memo (2019) 12:99–102
https://doi.org/10.1007/s12254-018-0445-6

memo
magazine of european medical oncology

Kaposi sarcoma following autoimmune hemolytic anemia in a patient with chronic lymphocytic leukemia

Utku Iltar · Vedat Aslan · Mesut Gocer · Fatma Aykac · İlknur Nizam · Mehmet Çelik · Faruk Gulec · Turgay Ulaş · Erdal Kurtoğlu

Received: 3 August 2018 / Accepted: 2 October 2018 / Published online: 11 October 2018

Summary
Background Kaposi sarcoma is a low grade angioproliferative disorder which requires infection with human herpes virus 8 for its development. Skin lesions can be observed frequently in chronic lymphocytic leukemia cases, but there is a limited number of cases of Kaposi sarcoma with chronic lymphocytic leukemia in the literature.
Case report Here, we present a case report of an iatrogenic Kaposi sarcoma in a 79-year-old man recently diagnosed with autoimmune hemolytic anemia secondary to chronic lymphocytic leukemia. After treatment with methylprednisolone and rituximab, the patient developed Kaposi sarcoma nodular lesions on his legs. After three courses of oral etoposide for Kaposi sarcoma, the lesions completely disappeared at the end of the third month of treatment.
Conclusion Even though the mortality rate is low with Kaposi sarcoma, it can cause physical and psychological burden for the patients. Additional investigations and raising awareness of Kaposi sarcoma while evaluating the differential diagnosis of skin lesions in chronic lymphocytic leukemia are needed. Short-term oral etoposide was tolerated well in this patient with a good clinical response.

U. Iltar, M.D (✉) · V. Aslan · M. Gocer · F. Aykac · İ. Nizam · M. Çelik · E. Kurtoğlu
Department of Hematology, Antalya Training and Research Hospital, Antalya, Turkey
utq_07@hotmail.com

F. Gulec
Department of Pathology, Antalya Training and Research Hospital, Antalya, Turkey

T. Ulaş
School of Medicine, Department of Internal Medicine, Division of Hematology, Near East University, Nicosia, Cyprus

Keywords Kaposi's sarcoma · Chronic lymphocytic leukemia · Human herpes virus-8 · Rituximab · Case report

Introduction

Kaposi sarcoma (KS) is a low grade angioproliferative disorder thought to be derived from endothelial cell lineage that requires infection with human herpes virus 8 (HHV-8) for its development. This condition carries a variable clinical course ranging from an early patch stage to nodular (tumor) stage. Histologically, KS lesions are comprised of spindle-shaped tumor cells, abnormal vessels and a variable chronic lymphoplasmacytic inflammatory infiltrate. KS can be primarily categorized into four types: classic (sporadic), endemic (African), iatrogenic (immunosuppression-associated) and epidemic (acquired immunodeficiency syndrome associated) [1].

Iatrogenic KS is seen in patients with solid-organ transplantations and those treated with immunosuppressive agents. Drugs that are implicated in the development of iatrogenic KS include cyclosporine, azathioprine, corticosteroids, and rituximab. These are particularly important in the setting of transplantation, but they are also relevant in the setting of chronic immunosuppression for autoimmune conditions or treatment of HHV 8-infected patients with other malignancies [2].

Immunosuppression is well described as a risk factor for KS but there are conflicting data on associations with malignancies. The largest retrospective study was an analysis of 16,367 patients with chronic lymphocytic leukemia (CLL) enrolled in the Surveillance, Epidemiology and End Results program and followed for an average of 5.2 years. Significant excesses were found for malignant melanoma and KS [3].

