Kaposi Sarcoma, De Novo, in a Kidney Transplant Surgical Scar☆

Sarcoma de Kaposi, *de novo*, en una cicatriz quirúrgica de transplante de riñón

Dear Editor:

A 56 years old Caucasian man presented to our Dermatology consultation with a slow-growing solitary skin lesion on the abdomen of 3-4 months of evolution, accompanied of slight burning sensation. He had a medical history of hypertension, chronic kidney disease and secondary hyperparathyroidism, that had undergone kidney transplantation 5 months before. He was being treated with tacrolimus, mycophenolate mofetil, prednisolone, nifedipine, carvedilol and cotrimoxazole.

Clinical examination revealed a 20 cm large purple plaque located at the inferior extremity of the abdominal surgical scar with no other skin or mucosal lesions (Fig. 1).

A punch biopsy demonstrated dermal proliferation of spindle shaped cells with mild cytologic atypia, which formed slit-like channels and stained positive for human herpesvirus 8. These features are characteristic of Kaposi sarcoma in plaque/nodular stage (Fig. 2).

After the diagnosis of Kaposi sarcoma, tacrolimus was replaced by everolimus and he was referred to the Oncology department, to proceed with exclusion of extra-cutaneous manifestations, that proved to be negative.

Gradually the skin plaque on the patient scar disappeared and was replaced by an hyperpigmented brown patch (Fig. 3).

Kaposi sarcoma (KS) is an angioproliferative disorder that is associated with infection with human herpes virus 8 (HHV-8).[1]

Iatrogenic, immunosuppressive drug-associated KS is frequent among renal transplant recipients, accounting for < 3-4% of all neoplasms.[2]

The incidence of KS among solid organ transplant recipients is 500 times greater as compared with the general population's, suggesting a role for immunosuppression in the development of the disease.[3] Iatrogenic Kaposi sarcoma presents mainly with cutaneous manifestations.[3,4] A presentation of Kaposi sarcoma, de novo, in a scar is extremely rare, and this location can be explained by the Koebner's phenomenon. The Koebner phenomenon is the localization of skin disease to a site of trauma in an individual who is susceptible to that disease.[5] A key role has been suggested for basic fibroblast growth factor (b-FGF), a mitogen for endothelial cells and keratinocytes. Trauma, like surgical intervention, to susceptible skin may cause the release of this and other cytokines (interleukin-1, interleukin- 6, tumour necrosis factor-alfa, vascular endothelial growth factor, platelet-derived growth factor, granulocyte–macrophage colony-stimulating factor) triggering angiogenesis. The increased angiogenesis and the reactivation of the HHV-8 would contribute to the development of Kaposi sarcoma.[4]

The advent of inhibitors of the mammalian target of rapamycin (mTOR inhibitors), such as sirolimus and everolimus,

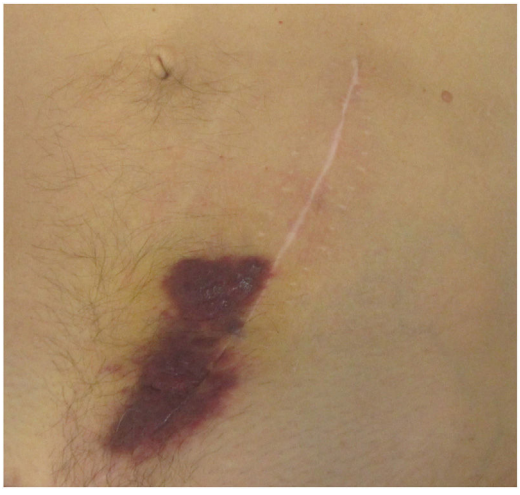

Figure 1 Cutaneous Kaposi sarcoma in the surgical scar.

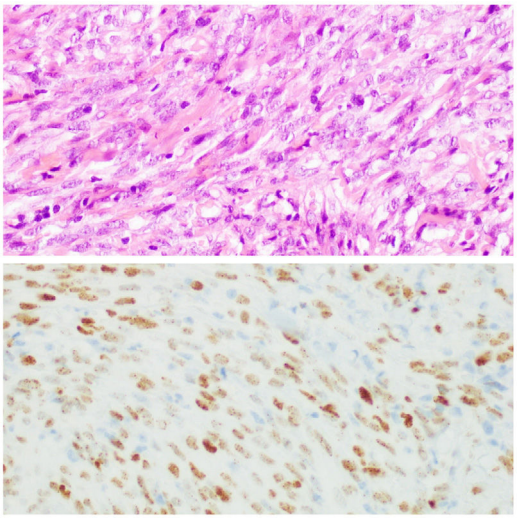

Figure 2 Histological examination characteristic of Kaposi sarcoma (hematoxylin-eosin stain; x400 magnification) and immunohistochemical staining for HHV8 (x400 magnification).

