

CASE REPORT

Auricular involvement of a multifocal non-AIDS Kaposi's sarcoma: a case report

Un caso di sarcoma di Kaposi, multifocale non-HIV correlato, dell'orecchio esterno

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SUMMARY

Kaposi's sarcoma (KS) is a multicentric, malignant neoplastic vascular disease, mainly involving skin and mucosae, characterized by the proliferation of endothelial cells. The aetiology of KS still is unknown. Nonetheless, it has been reported that several epidemiological and environmental factors may play a role in its pathogenesis. Viral factors (i.e. human herpes virus 8, HHV-8) have also been claimed to play a role in the onset of KS. Four main clinical presentations of KS have been described: classic (sporadic), African (endemic), iatrogenic (immunosuppression-associated) and AIDS-associated (epidemic). The authors present a case of KS involving the external ear of a HIV-negative patient with a history of non-Hodgkin lymphoma and tuberculosis.

KEY WORDS: Kaposi's sarcoma • External ear • Lymphoproliferative disorders

RIASSUNTO

Il Sarcoma di Kaposi (KS) è una patologia neoplastica maligna su base vascolare, che principalmente coinvolge la cute e le mucose, caratterizzata dalla proliferazione di cellule endoteliali. L'etiologia del KS è ancora sconosciuta, sebbene sia stato riportato che fattori epidemiologici, ambientali e virali (es Herpes virus umano 8, HHV-8) possano avere un ruolo nella patogenesi di tale affezione. Ad oggi, sono state descritte quattro forme principali di KS: classico (sporadico), africano (endemico), iatrogeno (associato a stati di immunosoppressione) ed AIDS-relato (epidemico). Gli Autori presentano un caso di KS con coinvolgimento del condotto uditivo esterno, in una paziente HIV-negativa con storia di linfoma non-Hodgkin e tubercolosi.

PAROLE CHIAVE: Sarcoma di Kaposi • Orecchio esterno • Disordini linfoproliferativi

Acta Otorhinolaryngol Ital:EPUB February 09, 2012

Introduction

Kaposi's sarcoma (KS) was first described in 1872 by Moritz Kaposi¹. KS is an angioproliferative disorder characterized by proliferation of spindle-shaped cells (SC), neoangiogenesis, inflammation and oedema, categorized as an intermediate neoplasm due to the absence of conventional features of malignancy²⁻⁴. The clinical appearance of KS is classically described as pink, red, purple, or violaceous macules, papules or raised plaques, although nodular and more distinctly neoplastic-looking forms have also been described⁵.

The pathogenesis of KS is now recognized to be multifactorial. It is influenced by genetic and environmental factors and is related to a state of immunosuppression. Moreover, the lesion is associated with a rhadinovirus, namely human herpes virus 8 (HHV-8)⁶. HHV-8 DNA sequences have been found in approximately 95% of KS lesions in patients with both AIDS and non-AIDS KS⁷.

The transmission modalities of HHV-8 are still unknown, even if the higher incidence of KS in HIV homosexual males suggests a possible sexual transmission (through faeces). Moreover, HIV patients with KS mainly have oral cavity and rectal lesions, which seems to suggest local direct spreading. A limited number of review articles focus on the incidence of non-AIDS KS in the head and neck area^{8,9}. The oral cavity is the most common site of presentation, and in these cases the KS lesion is usually coexistent with others¹⁰.

The clinical appearance of KS is classically described as pink, red, purple or violaceous macules, papules or raised plaques; at later stages they can become nodular or exophytic and sometimes becomes ulcerous. Oral lesions can ulcerate more often than skin lesions. Particularly due to ulceration, lesions within the oral cavity may manifest with pain, burning and bleeding.

We describe a case of KS of the pinna and external auditory canal that developed in an HIV-negative patient with a history of tuberculosis and non-Hodgkin lymphoma.

Case report

We report the case of a female patient aged 72 years, referred to the Audiology Department of the University Hospital of Ferrara, for the evaluation of a slow-growing, violaceous, macular lesion in the right pinna and external auditory canal (Fig. 1). The patient complained of itching and occasional discharge from the external auditory canal. Right otoscopic examination revealed the presence of a violaceous and thickened macular lesion with keratosis of the concha that also involved the antero-inferior wall of the external auditory canal until about 4 mm from the tympanic membrane. The tympanic membrane was intact. Left otoscopic examination was normal. The remainder of the ENT examination was unremarkable, and in particular the oral cavity was normal and no cervical nodes were present. Pure tone audiometry showed right sensorineural hearing loss in the high frequency range (4-8 kHz).

At the time of examination, other cutaneous lesions were also present on the right arm (Fig. 2) and the postero-medial surface of the left leg.

