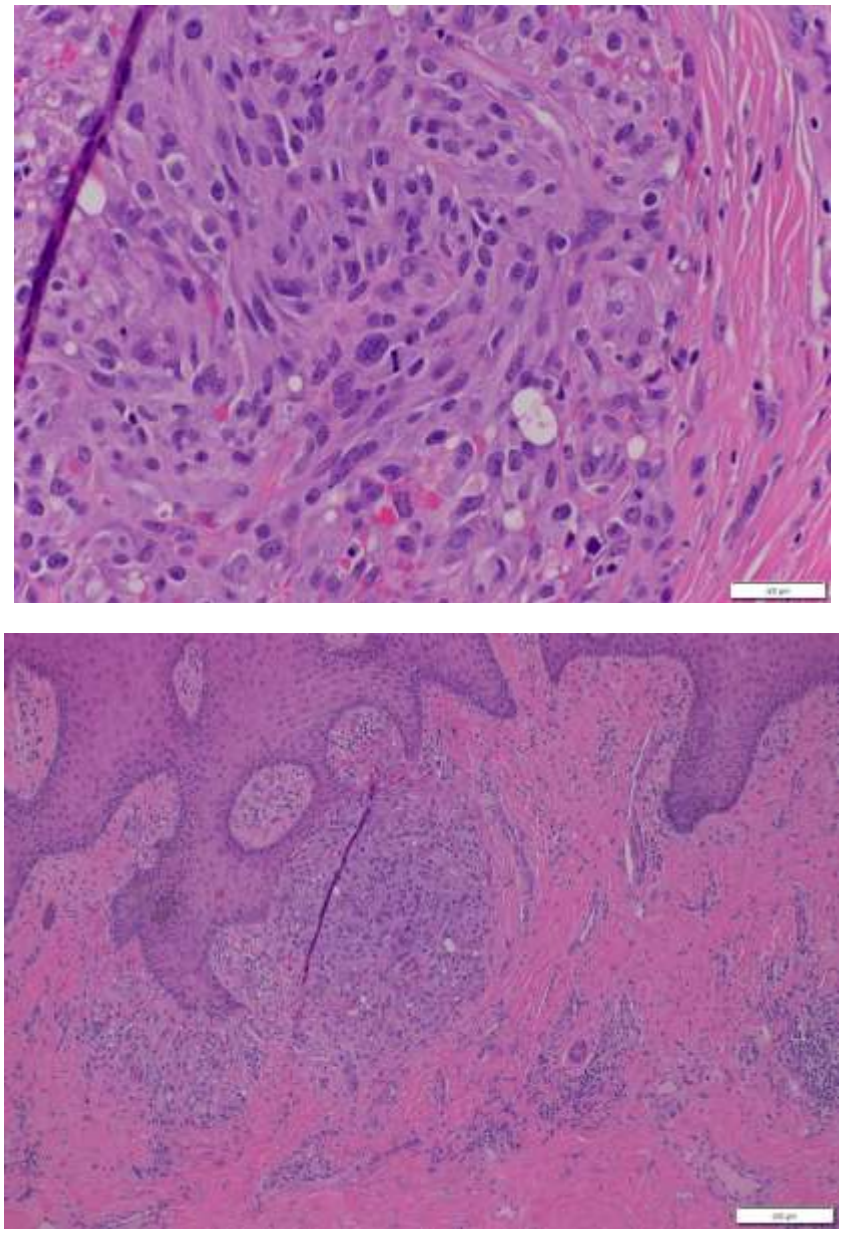


Figure 6:- (A) & (B) Tumor stage of KS, H&E stain showing nodules composed of intersecting fascicles of spindle cells with intracytoplasmic hyaline globules and numerous mitotic figures.

Discussion:-

The histological presentation of the various subtypes of Kaposi sarcomas tends to be relatively similar. The disease progress through three phases histologically: patch, plaque, and tumor (nodular).However, the patient might be present with more than one stage simultaneously (3). Early lesion (patch stage) of cutaneous Kaposi sarcomatypically has subtle features (especially at low power) including dilated vascular channels dissecting through collagen dermis with extravasated RBCs and hemosiderin deposition. This morphology might mimic stasis dermatitis or Acroangiodermatitis (pseudo-Kaposi sarcoma) (4). With no intervention, the lesion evolves from the patch into the plaque stage that shows more spindle cell proliferation with lymphoplasmacytic infiltration in addition to the aforementioned features of the patch phase.Ultimately,the tumor stage is characterized by discrete nodules composed of intersecting fascicles of relatively uniform spindle cells with intracytoplasmic hyaline globules and numerous mitotic figures.