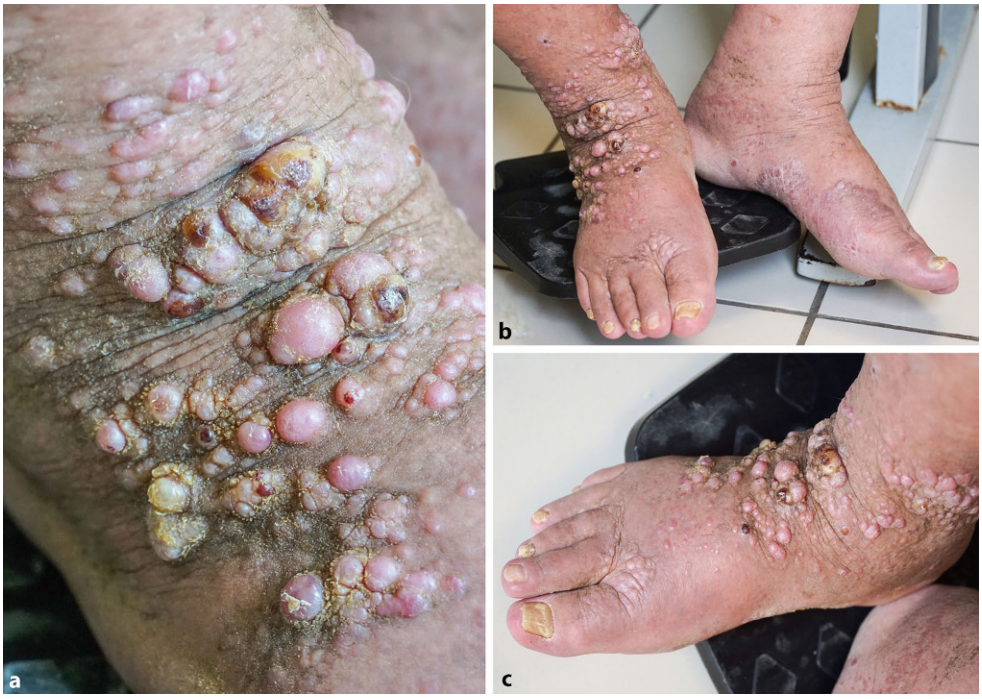

Fig. 1 KS(Kaposi sarcoma)-related nodules

To date, only a few publications have reported KS in patients with CLL [4–7].

Case report

A 79-year-old man recently diagnosed with autoimmune hemolytic anemia secondary to chronic lymphocytic leukemia was initiated therapy with 1 mg/kg per day of methylprednisolone. The patient's medical history was significant for atrial fibrillation and coronary artery disease. At home, he was on dabigatran 150 mg twice daily.

The patient had initial improvement in his hemoglobin concentration but remission was not maintained; high doses of methylprednisolone were needed. The methylprednisolone therapy was gradually tapered off and the treatment plan was then changed to include four weekly doses of rituximab at 375 mg/m^2 per dose, 8 weeks after the start of steroid treatment. Rituximab was initiated and just after the second rituximab infusion complete response was observed.

Before the last dose of weekly rituximab, the patient developed edematous legs and biopsy-proven KS nodular lesions on his legs (Fig. 1 and 2). The patient continued his treatment of rituximab and after the completion of treatment nodular lesions of KS gradually became enlarged and later spread towards the knees, while the edema progressed. He had normal immunoglobulin levels and was negative for the HIV antibody. For KS, the patient received oral etoposide 60 mg/m^2 on days 1–3 during the first course; 60 mg/m^2 on days 1–4 during the second course, and 60 mg/m^2 on days 1–5 during the third course; the courses were recycled every 3 weeks. In the first cycle of etoposide there was mild nausea and vomiting which improved with oral antiemetic drugs and which did not continue in subsequent etoposide cycles under oral emesis prophylaxis. After three courses of oral etoposide, the lesions had completely disappeared.

Discussion and conclusions

HHV-8 causes three human malignancies, KS, primary effusion lymphoma, and many cases of the plasmablastic form of multicentric Castleman's disease. Infection with HHV-8 is consistently observed in all forms of KS. While infection with HHV-8 is necessary for the development of KS, it alone may not be sufficient. Antiviral T-cell response in control of HHV-8 infection is fundamental [8]. Severe states of immunodepression may determine the development of KS through the imbalance of the lymphocyte subpopulation and the reactivation of HHV-8 from latency to replication. HHV-8 infects and transforms human endothelial cells which form the neoplastic spindle cell component of KS lesions [1].

Multiple studies have documented an increased incidence of KS with NHL (non-Hodgkin Lymphoma) but a few studies have documented KS with CLL [3, 9, 10]. Of significance, only one case of iatrogenic KS have been reported due to rituximab administration in a patient with CLL. The paper documented a possible relationship between CLL and KS in a 70-year-old man who was given a chemotherapy scheme of rituximab + fludarabine + cyclophosphamide combination for 6 cycles [4]. KS occurred in this patient a short time after chemotherapy completion.

