

Bullous lesions in the course of the classic form of Kaposi's sarcoma

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ABSTRACT

Kaposi sarcoma (KS) is a cancer originating from the endothelial cells of blood and lymphatic vessels. It develops multifocally as a result of pathological vascular hyperplasia. There are four forms of the disease: classic, endemic, iatrogenic, and epidemic. The treatment of Kaposi's sarcoma depends on the clinical form, stage of advancement, and the immunological condition of the patient. The article presents the case of an 82-year-old patient from the Dermatology Department of the Provincial Hospital in Elbląg diagnosed with Kaposi's sarcoma with bullous lesions.

Key words: Kaposi's sarcoma, Dermatology, Oncology

INTRODUCTION

Kaposi sarcoma (KS) is a cancer originating from the endothelial cells of blood and lymphatic vessels. The disease was first described by Moritz Kaposi in 1872. There are four clinical forms: classic, endemic, iatrogenic, and epidemic. The classic variant occurs in immunocompetent people, mainly older men. It is characterized by the presence of reddish-purple papules, nodules, and plaques, while blistering lesions are rarely observed. Skin eruptions are located mainly in the lower limbs. Sometimes internal organs are also affected. In our study, we would like to present the interesting case of a patient diagnosed with the classic form of Kaposi's sarcoma with rare bullous lesions.

CASE REPORT

An 82-year-old patient was admitted to the Dermatology Department of the Provincial Hospital in Elbląg in May 2023 for the diagnosis and treatment of skin lesions. The first skin eruptions, located on the shin, appeared about a year before hospitalization with concomitant pain. During the physical examination on the day of

admission to the department, blisters filled with serous-blood content, reddish-purple plaques, and nodules located in the shins and feet, as well as lymphatic edema of the lower limbs were observed. The patient denied the use of new medications, as well as allergies, sudden weight loss, and fever. A family history of autoimmune diseases and skin diseases was negative. The patient also had hypertension. She had been taking perindopril with amlodipine and torasemide. She had also used painkillers (tramadol with paracetamol). The skin lesions were not treated until admission to the department (Figs. 1a – 1d).

During hospitalization, basic laboratory tests were performed, which revealed an increased level of white blood cells (11,280,000/ μ L), total cholesterol (215 mg/dL), and LDL cholesterol (144 mg/dL) and a decreased level of iron (43 μ g/dL). In order to extend the diagnostics, a test for hepatitis B and C virus infection, as well as for infection with the human immunodeficiency virus, was ordered (returning with negative results). ANCA profile and ANA profile were also performed (negative results). Tumor markers Ca-125, Ca 15-3, and Ca 19-9 remained normal. No occult blood was detected in the stool. For the purpose of

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differential diagnosis, a serum test was performed for the presence of pemphigoid and pemphigus antibodies, and a biopsy was taken from apparently healthy skin in the area of the lesion for immunopathological assessment (no features consistent with autoimmune bullous disease were detected). Additionally, a swab was taken from the bladder contents of the lower limb and submitted for microbiological evaluation (no pathogenic microorganisms were detected). Imaging tests performed an ultrasound of the abdominal cavity and retroperitoneal space, revealing a cyst in the left kidney with a diameter of 7 mm. Chest radiological examination revealed fibrosis in the apical region of the heart, sclerotic aorta, and degenerative changes in the thoracic spine. Due to the reported deterioration of visual acuity, the patient was consulted by an ophthalmologist. The examination revealed a retraction of the lower eyelid of the right eye and cortical-nuclear cataracts in both eyes.

During the stay at the dermatology department, two biopsy specimens were taken from the affected skin for histopathological evaluation. The study described hyperkeratotic epidermis with focal sponging and chronic mild perivascular inflammation with a multiplication of vessels in the dermis. The immunohistochemical staining performed was positive

for the following antigens: CD34/+, CD31/+, F8/+, ERG/+, HHV8/+, and SMA/-. Staining for Ki 67 was positive in approx. 8% of the cells. In the videodermatoscopic examination of skin lesions, the rainbow sign was observed (occurring, among others, in Kaposi's sarcoma, basal cell carcinoma, squamous cell carcinoma, and melanoma) (Fig. 2).

Based on the clinical picture and dermoscopic examination and histopathological examination results, the classic form of Kaposi's sarcoma with rare bullous lesions was diagnosed.