The clinical history of the patient included peripheral polyneuropathy, miliary tuberculosis (pleural, intestinal and vesical), ankylosing spondylitis, pulmonary hypertension and chronic pericarditis. She also suffered from T-cell non-Hodgkin lymphoma for which she had been treated with 4 cycles of chemotherapy (CHOP: cyclophosphamide, doxorubicin, vincristine and prednisone). KS was diagnosed 8 months before by biopsying a lesion in the left leg. The exam showed the presence of a bi-phasic vascular spindle-cell growth occupying the entire thickness of the dermis.

Laboratory tests revealed that the patient was seropositive for human herpes virus type 4 (HHV-4; EBV) and HHV-8; she was HIV seronegative. The patient was taking prednisone, 5 mg/day, as maintenance therapy for non-Hodgkin's lymphoma.

The external ear lesion was treated with a local disin-



Fig. 2. Multiple skin lesions on the right arm.

fectant and with periodical toilette under microscopic guidance (local medication with gentamicin and betamethasone), thus avoiding the onset of infections and accumulation of debris in the external auricular canal. This led to rapid clearing of ear symptoms, while the macular lesion did not resolve.

At follow-up, after 18 months, no other localizations have appeared in the external ear.

Discussion

Four main clinical presentations of KS have been described: classic (sporadic), African (endemic), iatrogenic (immunosuppression-associated) and AIDS-associated (epidemic). Lesions are bluish-red macules or nodules and usually have multiple cutaneous localizations, but also lymph nodes and viscera have been described at the sites of presentation¹¹. The literature focuses particularly on HIV-related KS. In contrast, the other types of KS are underrepresented. About 60% of non-AIDS KS are localized on the skin (lower and upper limbs or trunk), and the head and neck is rarely involved¹²⁻¹⁵. The most recurrent sub-localization of the head and neck is the oral cavity. The oropharyngeal and conjunctiva mucosa have been observed in immunosuppressed-associated KS. The incidence of auricular lesions is lower, but in recent years has increased likely due to the greater use of immunosuppressive agents (i.e. organ transplantations, diffusion of chemotherapy)^{11 16 17}. At onset, they can appear as violaceous maculae that can become nodules or ulcerous. Normally the sites of tumour are coexistent and multifocal. For non-AIDS related KS, the male to female ratio is significantly lower¹⁵. Nevertheless, the mean age was also over 50 years. While most cases seen in Europe and North America occur in elderly men of Italian or Eastern European Jewish ancestry, the neoplasm also occurs in several other distinct populations: young black African adult males, prepubescent children,



Fig. 1. Lesion of the external ear involving the concha.

renal allograft recipients and other patients receiving immunosuppressive therapy¹⁸.

The aetiology of KS is unknown. However, it has been reported that several epidemiologic and environmental factors, as well as immunosuppression, play a role in the development and clinical course of the disease. In the last decade, epidemiologic and biologic evidence has suggested that a recently discovered herpes virus, namely KS herpes virus or HHV-8, is a required infectious cofactor responsible for all known forms of KS¹⁸. In particular, in non-AIDS associated KS immunodeficiency of any kind, iatrogenic, due to malignancy, tuberculosis¹⁹ or chemotherapy has been claimed to be the main causal factor in the development of KS²⁰. In the case presented, the previous history of miliary tuberculosis as well as previous chemotherapy could be related to the development of KS, as sources of immunodepression.

KS has a similar histopathologic appearance in all clinical subtypes. The early lesion (patch stage) is characterized by a proliferation of small veins and capillaries around one or more dilated vessels. A pronounced mononuclear inflammatory cell infiltrate, including mast cells, is often noted, as are scattered erythrocytes and hemosiderin deposits. There may be inconspicuous perivascular proliferation of spindle cells, but cellular atypia is minimal.

More advanced lesions are nodular and show increased numbers of small capillaries or dilated vascular channels interspersed with proliferating sheets of sarcomatous or atypical spindle cells, often with large numbers of extravasated erythrocytes and abundant hemosiderin deposition¹¹.

Main therapeutic options for KS include systemic treatments (i.e. chemotherapy or biological therapy particularly with recombinant interferon- α [IFN- α]), due to its immunomodulating and anti-angiogenic properties²¹ and local treatments (i.e. surgical excision; radiotherapy) mainly indicated for selected, small lesions. Optimal therapy for KS patients is still undecided in the literature as systemic therapy can be given in disseminated, progressive or symptomatic KS, while surgical excision and radiotherapy can be reserved for local disease²². It has been advocated that new advances in understanding the pathogenesis of KS, particularly the role of angiogenesis and growth factors, may help in the future development of additional therapies and in establishing a standardized protocol²².

Conclusions

Auricular involvement in KS is relatively rare: we found 4 previously-reported cases of KS involvement of the external ear^{11 16 17 23}. In 1983, Stearns described a case of KS arising as a primary lesion in the external auditory meatus, treated with surgical excision¹¹. In 1998, Delbruck described a case of external auditory canal KS with exten-

sion to mastoid, treated with radiotherapy¹⁶. Another case report concerns a solitary lesion of KS occurring in the helix of the ear in a healthy young patient, treated with surgical excision¹⁷. The last case described is a KS that developed in an HIV-negative patient affected by tuberculosis, which completely regressed with antituberculous therapy²³.

