Kaposi Sarcoma in a Non-Immunocompromised Patient – A Potential Diagnostic Pitfall

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Summary

Introduction. Kaposi sarcoma is a rare soft tissue tumor that may form masses in the skin, lymph nodes, mucosa and many other organs. It has a strong male predilection and is usually seen in the older population. It is caused by human herpes virus 8. Risk factors include compromised immune system, typically seen in patients with human immunodeficiency virus infection or organ transplant recipients. Case Report. We report a 66-year-old Caucasian woman with no previous history of human immunodeficiency virus infection, immunosuppressive therapy or organ transplantation. She was referred to a plastic surgeon by a dermatologist due to a suspected dermatofibroma presenting with one solitary, firm nodule on the dorsal aspect of the foot that she reported to have occurred a year before. A surgery was scheduled in 6 months, as the tumor was assessed as benign. After excisional biopsy and histological evaluation without immunohistochemical staining, that was not available, a diagnosis of benign myofibroblastic tumor was made. Later on, a new similar tumor on the hand appeared and the diagnosis was changed into a malignant tumor. Further pathological examination, using immunohistochemical staining, confirmed Kaposi sarcoma. The malignant cells showed positive immunostaining for CD34, CD31, D2-40, WT1, bcl-2, and human herpes virus 8, but they were CD99 negative. Conclusion. Non-specific clinical presentation and absence of risk factors may mislead the doctors, delay the biopsy and thus delay adequate treatment. In the same time, histological similarities with other disorders and tumors may be challenging for pathologists and lead to wrong diagnosis. Key words: Sarcoma, Kaposi; Risk Factors; Dermatofibroma; Benign; Fibrous; Immunity; Diagnosis, Differential; Morphological and Microscopic Findings; Immunohistochemistry

Introducion

Kaposi sarcoma (KS) was first described by Moritz Kaposi in 1872, but it became well known in the 80’s leading to stigmatisation of persons with acquired immune deficiency syndrome (AIDS). It is a rare angioproliferative soft tissue tumor that can form masses in the skin, lymph nodes, mucosa and many other organs. KS has strong male predilection (in classic forms with a male to female ratio 17:1) and is usually seen in older population of Mediterranean origin [1]. It is caused by human herpes virus 8 (HHV-8) and it shows the distribution of this virus in the world. Risk factors include compromised im-
mune system, either as a result of a disease or some medication (iatrogenic form), typically seen in human immunodeficiency virus (HIV) patients or organ transplant recipients. Clinically, there are four subtypes of KS: classic, endemic, epidemic (HIV-related) and immunosuppressive therapy related. The classic form is most common in elderly men, localized on legs and has a slow progression. Endemic is seen in adult men and children in Africa and it can be aggressive with generalized lymph node involvement. Epidemic form occurs in people with AIDS and it usually affects many body parts. Immunosuppressive therapy related KS can be seen in transplant patients and usually involves the skin.

The diagnosis is made by tissue biopsy and the extent of disease can be assessed by different imaging procedures. The therapy depends on the extent of disease, subtype and immunological status of patients and can involve surgery, local radiotherapy and in widespread forms biologic therapy and chemotherapy. The most aggressive anaplastic forms of KS may have a fatal outcome.

Case Report

We report a 66-year-old Caucasian woman with no previous history of HIV infection, immunosuppressive therapy or organ transplantation. She was referred to a plastic surgeon by a dermatologist due to a suspected dermatofibroma of the skin presenting as a solitary, firm, non-tender nodule on the dorsal aspect of the left foot that she reported to have for a year. Without specific medical history and no specific clinical presentation, KS was not considered as differential diagnosis and the surgeon agreed with the dermatologist’s on clinical diagnosis of dermatofibroma. The tumor was a 5 mm nodule of pinkish-brown color with smooth surface and firm consistency (Figure 1). The patient was scheduled for surgery in 6 months, since clinically the tumor was assessed as benign. After excisional biopsy, standard hematoxylin-eosin staining was performed and histological evaluation was done. The pathologist described a small tumor situated in the mid dermis, composed of fascicles of spindle cells, with small number of blood vessels. There was no cytological atypia or tumor necrosis, only a few mitoses, so the lesion was diagnosed as myofibroblastic tumor (Figure 2). Immunohistochemical analysis was not available at that moment. One year later, the patient presented with a recurrent tumor similar to the previous one, on the dorsum of her hand. We performed an excisional biopsy of both tumors. The tumors were CD34 and bcl-2 positive, with some mitotic figures, affecting two separate body parts (foot and hand), so the diagnosis of solitary fibrous tumor was made, presuming that it must be considered as malignant (Figures 3 and 4). In the meantime, the patient developed multiple nodules on both feet in a short pe-

**Abbreviations**

KS – Kaposi sarcoma  
HIV – human immunodeficiency virus  
AIDS – acquired immune deficiency syndrome  
HHV-8 – human herpes virus 8  
PG – pyogenic granuloma

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**Figure 1.** Clinical presentation of tumors in KS patient (A- KS close view, B- KS presentation on plantar side of foot, C- multiple KS tumors on dorsal side of foot, D- KS on hand)

