

## Clinical Remission of Classic Kaposi Sarcoma with Topical 5% Imiquimod

### Remisión Clínica de Sarcoma de Kaposi Clásico con Imiquimod Tópico al 5%

To the Editor:

Kaposi sarcoma, in view of its benign and chronic nature, is usually now considered to be a vascular hyperplasia rather than a true tumor. It is always linked to *Human herpesvirus* (HHV) 8, which is a necessary though alone insufficient condition for the development of the lesions.<sup>1</sup> Four variants have been described: classic, endemic African, immunosuppression-associated, and human immunodeficiency virus (HIV) related.

The classic variant is most common in the Mediterranean population over 50 years of age. Clinically it presents as small, violaceous papules and macules situated particularly on the lower limbs and, less frequently, on the upper arms, forearms, trunk, eyelids, and genital area. Its clinical course is variable and although spontaneous resolution has been observed very occasionally, there is a tendency of pre-existing lesions to grow and for new lesions to appear.<sup>2</sup>

We present the case of a patient with classic Kaposi sarcoma, in whom the lesions had recurred after multiple treatments but then responded favorably to topical imiquimod, which led to their complete clinical and histological disappearance.

The patient was a 72-year-old man who was first seen in the dermatology department in 1998 for multiple, small, violaceous papules on the right foot. Biopsy of one of the lesions gave a diagnosis of Kaposi sarcoma and serology for hepatitis B and C viruses and HIV were negative. Thus, with the diagnosis of classic Kaposi sarcoma, treatment was started with local radiation therapy.

After remaining asymptomatic for a year, the lesions reappeared on the same foot (first at a distance from the irradiated area and years later in the same area) and then on the left foot and on the glans penis. Periodic treatment with electrocoagulation and curettage was applied to

both feet and continued up to the present time, without achieving complete resolution, and after several attempts at eradication of the lesions on the penis by means of surgical excision, it was decided to use local radiotherapy.

In view of the multiple recurrences on both feet (Figures 1A and 2A), it was finally decided to start treatment with 5% imiquimod cream on the lesions on the dorsum of the right foot on alternate days for a period of 10 weeks.

During the treatment with imiquimod the patient suffered very little inflammation in the treated area, and after 1 month the lesions had practically resolved; complete healing was achieved at 10 weeks (Figures 1B, 2B, and 2C).

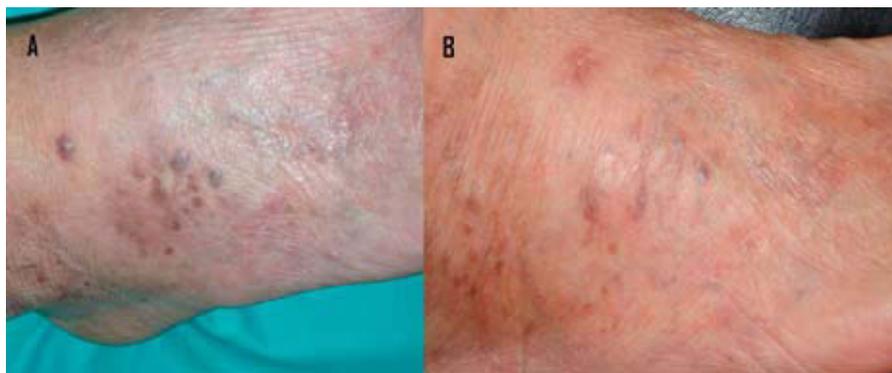
At the time of writing this report, 3 months after completing treatment, the patient remains in complete clinical and histological remission of the lesions on the right foot and has started the same treatment on the lesions of the left foot.

Classic Kaposi sarcoma is a variant with a very prolonged and benign clinical course. Some authors consider that, in addition to HHV-8, diabetes and chronic systemic corticosteroid treatment<sup>2,3</sup> are risk factors for the appearance of Kaposi sarcoma due to the associated immunosuppression, and that smoking acts as a protective factor.<sup>4</sup>