In addition, various Kaposi sarcoma histological patterns have been well reported in the literature review, including lymphangioma-like, telangiectatic, ecchymosis, glomeruloid, intravascular, hyperkeratotic, keloidal, micronodular, pyogenic granuloma-like, Kaposi sarcoma "in-situ"and anaplastic pleomorphic variants (5).It's worth noting that some variants are linked with specific clinical symptomsor as a consequence of specific medication, but the histogenesis of others is unknown or uncertain. For instance, Intravascular KS, could either originate primarily as an intravascular proliferation or develop as a result of the intravascular extension of a lesion breaching the vessel wall. On the contrary, Hyperkeratotic KS is developed in patients with chronic lymphedema of the lower extremities. Meanwhile, Anaplastic or pleomorphic KS has an adverse prognosis and exhibits a wide range of morphologies with nuclear atypia, mitosis, and a high mitotic index (5-20/hpf).

A wide variety of variants and morphology make KS a great mimicker and consequently has a diagnostic dilemmafor pathologists. Utilizing the ancillary studiesand clinical information with recognizing the different histological variants can lead to a definite diagnosis and treatment. The epithelioid variant is a rare recent histological variant documented in the literature (6). Only three cases of KS with an epithelioid form were found in the literature review (Table 1) (6,7 & 8). According to Kaitlyn M. Yim, who reported the third case, argued that the tumor cells transformed convert into the epithelioid as a result of chronicity or untreated disease (7). Microscopically, it shows nests and sheets of plump pleomorphic cells with extravasated RBCs, numerous mitotic figures, and scattered plasma cells.In such a case, several epithelioid vascular neoplasms would be included in the differential diagnosis including cutaneous epithelioid angiosarcoma, epithelioid hemangioendothelioma, and epithelioid hemangioma.The distinction between such entities is critical, and misdiagnosis or a delay in diagnosis can be fatal.It is crucial to keep in your mind the distinct clinicopathology features of these entities especially angiosarcoma (Table2).

Our patient is a known case of KS for almost 9 years presents with the same epithelioid morphology. It has been noticed that all the reported cases including our case known to have long-term KS and they received almost the same kind of treatment. Given that the epithelioid morphology could be a result of long-standing or recurrentKS leading to an undifferentiated tumor. In addition, this kind of morphology might be also due to the treatment effect (chemotherapy). However, the epithelioid variant must be included within the known variants of KS to avoid misdiagnosis or delay in a proper intervention that may result in adverse consequences.

Table.1:- Clinicopathological features of reported cases of Epithelioid variant of Kaposi Sarcoma.

Study	Sex	Ethnicity	HIV/AIDS	Tumor location	Duration
Basra et al. (8) 2018	M	White	Yes	Disseminated (Leg, chest, back, and abdomen)	Since 2008 (13 years)
Alvarez P et al. (6) 2021	M	Hispanic	No	Both feet	2 years
Yim KM et al. (7) 2021	M	African-American	Yes	Both lower extremities	NM
Our case	M	White	No	Right foot	Since 2013 (9 years)

Abbreviations: M- Male, F- Female. NM- Not mentioned

Table.2:- Comparison of clinicopathologic features of the epithelioid variant of Angiosarcoma and Kaposi sarcoma.

	Epithelioid Angiosarcoma	Epithelioid Kaposi sarcoma
Etiology	Primary (idiopathic) and secondary to radiation and chronic lymphedema	Caused by Human herpesvirus-8(HHV-8) and often associated with HIV/AIDS

Preferntial sites	Usual arises in head/neck of sun damaged elderly or at site of irradiation.	Lower extremity skin
Distinct Histopathological features	Marked atypia and mitosis	The background of classic uniform spindle cells associated with different stages of the KS
Distinct IHC analysis	HHV8 (LANA1) negative	HHV8 (LANA1) positive

Abbreviations:
LANA1 (Latency Associated Nuclear Antigen).

Ethical Disclaimer
A written consent has been obtained from the patient for publication of this case report and accompanying images.

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