**Slika 1.** Klinička prezentacija tumora kod pacijenta sa Kapošijevom sarkomom (KS) (A-KS uvećano, B- KS na plantarnoj strani stopala, C- višetruki KS tumori na dorzalnoj strani stopala, D- KS na šaci)

**Figure 2.** Histopathological presentation of the tumor stage Kaposi sarcoma – first surgery (A-HE x 100, B-HE x 200)

**Slika 2.** Patohistološka prezentacija tumora Kapošijevog sarkoma-prva operacija (A-HE x 100, B-HE x 200)
period of time. As the diagnosis was changed from a solitary benign to recurrent malignant tumor with multiple similar nodules, we decided to take off all five new nodules on both feet and to consider revision of previous histopathological reports. The final diagnosis was KS of the skin. The tumor was located in the whole dermis, and one of the excised lesions already affected the subcutaneous tissue. The tumor tissue consisted of fascicles of spindle cells and some whorled patterns, with some extravasated red blood cells in the intercellular spaces. The nuclei were oval, elongated, without pleomorphism, but with some visible mitosis. The capillary network was rather prominent with areas of slit-like vascular spaces. The malignant cells were positive for CD34, CD31, D2-40, WT1, bcl-2, and HHV-8, but CD99 negative. The patient was referred for further oncological care. Chest computerized tomography (CT) and abdominal magnetic resonance (MR) were done. No mucosal lesions were detected, no lymph node infiltrations and no visceral manifestations of the disease, so close follow up of the patient was planned without additional therapy for the time being.

Discussion

Although the incidence of KS has increased 20-fold during the spread of HIV infection in the 80’s and 90’s, it is still a rare tumor, especially in general population of non-immunocompromised people. The classic form of KS that was diagnosed in our patient is usually seen in older men presenting as slowly growing lesions that appear in small number and are bilaterally located on the lower limbs. They are usually red-brown macules that slowly progress to plaques and nodules. In more aggressive forms of KS, usually HIV associated, lymph nodes may also be involved.

In this case, the patient had a quite unusual development of the disease with one solitary nodule that persisted for a year as a tumor mimicking dermatofibroma that at one point developed sudden “dissemination” with multiple nodules without macular phase, with both hand and foot involvement. The nonspecific clinical presentation firstly of a solitary, firm nodule deceived the dermatologist and the surgeon and postponed the need for urgent biopsy. If the patient presented with an advanced phase of the disease, with multiple nodules, that might have triggered the doubt that it was something else. The recurrent tumor and occurrence on a remote area (opposite site hand) with very similar histology helped making the diagnosis of malignancy after all. On the other hand, different manifestations of classic KS, such as disseminated lymphadenopathy as described by Jeong and colleagues, can mislead the doctor in other direction, in this case mimicking aggressive lymphoma [2]. Hand involvement, as seen in our patient is rare. Considering the fact that Sbiyaa et al. presented a case with an aggressive form of classic KS with hand bone involvement, we made an X-ray of the affected hand, but no bone involvement was noticed [3].

A similar problem was noticed with pyogenic granuloma (PG) as described by Harmelin A. et al., where KS was mimicking another tumor [4]. As clinical presentations of skin tumors may vary, we expect that histological evaluation will give us straight and clear answers and solve all our dilemmas. Scott PL.
et al. described a case where besides clinical features, similar histological presentations were found in KS and pyogenic granuloma-like KS, and emphasized that histological diagnosis can also be very challenging [5]. Overlapping histological features of PG and PG-like KS, such as epidermal collarette resulting from nodular prominence, ulceration and inflammation, and lobular proliferation of capillaries can create a problem for pathologists [6]. In the early patch stage of KS the histological appearance of the lesion can be close to various inflammatory dermatoses, granulomatous and interstitial skin diseases and tumors. As Grayson W. et al. emphasized, differential diagnosis can be challenging as there are many conditions and diseases varying from completely benign to many different malignant ones, that can have a similar, not only clinical, but also histopathological presentation [7].

Since the waiting list for surgery of presumed benign skin lesions is rather long, and we clinically assumed that this was a dermatofibroma, the histological appearance of spindle cell lesion in a rather uncommon location, with absence of immunohistochemical markers, it postponed the final diagnosis of a malignant disease. Another issue is that doctors tend to think about specific diseases as part of some syndromes, in this case immunosuppressive conditions such as AIDS or a transplant recipient, and thus miss a wider picture that involves absence of risk factors and atypical presentations. Health care providers of any specialization, especially dermatologists and dentists, should think about this disease even in non-risk related groups, in order to reduce underestimation of any suspicious plaque or nodule and thus postpone adequate treatment.

**Conclusion**

Since Kaposi sarcoma is not widespread in general population, and Europe is a non-endemic territory, we usually do not think about it if the patient is not in typical risk groups. Nonspecific clinical presentation, unusual location and absence of risk factors can mislead the physician, delay the biopsy and thus also delay adequate treatment. At the same time, histological similarities with other disorders and tumors can be challenging for pathologists and sometimes lead to wrong diagnosis. Raising awareness of Kaposi sarcoma is important as it can prevent delay of adequate treatment.

**References**