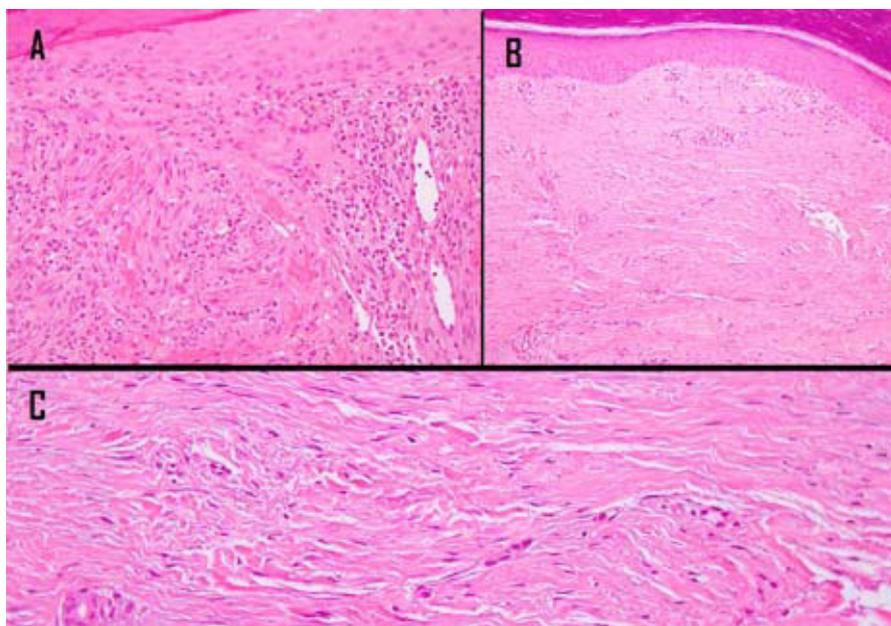
The lesions are unlikely to show spontaneous regression and, despite the use of multiple treatments, they usually recur. Treatment must be individualized, taking into account the patient's underlying conditions (presence or absence of immunosuppression), whether the lesions are single or multiple, and whether or not they affect regions other than the skin. Surgical excision is therefore a good therapeutic option in isolated, easily accessible lesions in immunocompetent patients, and local radiation therapy can be used in the case of multiple lesions.

Other treatments used include intralesional injection of vinblastine, the application of alitretinoin cream,<sup>5</sup> cryotherapy, laser or photodynamic therapy, and systemic chemotherapy in cases of visceral involvement.

With respect to topical imiquimod, apart from its functions as an immune response modifier,<sup>6</sup> it has been shown to have apoptotic and antiangiogenic activity; this is



**Figure 1** A, Multiple violaceous papules on the dorsum of the right foot prior to treatment with imiquimod. B, Clinical image of complete remission after 10 weeks of treatment.



**Figure 2** A, multiple vessel lumens in the dermis surrounded by a lymphocytic inflammatory infiltrate, observed in the Kaposi sarcoma lesion prior to starting treatment with imiquimod. B and C, Endothelial hyperplasia and fibrosis with no signs of Kaposi sarcoma in the treated lesion.

the basis on which it is starting to be used in other diseases such as Kaposi sarcoma<sup>7</sup> and infantile hemangiomas.<sup>8</sup>

In 2008, a prospective study of 17 immunocompetent patients was presented in which topical imiquimod was applied 3 times a week for 24 weeks.<sup>7</sup> Half of the patients showed a marked improvement and complete remission was achieved in 2 cases. Inflammation and irritation localized to the area of application was reported as an adverse effect.

In summary, we present a new case of classic Kaposi sarcoma treated with topical 5% imiquimod. This is the third reported case in which complete clinical remission has occurred after its use, and this therefore provides a new therapeutic option with minimal adverse effects and no systemic repercussions for a chronic and recurring disease.

### Conflicts of Interest

The authors declare no conflicts of interest.

### References

- Sullivan RJ, Pantanowitz L, Casper C, Stebbing J, Dezube BJ. Epidemiology, pathophysiology, and treatment of Kaposi sarcoma—associated herpesvirus disease: Kaposi sarcoma, primary effusion lymphoma, and multicentric Castlemann disease. *Clin Infect Dis*. 2008;47:1209-15.
- Sanmartín Jiménez O, Febrer Bosch I, Botella Estrada R, Oliver Martínez V, Calvo Catalá J, Aliaga Boniche A. Sarcoma de Kaposi con afectación visceral en paciente con artritis reumatoide en tratamiento esteroideo. *Med Cut ILA*. 1994;22:83-6.
- González-Sixto B, Conde A, Mayo E, Pardavila R, De la Torre C, Cruces M. Sarcoma de Kaposi asociado a corticoterapia sistémica. *Actas Dermosifiliogr*. 2007;98:553-5.
- Mbulaiteye SM, Atkinson JO, Whitby D, Wohl DA, Gallant JE, Royal S, et al. Risk factors for human herpesvirus 8 seropositivity in the AIDS Cancer Cohort Study. *J Clin Virol*. 2006;35:442-9.
- González de Arriba A, Pérez-Gala S, Goiriz-Valdés R, Ríos-Buceta L, García-Díez A. Sarcoma de Kaposi clásico tratado con alitretinoína tópica. *Actas Dermosifiliogr*. 2007;98:50-3.
- Schön MP, Schön M. Imiquimod: mode of action. *Br J Dermatol*. 2007;157:8-13.
- Célestin Schartz NE, Chevret S, Paz C, Kerob D, Verola O, Morel P, et al. Imiquimod 5% cream for treatment of HIV-negative Kaposi's sarcoma skin lesions: A phase I to II, open-label trial in 17 patients. *J Am Acad Dermatol*. 2008;58:558-91.
- Barry RB, Hughes BR, Cook LJ. Involution of infantile haemangiomas after imiquimod 5% cream. *Clin Exp Dermatol*. 2008;33:446-9.

B. Echeverría-García, O. Sanmartín, and C. Guillén

Servicio de Dermatología, Instituto Valenciano de Oncología (IVO), Valencia, Spain

\*Corresponding author.

E-mail address: osanmartinj@gmail.com (O. Sanmartín).