The patient was referred to the oncology clinic to extend the diagnostics and select appropriate oncological therapy. The patient was treated with Paclitaxel, achieving a partial reduction of the skin lesions with satisfactory therapeutic and aesthetic effects. The patient continues chemotherapy treatment at the oncology clinic (Figs. 3a and 3b).



Figure 1: (a) Bullous lesions on the patient's right foot. (b) Blisters filled with serous-blood content. (c) Bullous lesions on the patient's left foot. (d) Blisters, reddish-purple plaques, and nodules located on the shins and feet.

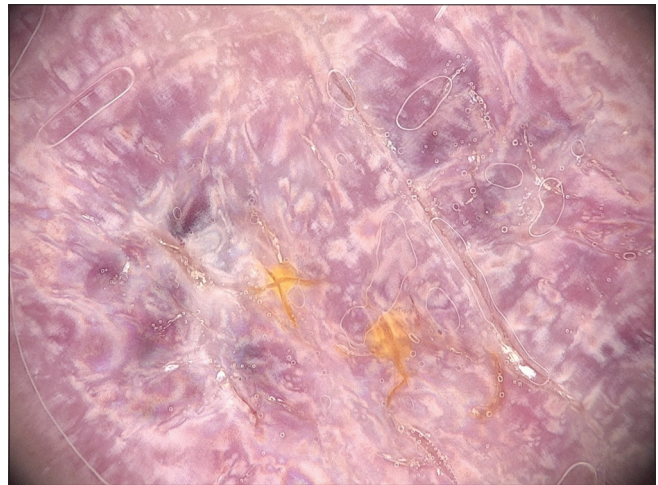


Figure 2: Rainbow sign on videodermatotomy.



Figure 3: (a) The patient around three months after chemotherapy. (b) Close-up of the skin lesions after treatment.

DISCUSSION

Kaposi sarcoma (KS) is a rare dermatological diagnosis that mainly affects older men, patients infected with HIV or receiving immunosuppressive treatment. There is ongoing controversy about whether Kaposi's sarcoma is a cancer of the endothelial cells of blood and lymphatic vessels or a multifocal systemic disease leading to hyperplasia of these cells [1].

In the U.S. and Northern Europe, the prevalence of KSHV infection in the general population is low and estimated to be approx. 6%. In regions with low seroprevalence, the highest values are observed in HIV-infected men who have sex with men (MSM) (30–60%) and HIV-uninfected MSM (20–30%).

Kaposi's sarcoma is a highly vascularized tumor composed of spindle-shaped cells. The clinical picture of this disease may include reddish-brown, blue, slowly enlarging spots, papules, and larger nodules. Kaposi's sarcoma may be located in various areas and cause a wide range of symptoms, e.g., on the skin, being almost asymptomatic, or in the lungs, where it may even be life-threatening. Frequently affected areas include the face (especially the orbital, paranasal, and retroauricular regions), upper torso, and lower limbs [2].

KS lesions evolve from early spots to plaques, which may then develop into larger nodules (cancer stage). These tumors may ulcerate, cause significant lymphedema, present as exophytic growths (e.g., cutaneous horns), or invade adjacent tissues (e.g., underlying bone). Different stages may coexist in the same person at the same time. Similar stages of KS growth concern both skin and mucous membrane lesions.

On histopathological examination, well-developed KS tumors consist of several bundles of spindle-shaped tumor cells, often admixed with a variable chronic inflammatory infiltrate consisting of lymphocytes, plasma cells, and dendritic cells. Macrophages loaded with hemosiderin may also be observed in Kaposi's sarcoma. In cross section, KS nodules have a sieve-like appearance caused by the intersection of spindle cells with intervening slit spaces. Typical lesions in KS are devoid of clear cellular pleomorphism, necrosis, or a significant number of mitotic figures.

In advanced stages of KS, CD34 tends to be expressed more strongly than CD31 in immunohistochemistry. Kaposi's sarcoma spindle cells may also present several

lymphatic system-specific markers, such as D2-40 (which binds to podoplanin antigen), LYVE-1 (CD44 glycoprotein receptor homolog for hyaluronan), VEGFR-3 (vascular endothelial growth factor receptor C), and Prox-1 [3].

