KAPOSI'S SARCOMA IN AN HIV-POSITIVE PATIENT

Mięsak Kaposiego u pacjenta zakażonego HIV

Vasiliki Chwiałkowska, Karolina Parciak, Joanna Zalewska, Anna Płatkowska, Elwira Paluchowska, Witold Owczarek

Military Institute of Medicine – National Research Institute, Department of Dermatology, Poland

Abstract

Kaposi's sarcoma is a malignancy arising from vascular endothelial cells, associated with infection with the human herpes virus-8 (HHV-8). It has four clinical forms: classic, endemic, epidemic (associated with HIV/AIDS) and iatrogenic. We present a case of a 38-year-old male patient who was admitted to the Dermatology Clinic due to numerous, scattered blue-violet macules, plaques, and nodules. HIV infection was revealed during the diagnostic process. Kaposi's sarcoma was diagnosed based on the clinical picture and histopathological findings. The patient was referred to the Department of Infectious Diseases for antiretroviral treatment and to the Department of Oncology, where he received treatment with paclitaxel with remission of the lesions. The clinical picture of Kaposi's sarcoma, which includes macules, plaques, and nodules, is not sufficient to make the diagnosis. A biopsy followed by a histopathological examination should be performed. Current guidelines do not recommend serological testing to detect antibodies or the HHV-8 genome. Topical or systemic treatment can be used for Kaposi's sarcoma, depending on the extent of skin lesions, accompanying systemic symptoms and involvement of other organs.

Streszczenie

Mięsak Kaposiego jest nowotworem wywodzącym się z komórek śródbłonka naczyń, związanym z infekcją ludzkim wirusem opryszczki HHV-8. Wyróżnia się cztery postaci kliniczne choroby: klasyczną, endemiczną, epidemiczną związaną z HIV/AIDS i jatrogenną. W artykule przedstawiono historię 38-letniego pacjenta, który został przyjęty do Kliniki Dermatologii z powodu licznych, rozsianych sino-fiołkowych plam, blaszek, guzków oraz guzów. W trakcie diagnostyki ujawniono zakażenie HIV, a następnie na podstawie obrazu klinicznego i wyniku biopsji rozpoznano mięsaka Kaposiego. Pacjenta skierowano na oddział chorób zakaźnych w celu rozpoczęcia leczenia przeciwretrowirusowego i na oddział onkologii, gdzie otrzymał leczenie paklitakselem, po którym uzyskano remisję zmian. W obrazie klinicznym mięsaka Kaposiego we wszystkich odmianach występują plamy, blaszki oraz guzki, jednak sam obraz kliniczny nie jest wystarczający do ustalenia rozpoznania. W tym celu należy wykonać biopsję, a następnie badanie histopatologiczne. Aktualne wytyczne nie zalecają stosowania diagnostyki serologicznej w celu wykrywania przeciwciał lub genomu HHV-8. Leczenie mięsaka Kaposiego może być miejscowe lub ogólnoustrojowe, o czym decyduje rozległość zmian skórnych, towarzyszące objawy ogólne i zajęcie innych narządów.

Keywords: Kaposi's sarcoma, immunodeficiency, human herpes virus-8 (HHV-8), human immunodeficiency virus (HIV)

Słowa kluczowe: mięsak Kaposiego, niedobór odporności, ludzki wirus opryszczki typu 8 (HHV-8), ludzki wirus niedoboru odporności (HIV)

DOI 10.53301/lw/176198

Received: 21.11.2023

Accepted: 01.12.2023

Corresponding author:
Joanna Zalewska
Military Institute of Medicine – National Research Institute, Department of Dermatology, Warsaw
e-mail: joannaezalewska@gmail.com

Introduction

Kaposi's sarcoma (KS), first described in 1872 by Moritz Kaposi [1], is a malignancy arising from the endothelial cells. There has been no consensus on the origin of the endothelial cells so far. Neoplastic proliferation of lymphatic as well as blood vessel cells is postulated. Endothelial cells undergo neoplastic transformation as a result of infection with the oncogenic human herpesvirus-8 (HHV-8).

There are four forms of Kaposi's sarcoma:

- classic – usually affecting men aged over 50 years, from the Mediterranean and Eastern European countries;
- endemic (African) – affecting HIV-negative children and young adults in Africa;
- iatrogenic – associated with the use of immunosuppressive therapy in organ transplant recipients;
- epidemic (AIDS-related KS) – an indicator disease mostly affecting men who have sex with men (MSM) [2].