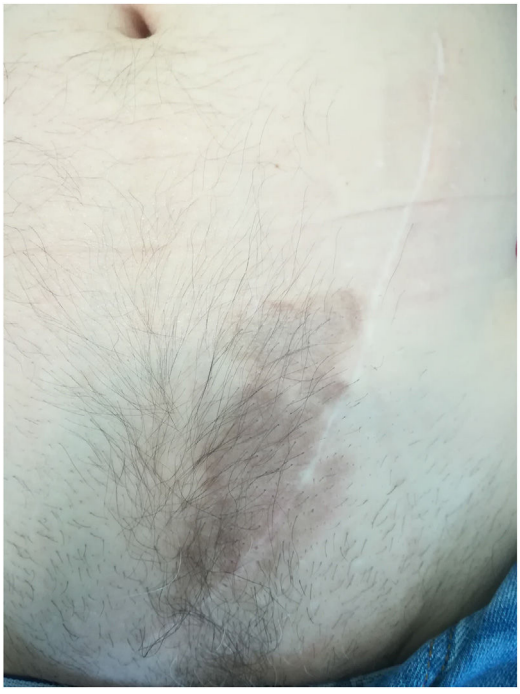

Figure 3 Regression of Kaposi sarcoma after switch of tacrolimus to everolimus.

☆ Please cite this article as: Santos Silva LF, Miroux Catarino A, Sordo Amaro C, Faro Viana I. Sarcoma de Kaposi, *de novo*, en una cicatriz quirúrgica de transplante de riñón. Actas Dermosifiliogr. 2021;112:671–672.

represents an alternative for the antirejection maintenance therapy. Furthermore, they can have a role in the treatment of Kaposi's sarcoma, since they also decrease the production of VEGF and inhibit the response of vascular endothelial cells to stimulation by VEGF. Therefore, mTOR inhibitors, not only inhibit the growth of certain vascularized tumors, while maintaining a lower risk of losing the renal graft.[6]

In the present case the patient presented only with a cutaneous lesion due to Kaposi Sarcoma, that resolved with the switch from tacrolimus to everolimus. This fact supports that mTOR inhibitors represent an alternative that allows the preservation of the renal graft, while treating Kaposi sarcoma.

References

1. Gao SJ, Kingsley L, Li M, Zheng W, Parravicini C, Ziegler J, et al. KSHV antibodies among Americans, Italians and Ugandans with and without Kaposi's sarcoma. Nat Med. 1996;2:925.
2. Penn I. Kaposi's sarcoma in organ transplant recipients. Transplantation. 1981;27:8–11.
3. Yaich S, Charfeddine K, Zaghdane S, Aoud N, Jarraya F, Kharrat M, Hachicha J. Sirolimus for the Treatment of Kaposi Sarcoma After Renal Transplantation: A Series of 10 Cases. Transplant Proc. 2012;44:2824–6, http://dx.doi.org/10.1016/j.transproceed.2012.09.025.
4. Kin D, Zcan G, Demirag A, Hizel N, Haberal M. The Koebner phenomenon in Kaposi's sarcoma in a renal transplant recipient. Br J Dermatol. 1998;139:346–8.
5. Stoebner P, Fabre C, Kabbaj N, Bismuth M, Pageaux GP, Meunier L. Koebnerizing Kaposi's Sarcoma Mimics a Laparotomic Hypertrophic Scar in a Liver Transplant Recipient. Liver Transpl. 2009;15:994–6, http://dx.doi.org/10.1002/lt.21739.
6. Detroyer D, Deraedt K, Scheoffski P, Hauben E, Lagrou K, Naesens M, et al. Resolution of diffuse skin and systemic Kaposi's sarcoma in a renal transplant recipient after introduction of everolimus: a case report. Transpl Infect Dis. 2015;17:303–7, http://dx.doi.org/10.1111/tid.12357.