Cancer cells in KS show some similarity to endothelial cells (lining blood vessels), smooth muscle cells, and macrophages (cells of the immune system). Malignant transformation probably occurs due to infection with human herpesvirus 8 (HHV-8). A contributing factor is chronic immunosuppression, especially HIV infection [4].

Four clinical forms of this disease have been distinguished in Kaposi's sarcoma. The classic form occurs mostly in men of Mediterranean, Eastern European, and Ashkenazi Jewish descent. About 2/3 of patients develop symptoms after the age of fifty. This form affects immunocompetent people. Typical lesions are painless, slowly growing, having the form of blue spots or lumps, almost always located on the feet or lower legs. The lesions slowly harden and coalesce into larger plaques or nodules. Exceptionally, they occur only on mucous membranes, although cases of the involvement of internal organs, mainly the gastrointestinal tract, have been described. Additionally, infiltrates affect the liver and spleen.

Another variant of KS is the endemic African form with generalized involvement of the lymph nodes. It occurs mainly in the pediatric population in Africa. In adults, it is much more aggressive than the classic form and may occur in three forms: nodular, aggressive, or bright red. In the pediatric form, there is a sudden enlargement of the cervical lymph nodes, resembling Burkitt's lymphoma, and disseminated lesions, which may lead to death.

Another form of KS is that with HIV infection, occurring in patients not treated with HAART therapy, with widespread involvement of the skin and internal organs. Mucous membranes are often involved, and numerous facial lesions occur, which rarely occur in other forms.

Another form is iatrogenic in patients with immunosuppression, which occurs after solid organ transplants and the use of immunosuppressive drugs, such as corticosteroids, cyclosporine, azathioprine, calcineurin inhibitors. It may present with diffuse involvement of the skin and internal organs. The

changes sometimes regress after the discontinuation of immunosuppressive treatment [2,5,6].

Bullous lesions in Kaposi's sarcoma are rare, therefore it is difficult to find descriptions of similar cases in the scientific literature. In "Histopathological analysis of vesicular and bullous lesions in Kaposi sarcoma" from 2012 published in *Diagnostic Pathology*, 178 biopsy materials taken from 75 patients diagnosed with the classic form of Kaposi's sarcoma were assessed. The study included patients diagnosed between 2001 and 2010 at the Department of Pathology of the University of Karaemas and Dr. Lütfi Kırdar Training and Research Hospital. None of the patients had a history of organ transplantation or taking immunosuppressive drugs, and all patients were HIV-seronegative. In the analyzed materials, vesicular changes were observed in 21 (12%) of 178 biopsy materials, and bullous changes in only four (2%). Clinical vesicular lesions were not visible in any of the cases where they were detected microscopically, yet vesicular lesions were clinically observed in all cases where they were present on microscopic examination. Among patients with bullous lesions, the male-to-female ratio was 3:1. The lesions were located on the lower limbs ($n = 2$), upper limbs ($n = 1$), and head and neck ($n = 1$). All cases involved KS in the nodular stage. In all cases, histopathological features were similar: hyperkeratosis and serous exudate in the epidermis, marked edema of the dermis, enlarged lymphatic vessels, and chronic inflammation [7,8].

The choice of the appropriate treatment method for Kaposi's sarcoma depends mainly on its clinical form and stage of advancement. Particular attention should also be paid to the patient's immunological status. In stage I of the disease, regardless of its form, if only single lesions are present, they may be surgically removed. In stages I and II of advancement, local treatment methods are used. These include cryotherapy, laser resection, photodynamic therapy, intralesional injections of vinca alkaloids (vinblastine, vincristine), the use of 0.1% alitretinoin preparations and 5% imiquimod. Another form of treatment used is radiotherapy with low doses of ionizing radiation [6,9,10-12]. General treatment is usually used when the lesions are disseminated or when the internal organs are involved. For the epidemic form of Kaposi's sarcoma, the key element of treatment is highly active antiretroviral therapy (HAART). General therapy associated with HAART in the case of HIV infection includes the use of pegylated interferon α , paclitaxel, liposomal doxorubicin, or daunorubicin. Polychemotherapy according to the ADV regimen

(doxorubicin, vincristine, bleomycin) is also used (mainly in severe cases of Kaposi's sarcoma) [6,10,12,13]. In the iatrogenic form (related to immunosuppressive treatment after transplantation), regardless of the stage of advancement, the first step should be to consider the possibility of modifying this treatment, i.e., reducing the dose or changing the immunosuppressive drug to another one. Significant benefits of switching from cyclosporine to sirolimus (rapamycin), an mTOR inhibitor, have been demonstrated [14-16]. In the case of our patient, treatment with Paclitaxel was initiated, resulting in a significant reduction of skin lesions and quite good tolerance of the therapy.