All KS variants share a similar clinical and histological picture of skin lesions [3]. HHV-8 infection is another common feature [4]. HHV-8 is spread horizontally, most often through saliva, less commonly through sperm or blood [5]. KS is a rare malignancy, as evidenced by the fact that only 26 KS cases were recorded among men and 14 among women in Poland in 2020, as confirmed by the Statistics of the National Cancer Registry [6].

A case report

A 38-year-old male patient was admitted to the Department of Dermatology due to multiple, scattered blue-violet spots, plaques, and nodules (fig.). The first skin lesion had appeared three months prior to admission and was located on the fourth toe of the left foot. Subsequent, ascending lesions involved the lower limbs, trunk, and face.

The patient reported no history of chronic diseases, but he had sexual contacts with other men (he belonged to the MSM group). As part of outpatient diagnosis, he had undergone two biopsies before admission to the Department. The first histopathological result suggested drug-induced lesions. The results obtained one month later indicated that the image could correspond with dermatofibrosarcoma protuberans, but it should be differentiated from other sarcomas of vascular origin. During hospitalization, serological diagnosis of HIV infection was performed - both screening and confirmation tests turned out to be positive. EBV, CMV, hepatitis B and C infections were excluded. Abdominal ultrasound revealed three vascular hepatic lesions up to 11 mm in size. Furthermore, ultrasound of the peripheral lymph nodes revealed multiple enlarged cervical, supraclavicular, axillary and inguinal lymph nodes with blurred echostructure and increased blood flow.

The clinical picture and histopathological findings led to the diagnosis of Kaposi's sarcoma. The patient was referred to the Department of Infectious Diseases for antiretroviral treatment, as well as to the Department of Oncology, where it was decided to initiate chemotherapy (paclitaxel). Remission was achieved and no new skin lesions appeared.

Discussion

The early clinical picture of all KS variants encompasses patches, identifiable only by changes in skin colour, which may pose a major diagnostic challenge [7]. Lesions involve both skin and mucous membranes, and subsequently evolve into plaques and nodules. The latter ones may ulcerate, form exophytic lesions, cause significant lymphedema and infiltrate adjacent tissues, such as bones. The clinical picture may include coexisting skin lesions at various stages of advancement [8]. The lesions usually develop on the lower limbs, with the first manifestation on the foot in the vast majority of cases [9]. Common extracutaneous locations of KS include lymph nodes, abdominal organs, and airways [2]. Rare cases of the disease occurring in the musculoskeletal system, central and peripheral nervous system, larynx, eyeball, salivary glands, heart, thoracic duct, urinary system, and breasts are also described in the literature [10].

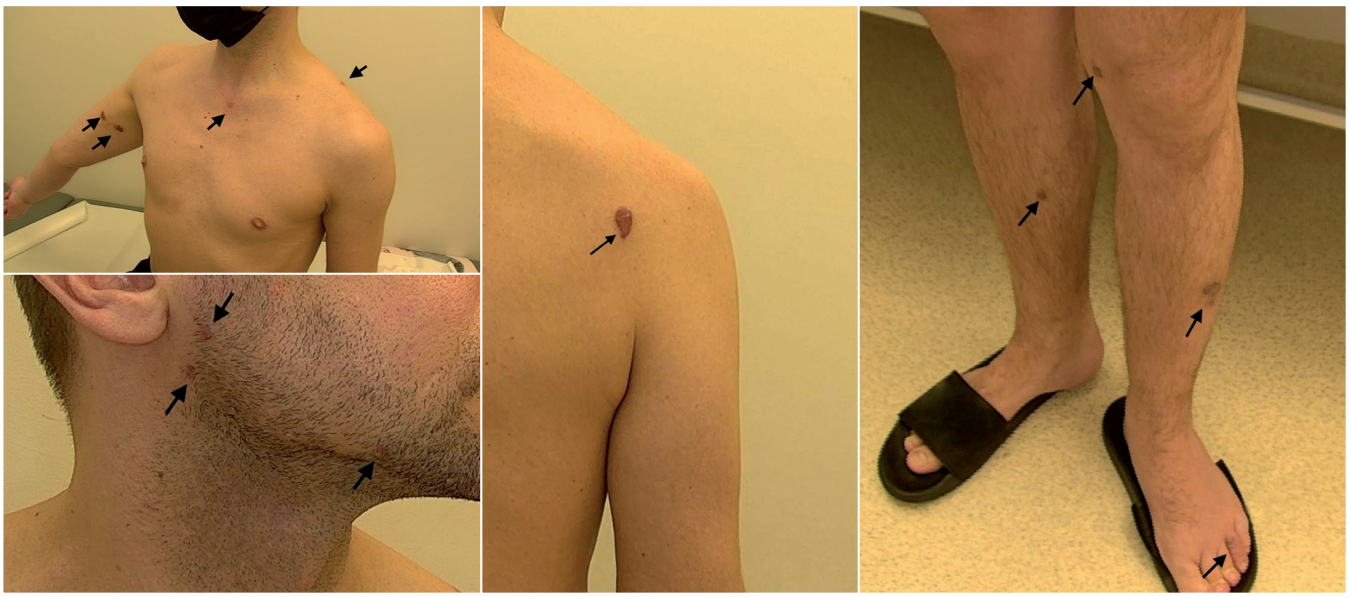

Figure. A. Blue-violet nodules on the right arm and patches around the sternum and right arm. **B.** Blue-violet patches on the face. **C.** A blue-violet nodule on the right shoulder. **D.** Blue-violet nodules on the lower limbs