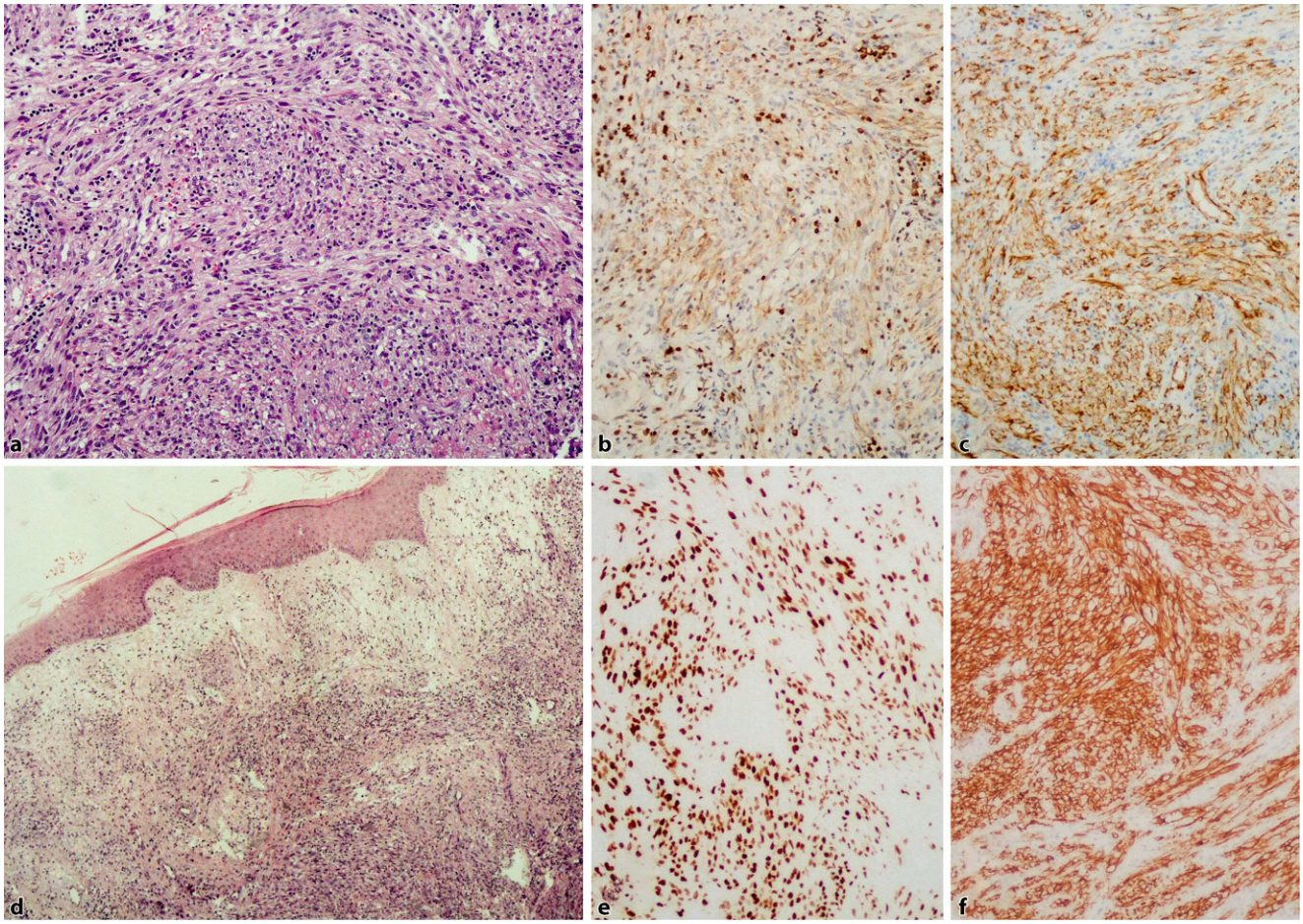

Fig. 2 Histology and immunohistochemistry of KS specimens. Proliferating spindle-shaped cells expressed CD31, CD34 and human herpes virus 8 (HHV-8). **a** Hematoxylin and eosin staining, original magnification, ×100. **b** BCL2. **c** CD31. **d** Hematoxylin and eosin staining, original magnification, ×40. **e** HHV8. **f** CD34

This is a case report of iatrogenic KS in a patient with CLL. The lesions developed while being treated with methylprednisolone and rituximab for autoimmune hemolytic anemia secondary to CLL and did not resolve, even months after stopping these medications.