References

- 1 Kaposi M. *Idiopathisches multiples Pigmentsarkom der Haut*. Arch Dermatol Syph 1872;4:265-73.
- 2 Ramírez-Amador V, Martínez-Mata G, González-Ramírez I, et al. *Clinical, histological and immunohistochemical findings in oral Kaposi's sarcoma in a series of Mexican AIDS patients. Comparative study*. J Oral Pathol Med 2009;38:328-33.
- 3 Feller L, Lemmer J, Wood NH, et al. *HIV-associated oral Kaposi sarcoma and HHV-8: a review*. J Int Acad Periodontol 2007;9:129-36.
- 4 Fletcher CD, Unni KK, Mertens FLamovec J, et al. *Kaposi sarcoma*. In: Fletcher CD, Unni KK, Mertens F, editors. *Pathology and genetics of tumours of soft tissue and bone. World Health Organization classification of tumours*. Lyon, France: IARC Press; 2002. pp. 170-2.
- 5 Schwartz RA. *Kaposi's sarcoma: an update*. J Surg Oncol 2004;87:146-51.
- 6 Chang Y, Cesarman E, Pessin MS, et al. *Identification of herpesvirus-like DNA sequences in AIDS-associated Kaposi's sarcoma*. Science 1994;266:1865-9.
- 7 Moore PS., Gao S-J, Dominguez, G, et al. *Primary characterization of a herpesvirus agent associated with Kaposi's sarcoma*. J Virol 1996;70:549-58.
- 8 Jindal JR, Campbell BH, Ward TO, et al. *Kaposi's sarcoma of the oral cavity in a non-AIDS patient: case report and review of the literature*. Head Neck 1995;17:64-8.
- 9 Mohanna S, Ferrufino JC, Sanchez J, et al. *Epidemiological and clinical characteristics of classic Kaposi's sarcoma in Peru*. J Am Acad Dermatol 2007;53:435-41.
- 10 Eisele DW, Forastiere AA, Ang KK, et al. *National Comprehensive Cancer Network, Head and neck cancers*. J Natl Compr Canc Netw 2008;6:646-95.
- 11 Stearns MP, Hibbard AA, Patterson HC. *Kaposi's Sarcoma of the ear: a case study*. J Laryngol Otol 1983;97:641-5.
- 12 Farman AG, Uys PB. *Oral Kaposi's sarcoma*. Oral Surg 1975;39:288-96.
- 13 Beckstead JH. *Oral presentation of Kaposi's sarcoma in a patient without severe immunodeficiency*. Arch Pathol Lab Med 1992;116:543-5.
- 14 Schiff NF, Annino DJ, Woo P, et al. *Kaposi's sarcoma of the larynx*. Ann Otol Rhinol Laryngol 1997;106:563-7.
- 15 Gourin CG, Terris DJ. *Head and neck cancer in transplant recipients*. Curr Opin Otolaryngol Head Neck Surg 2004;12:122-6.
- 16 Delbrouck C, Kampouridis S, Chantrain G. *An unusual localisation of Kaposi's sarcoma: the external auditory canal*. Acta Otorhinolaryngol Bel 1998;52:29-36.

- ¹⁷ Babuccu O, Kargi E, Hoşnüter M, et al. *Atypical presentation of Kaposi's sarcoma in the external ear*. *Kulak Burun Bogaz Ihtis Derg* 2003;11:17-20.
- ¹⁸ Iscovich J, Boffetta P, Franceschi S, et al. *Classic Kaposi sarcoma: Epidemiology and risk factors*. *Cancer* 2000;88:500-17.
- ¹⁹ Castro A, Pedreira J, Soriano V, et al. *Kaposi's sarcoma and disseminated tuberculosis in HIV-negative individual*. *Lancet* 1992;339:868.
- ²⁰ Jakob L, Metzler G, Chen KM, et al. *Non-AIDS associated Kaposi's sarcoma: clinical features and treatment outcome*. *PLoS One* 2011;6:e18397.
- ²¹ Sullivan RJ, Pantanowitz L, Dezube BJ. *Targeted therapy for Kaposi sarcoma*. *Bio Drugs* 2009;23:69-75.
- ²² Aldenhoven M, Barlo NP, Sanders GJC. *Therapeutic strategies for epidemic Kaposi's sarcoma*. *Int J STD AIDS* 2006;17:571-8.
- ²³ Guler ZM, Kanbay A, Ciftci B, et al. *Kaposi sarcoma secondary to pulmonary tuberculosis: a rare case*. *South Med J* 2005;98:933-4.

Received: June 6, 2011 - Accepted: July 2, 2011

EPUB

The authors declare that there are no conflicts of interest.

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