The differential diagnosis of KS includes vascular pathologies with a similar clinical picture, i.e. angiosarcomas, vascular granulomas, haemangiomas and IgA vasculitis [2].

However, the clinical picture is not sufficient to diagnose KS. For this purpose, a biopsy followed by histopathological examination, and optionally immunostaining should be performed, The histopathological picture of KS depends on the stage of the disease. In the patch stage, superficial proliferation of small, dilated vessels lined by endothelial cells may be observed. These vessels tend to separate the collagen bundles. They are accompanied by an infiltrate consisting of lymphocytes and plasma cells. When the patches become more advanced, vascular lesions can invade the deeper layers of the skin and subcutaneous tissue. In the nodular phase, spindle cells are separated by characteristic slit-like spaces containing erythrocytes. This image forms a cribriform pattern typical of sarcoma. The nodules are often surrounded by hemosiderin deposits, lymphocytes and plasma cells [11]. Furthermore, the identification of HHV-8 in the affected cells using a monoclonal antibody against HHV-8 is the most diagnostically useful immunostaining technique [12]. Current guidelines do not recommend serological diagnostics to detect antibodies or the HHV-8 genome in screening, diagnosis or monitoring of any KS variant [13].

Local or systemic treatment can be used for KS. The most optimal therapeutic outcomes are achieved in the classic form of KS, which requires only local treatment [3]. The choice of therapy is determined by the extent of skin lesions, the accompanying systemic symptoms, and the involvement of other organs. Local treatment is recommended for single, small lesions and includes surgical excision, radiotherapy, and cryotherapy [14]. Local treatment using alitretinoin, imiquimod and timolol has also been described in the literature. All three demonstrate significant clinical efficacy with minimal adverse effects [15]. Systemic treatment is recommended for disseminated and symptomatic forms of KS. It includes chemotherapy with doxorubicin, which is effective in patients with classic KS [16], and paclitaxel, which is used in patients with both classic and AIDS-related KS [17], as in described case. Furthermore, the literature also describes therapy with vinblastine [18], etoposide [19] and gemcitabine [20]. All are effective for classic and AIDS-related KS. Other therapeutic options include immunotherapy (pembrolizumab [21] and nivolumab in combination with ipilimumab [22]), biological therapy (a.o. recombinant interferon alpha due to its immunomodulatory and antiangiogenic properties [23]) and antiretroviral therapy (HAART), which allows to achieve remission in many HIV-positive patients [24].

Conclusions

Kaposi's sarcoma is a rare tumour that poses significant diagnostic difficulties. The clinical picture may include a variety of skin lesions, such as patches, plaques, and nodules. Several biopsies performed in different pathomorphology centres are sometimes needed to establish the diagnosis.

The patient's consent for the publication of photographs was obtained.