L.F. Santos Silva,* A. Miroux Catarino, C. Sordo Amaro, I. Faro Viana

Departamento de Dermatología, Hospital de Egas Moniz, Centro Hospitalario de Lisboa Occidental, Lisboa, Portugal

* Corresponding author.
E-mail address: leandrofilipe@hotmail.com (L.F. Santos Silva).

https://doi.org/10.1016/j.adengl.2021.03.014

Advanced Cutaneous Squamous Cell Carcinoma Treated with Pembrolizumab☆

Carcinoma epidermoide cutáneo avanzado tratado con pembrolizumab

To the Editor:

Cutaneous squamous cell carcinoma (CSCC) metastatic to lymph nodes is an entity with low incidence (2.4% in males and 1.1% in females), which often poses a therapeutic challenge. Traditionally, systemic treatment of nonresectable cases has involved platinum-based antineoplastic drugs and epidermal growth-factor inhibitors, with or without radiation therapy. Recent studies, however, increasingly point to immune checkpoint inhibitors as the most effective and safe alternative for treatment of locally advanced or metastatic disease. We report the case of a patient with CSCC metastatic to the lymph nodes, who showed a complete objective response after 6 months of treatment with pembrolizumab.

The patient was an 83-year-old woman who was treated for moderately differentiated and infiltrating CSCC with a thickness of 8 mm, with no lymph-vessel or perineural involvement and spared margins, in the right mandibular ramus. Expression of programmed cell death ligand (PD-L1) was 30% in cancerous cells. The patient's personal history included a diagnosis of invasive ductal carcinoma that did not progress and was not treated. Three months after the intervention, the patient developed a metastatic conglomerate lymph-node mass in the angle of the right side of the jaw, measuring 4.5 cm; the mass was confirmed to be squamous cell carcinoma by means of fine-needle aspiration cytology. Curative radiation therapy was performed but the lymph-node disease progressed and an anterior cervical mass measuring up to 8 cm developed. In light of the nonresectable nature of the disease and its progression despite radiation therapy, with an ECOG score of 0, permission was sought for off-label use of pembrolizumab. The patient began treatment with pembrolizumab at a dosage of 2 mg/kg every 3 weeks, with rapid reduction in tumor size after 4 cycles and complete clinical and radiologic remission maintained over 6 (Figs. 1 and 2). The treatment was well tolerated, and the patient presented only a syndrome similar to rheumatic polymyalgia, which remitted with analgesics and 200 mg of hydroxychloroquine every 12 hours. At the same time, the ductal carcinoma showed no alternations in the control mammograms.

The role of immunotherapy in skin cancer is becoming increasingly important. PD-1 inhibitors are producing highly promising results for the treatment of locally advanced and metastatic CSCC,[1–5] with a response rate of up to 60% according to the latest reviews - mostly in the form of partial responses.[4] Cemiplimab, a programmed cell death receptor 1 (PD-1) antibody, has recently been approved with indications by the EMA and the FDA for locally advanced CSCC. Pembrolizumab is an anti-PD-1 monoclonal antibody indicated as adjuvant treatment in resected stage III melanoma, advanced melanoma, Hodgkin lymphoma, urothelial carcinoma, non-small cell lung cancer, and squamous cell carcinoma of the head and neck. Its mechanism of action affects the immunological synapse, inhibiting the coinhibitory activity of PD-1, thus favoring destruction of the tumor by intratumoral CD8 T cells.[6] Studies exist on the expression of PD-1 and PD-L1, and on the type of intratumoral inflammatory infiltrate and its relation to tumor characteristics[7] and treatment response.[8]

It is not clear that a cutoff exists in the expression of PD-1 and PD-L1 in CSCC tumor cells and its relation to the response to anti-PD-1 drugs, although a positive correlation appears to exist.[7,8] Similarly, expression of PD-L1 has also been linked to high-risk characteristics such as the infiltration pattern, perineural invasion, and immunosuppression.[7] To date, most publish results are of partial responses,[4] although

☆ Please cite this article as: Villegas-Romero I, Jiménez-Gallo D, Gutiérrez-Bayard L, Linares-Barrios M. Carcinoma epidermoide cutáneo avanzado tratado con pembrolizumab. Actas Dermosifiliogr. 2021;112:672–675.