We cannot eliminate the possibility that corticosteroids may have contributed to the iatrogenic KS described in our case because corticosteroid is one of the drugs implicated in the development of iatrogenic KS. Although it is certain that both rituximab and corticosteroids contribute to the development of KS, it can be considered that the main agent is rituximab because the lesions developed after stopping corticosteroids and during rituximab treatment.

It is known that skin lesions can be observed more frequently in CLL cases, but there is a limited number of KS reported in CLL cases in the literature. Therefore, KS should not be overlooked in the differential diagnosis of the clinician for the lesions observed in CLL cases.

Not all patients infected with HHV8 and treated with chemotherapy develop KS. There may be other factors. Some types of infections along with HHV8 may also play a part in a person developing KS. Additional investigations of KS after CLL are needed for extending the knowledge of the pathophysiology of the disease.

Compliance with ethical guidelines

Conflict of interest U. Iltar, V. Aslan, M. Gocer, F. Aykac, İ. Nizam, M. Çelik, F. Gulec, T. Ulaş, and E. Kurtoğlu declare that they have no competing interests.

Ethical standards This article does not contain any studies with human participants or animals performed by any of the authors. For images or other information within the manuscript which identify patients, consent was obtained from them and/or their legal guardians.

References

1. Douglas JL, Gustin JK, Dezube B, Pantanowitz JL, Moses AV. Kaposi's sarcoma: a model of both malignancy and chronic inflammation. Panminerva Med. 2007;49(3):119–38.
2. Vangipuram R, Tyring SK. Epidemiology of Kaposi sarcoma: review and description of the nonepidemic variant. Int J Dermatol. 2018; https://doi.org/10.1111/ijd.14080.

3. Hisada M, Biggar RJ, Greene MH, Fraumeni JF Jr, Travis LB. Solid tumors after chronic lymphocytic leukemia. Blood. 2001;98(6):1979–81.
4. Hacioglu MB, Sahin S, Karatas F, Aytekin A. A rare coexistence—chronic lymphocytic leukemia and Kaposi sarcoma: case report and review of the literature. J Cancer Res Ther. 2015;11(4):954–6.
5. Wijermans PW, van Groningen K, van Royen EA, Bruijn JA. Kaposi's sarcoma in an HIV-negative CLL patient as the cause of thrombocytopenia. Ann Hematol. 1994;68(6):307–10.
6. Kose F, Kocer NE, Sumbul AT, Sezer A, Yilkan O. Kaposi's sarcoma following chronic lymphocytic leukemia: a rare entity. Case Rep Oncol. 2012;5(2):271–4.
7. Contu L, Carcassi C, La Nasa G, Zurrida SM, Sirigu F, Del Giacco S, Cerimele D, Longinotti M, Pitzus F. A case of classical Kaposi's sarcoma in B-cell chronic lymphocytic leukemia (B-CLL). Tumori. 1986;72(4):365–74.
8. Wang QJ, Jenkins FJ, Jacobson LP, Kingsley LA, Day RD, Zhang ZW, Meng YX, Pellett PE, Kousoulas KG, Baghian A, Rinaldo CR Jr.. Primary human herpesvirus 8 infection generates a broadly specific CD8(+) T-cell response to viral lytic cycle proteins. Blood. 2001 Apr 15;97(8):2366–73. Erratum. Blood. 2002;99(10):3499.
9. Manusow D, Weinerman BH. Subsequent neoplasia in chronic lymphocytic leukemia. JAMA. 1975;232(3):267–9.
10. Brewer JD, Shanafelt TD, Call TG, Cerhan JR, Roenigk RK, Weaver AL, Otley CC. Increased incidence of malignant melanoma and other rare cutaneous cancers in the setting of chronic lymphocytic leukemia. Int J Dermatol. 2015;54(8):e287–e93.