References

1. Kaposi M. Idiopatisches multiples Pigmentsarkom der Haut [German]. Arch Dermatol Syph, 1872; 4: 265–273. doi: 10.1007/BF01830024
2. Gajda P, Olszewska M. Mięsak Kaposiego. In: Rudnicka L, Olszewska M, Rakowska A, Sar-Pomian M, eds. Współczesna dermatologia Tom I. Warszawa, Wydawnictwo Naukowe PWN, 2022: 105–107
3. Roszkiewicz J, Nedoszytko B, Lange M. Sarcoma Kaposi's – fascinating story of contemporary medicine. Forum Medycyny Rodzinnej, 2010; 4: 246–254
4. 4. Iscovich J, Boffetta P, Franceschi S, et al. Classic Kaposi sarcoma: epidemiology and risk factors. Cancer, 2000; 88: 500–517
5. Iftode N, Rădulescu M, Aramă Ş, Aramă V. Update on Kaposi sarcoma-associated herpesvirus (KSHV or HHV8) – review. Rom J Intern Med, 2020; 58: 199–208. doi: 10.2478/rjim-2020-0017
6. Wojciechowska U, Brańska K, Michałek I, Olasek P, et al. Nowotwory złośliwe w Polsce w 2020 roku. Warszawa, Krajowy Rejestr Nowotworów, 2022
7. Rothman S. Some clinical aspects of Kaposi's sarcoma in the European and North American populations. Acta Unio Int Contra Cancrum, 1962; 18: 364–371
8. Radu O, Pantanowitz L. Kaposi sarcoma. Arch Pathol Lab Med, 2013; 137: 289–294. doi: 10.5858/arpa.2012-0101-RS
9. Richter P, Black J. Kaposi's sarcoma of the foot: case report and review. Mil Med, 1984; 149: 631–634
10. Pantanowitz L, Dezube BJ. Kaposi sarcoma in unusual locations. BMC Cancer, 2008; 8: 190. doi: 10.1186/1471-2407-8-190
11. North PE. Vascular neoplasms and neoplastic-like proliferations. In: Bolognia JL, Schaffer JV, Cerroni L, eds. Dermatology. Elsevier, 2018: 2020–2049
12. Lebbe C, Garbe C, Stratigos A, et al.; European Dermatology Forum (EDF), the European Association of Dermato-Oncology (EADO) and the European Organisation for Research and Treatment of Cancer (EORTC). Diagnosis and treatment of Kaposi's sarcoma: European consensus-based interdisciplinary guideline (EDF/EADO/EORTC). Eur J Cancer, 2019; 114: 117–127. doi: 10.1016/j.ejca.2018.12.036
13. Dupin N, Jary A, Boussouar S, et al. Current and Future Tools for Diagnosis of Kaposi's Sarcoma. Cancers (Basel), 2021; 13: 5927. doi: 10.3390/cancers13235927
14. PDQ Adult Treatment Editorial Board. Kaposi Sarcoma Treatment (PDQ®): Health Professional Version. 2023 Sep 21. In: PDQ Cancer Information Summaries [Internet]. Bethesda (MD): National Cancer Institute (US); 2002
15. Htet K, Waul M, Leslie K. Topical treatments for Kaposi sarcoma: A systematic review. Skin Health Dis, 2022; 2: e107. doi: 10.1002/ski2.107
16. Di Lorenzo G, Kreuter A, Di Trolio R, et al. Activity and safety of pegylated liposomal doxorubicin as first-line therapy in the treatment of non-visceral classic Kaposi's sarcoma: a multicenter study. J Invest Dermatol, 2008; 128: 1578–1580. doi: 10.1038/sj.jid.5701215
17. Cianfrocca M, Lee S, Von Roenn J, et al. Randomized trial of paclitaxel versus pegylated liposomal doxorubicin for advanced human immunodeficiency virus-associated Kaposi sarcoma: evidence of symptom palliation from chemotherapy. Cancer, 2010; 116: 3969–3977. doi: 10.1002/cncr.25362

18. Solan A, Greenwald E, Silvay O. Long-term complete remissions of Kaposi's sarcoma with vinblastine therapy. Cancer, 1981; 47: 637–639. doi: 10.1002/1097-0142(19810215)47:4<637::aid-cncr2820470402>3.0.co;2-b
19. Tas F, Sen F, Keskin S, Kilic L. Oral etoposide as first-line therapy in the treatment of patients with advanced classic Kaposi's sarcoma (CKS): a single-arm trial (oral etoposide in CKS). J Eur Acad Dermatol Venereol, 2013; 27: 789–792. doi: 10.1111/j.1468-3083.2011.04404.x
20. Zustovich F, Ferro A, Toso S. Gemcitabine for the treatment of classic Kaposi's sarcoma: a case series. Anticancer Res, 2013; 33: 5531–5534
21. Delyon J, Biard L, Renaud M, et al. PD-1 blockade with pembrolizumab in classic or endemic Kaposi's sarcoma: a multicentre, single-arm, phase 2 study. Lancet Oncol, 2022; 23: 491–500. doi: 10.1016/S1470-2045(22)00097-3
22. Zer A, Icht O, Yosef L, et al. Phase II single-arm study of nivolumab and ipilimumab (Nivo/Ipi) in previously treated classical Kaposi sarcoma (cKS). Ann Oncol, 2022; 33: 720–727. doi: 10.1016/j.annonc.2022.03.012
23. Sullivan R, Pantanowitz L, Dezube B. Targeted therapy for Kaposi sarcoma. Bio Drugs, 2009; 23: 69–75. doi: 10.2165/00063030-200923020-00001
24. PDQ Adult Treatment Editorial Board. Kaposi Sarcoma Treatment (PDQ®): Patient Version. 2023 May 17. In: PDQ Cancer Information Summaries [Internet]. Bethesda (MD): National Cancer Institute (US); 2002