

Topical Sirolimus 0.1% as Off-Label Treatment of Kaposi's Sarcoma

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Introduction

Kaposi's Sarcoma (KS, now more precisely referred to as Kaposi's Disease) is a vascular proliferative disorder associated with human herpesvirus 8 (HHV8) infection. Its classical form, Mediterranean Kaposi, is characterized by multiple red-purple macules, patches, and nodules typically involving the lower limbs of elderly subjects. Management of these patients can be challenging. Therapeutic options depend on various factors such as the number and types of lesions, the presence of lymphedema, age, immunosuppression, patients' compliance, and so on. For skin-limited KS, shaving or cryotherapy is an option for small macules or nodules, while the treatment of large patches and plaques is more complex. Many topical and systemic approaches have been evaluated, from elastic stocking to beta blockers, intra-lesional chemotherapeutic agents like vinblastine and bleomycin, electrochemotherapy, and so on [1].

Case Presentation

In our dermatology department, we treated thirteen patients with classical KS, mostly represented by large patches and plaques on the lower limbs, using topical galenic sirolimus (0.1% in Pentravan[®]) twice daily. The diagnosis was confirmed by a punch biopsy in all patients. Since June 2023, thirteen patients (eight males and five females, mean age 81.6) have been under treatment. The lesions mainly consisted in large plaques. They were previously treated with elastic compression without significant benefits. None of them was on beta blockers for other diseases. After three months, the lesions showed a significant reduction in skin infiltration, and after six months, some of the smallest ones had almost disappeared. Only two patient did not show any benefit. The patients are still under treatment, without any significant adverse events (Figure 1).



Figure 1. 79-year-old female patient's left foot. (A) panel shows a large red-purplish infiltrated plaque, confirmed as KS by an incisional biopsy. (B) panel shows the same foot after six month of sirolimus 0.1% in Pentrvan® applied morning and evening. At clinical examination, the infiltration has almost disappeared, while hyperpigmentation persists.

Conclusion

Sirolimus targets a serine threonine kinase known as mTOR (mammalian target Of rapamycin), which plays a crucial role in regulating cell growth, proliferation, and survival. For this reason, several novel anticancer drugs aim to inhibit this enzyme. Growth factors like IGF (insulin-like growth factor), EGF (epidermal growth factor), PDGF (platelet-derived growth factor), and VEGF (vascular endothelial growth factor) bind and activate receptors on the cell surface, initiating a cascade of intracellular pathways mediated by mTOR. Thus, increased activity of mTOR can alter metabolic pathways, increasing the risk of tumor development and neo-angiogenesis. HHV-8 genes like ORF-K1 and ORF-K15 are able to increase the levels of pro-inflammatory and pro-angiogenic mediators like VEGF, whose role has been established in KS pathogenesis [2]. Stallone et al. treated with systemic sirolimus 15 kidney-transplanted patients who had developed KS during immunosuppressive anti-reject treatment with cyclosporine. The authors showed that systemic sirolimus was effective in resolving KS without causing kidney rejection [3]. In our clinical practice, KS is mostly encountered in older people often with many

comorbidities. Therefore, our proposed approach involves using topical sirolimus 0.1% to be applied morning and evening, exerting an anti-proliferative action on endothelial cells without significant immunosuppression. The small cohort patients is the main limitation of this study, but the rationale is well-founded on the literature and clinical practice. More studies need to demonstrate the efficacy and safety of sirolimus 0.1% in the management of Mediterranean KS.

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