CONCLUSION

Kaposi's sarcoma is a relatively rare disease found in the Polish population. A preliminary diagnosis may be made based on the clinical picture, yet a histopathological examination is necessary to make a final diagnosis. Therefore, in dermatological practice, one must demonstrate extensive knowledge, experience, and inquisitiveness. Different clinical variants of Kaposi's sarcoma have different courses and prognoses, which is why a correct diagnosis is so important. We should not forget about the interdisciplinary approach when choosing a treatment method.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

REFERENCES

1. Liliashvili S, Pataraiia S, Galdava G, Ghibradze T. Mięsak Kaposiego u biorcy przeszczepu nerki. *Dermatol Rev.* 2022;109:460-3.
2. Iftode N, Rădulescu MA, Arama SS, Arama V. Update on Kaposi sarcoma-associated herpesvirus (KSHV or HHV8): A review. *J Intern Med.* 2020;58:199-208.
3. Radu O, Pantanowitz L. Kaposi sarcoma. *Arch Pathol Lab Med.* 2013;137:289-94.
4. Itrych B, Sadulaev Z, Brzeziński P. Mięsak Kaposiego: Od diagnostyki do leczenia. *Dermat Dypł.* 2019;1:1.
5. Marušić Z, Billings SD. Histopathology of spindle cell vascular tumors. *Surg Pathol Clin.* 2017;10:345-66.
6. Agrawal SN, Rawal AA, Jane SD. Classic Kaposi's sarcoma: A rare case with unusual presentation. *Our Dermatol Online.* 2014;5:68-70.

7. Kandemir NO, Barut F, Gün BD, Tekin NS, Keser SH, Özdamar SO. Histopathological analysis of vesicular and bullous lesions in Kaposi sarcoma. *Diagn Pathol.* 2012;7:101.
8. Borroni G, Brazzelli V, Vignoli GP, Gaviglio MR. Bullous lesions in Kaposi's sarcoma: Case report. *Am J Dermatopathol.* 1997;19:379-83.
9. Ouédraogo MS, Moï-Bohm Biatougou N, Ouédraogo NM, Ouangré/Ouédraogo A, Tapsoba GPML, Traoré A, et al. Iatrogenic Kaposi's sarcoma in a patient with bullous pemphigoid treated with an oral corticosteroid. *Our Dermatol Online.* 2023;14:73-6.
10. Kourouma HS, Gbandama KKP, Kouassi YI, Allou AS, Amani KLWG, Kouassi KA, et al. Systemic diseases with cutaneous expression and HIV infection in dark skin: Epidemiological and therapeutic aspects in Abidjan (Ivory Coast). *Our Dermatol Online.* 2023;14(Supp. 2):25-31.
11. Mai S, Mansouri S, Outznit M, Znati K, Senouci K, Meziane M. Anaplastic transformation in a classic Kaposi's sarcoma. *Our Dermatol Online.* 2020;11:329-30.
12. Roszkiewicz J, Nedoszytko B, Lange M. Mięsak Kaposiego: Fascynująca historia współczesnej medycyny. *Forum Med Rodz.* 2010;4:246-54.
13. Simon K, Knysz B, Szybejko-Machaj G, Gadysz A. Kaposi's sarcoma in patients with acquired immunodeficiency syndrome (AIDS): Our own observation. *Współcz Onkol.* 2000;1:21-4.
14. Abdelmouttalib A, Soumaya H, Meziane M, Ismaili N, Benzekri L, Senouci K. Iatrogenic Kaposi's sarcoma in the anovulvar area. *Our Dermatol Online.* 2023;14:109-10.
15. Mariggio G, Koch S, Schulz TF. Kaposi sarcoma herpesvirus pathogenesis. *Phil Trans R Soc B.* 2017;372:20160275.
16. Schneider JW, Dittmer DP. Diagnosis and treatment of Kaposi sarcoma. *Am J Clin Dermatol.* 2017;18:529-39.

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