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Successful Treatment of Suborbital Pyogenic Granuloma with Topical Imiquimod

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Abstract

Pyogenic granuloma (PG) is a benign vascular proliferation of the skin and mucosae, that has been treated with different regimens with variable success and recurrence rates; however, the management of PG still remains a challenging issue, particularly in children and in adult cases with lesions localized at sites difficult to access. Imiquimod, a member of the imidazoquinoline family of immune response modifiers, is a topically applicable TLR-7/8 agonist that reveals potent antiviral, antitumor, immunoregulatory and antiangiogenic properties. In the present paper we report the case of a 9-year old boy with suborbital pyogenic granuloma, successfully treated with topical daily application of imiquimod 5% cream without occlusion. 8 weeks after onset of topical imiquimod treatment a complete resolution of the lesion without any scarring was observed. No systemic side effects were seen and the patient remained well throughout the course of therapy. He is presently completing a 15-month follow-up and has revealed no relapse. The findings of the present study suggest that topical imiquimod is a safe, effective and well-tolerated treatment for PG in children, even at difficult to treat areas like the suborbital region.

Keywords

Pyogenic Granuloma, Imiquimod, Children, Angiogenesis

1. Introduction

Pyogenic granuloma (PG) (granuloma telangiectaticum or lobular capillary haemangioma) is a benign vascular proliferation of skin and mucosae. Typically, it presents as a mostly solitary, rapidly developing, hemorrhagic and ulceration-prone, purple, angiomatous papule or nodule usually located on the face, fingers, toes and trunk, and on mucous membranes, as well. Predisposing factors

for the occurrence of PG include minor trauma, chronic irritation, infection, viral oncogenes, increased levels of female sex-hormones (e.g. pregnancy), microscopic arteriovenous anastomoses and drugs (e.g. retinoids) [1] [2].

Although spontaneous resolution of PG is possible, therapy is usually necessary. A variety of therapeutic regimens have been used in the management of PG, with variable success and recurrence rates [3], including surgical and shave excision, curettage, electrodessication, laser therapy, cryotherapy, radiotherapy, sclerotherapy, topical and systemic steroids, microembolization, topical timolol or imiquimod and intralesional bleomycin [4] [5].

In the present paper we report the case of a 9-year-old boy with suborbital pyogenic granuloma, which was successfully treated with topical application of imiquimod 5% cream.

2. Case Report

A previously healthy 9-year-old boy presented with a three-week history of a solitary vascular lesion that had developed on his facial skin subsequent to minor trauma. Physical examination showed a healthy-looking boy with normal growth and development. In his right suborbital region, 1.2 cm under his lower eyelid, there was a red-violet spherical nodule with a diameter of 4 mm (**Figure 1(a)**) that was clinically consistent with pyogenic granuloma. The results of routinely performed laboratory investigations were either negative or within normal range. The parents of the patient were informed about the existing therapeutic options (described in the Introduction) and the possible side effects, declined the surgical excision of the lesion and gave their written consent for its topical treatment with imiquimod 5% cream once daily without occlusion. Considering the proximity of the lesion to the patient's eye, we chose this therapeutic approach due to its non-invasive nature and the minimal risk of scaring, as compared to tissue-destructive procedures. Already after 3 days of treatment, a progressive inflammation with swelling of the lesion and perilesional erythema became evident, whereas spontaneous bleeding with formation of hemorrhagic crusts has repeatedly occurred in the second and third week of treatment (**Figure 1(b)**). Thereafter, despite further topical application of imiquimod there was a progressive shrinking of the lesion (**Figure 1(c)**).

Finally, 8 weeks after onset of treatment a complete resolution of the lesion without any scarring was observed (**Figure 1(d)**). No systemic side effects were seen and the patient remained well throughout the course of therapy. He is presently completing a 15-month follow-up and has revealed no relapse. The parents of the patient gave their written consent for this case report to be published.

3. Discussion

Imiquimod, representative of the imidazoquinoline family of immune response modifiers, is a topically applicable TLR-7/8 agonist known to stimulate the cutaneous innate immunity and the cellular arm of the adaptive immune response

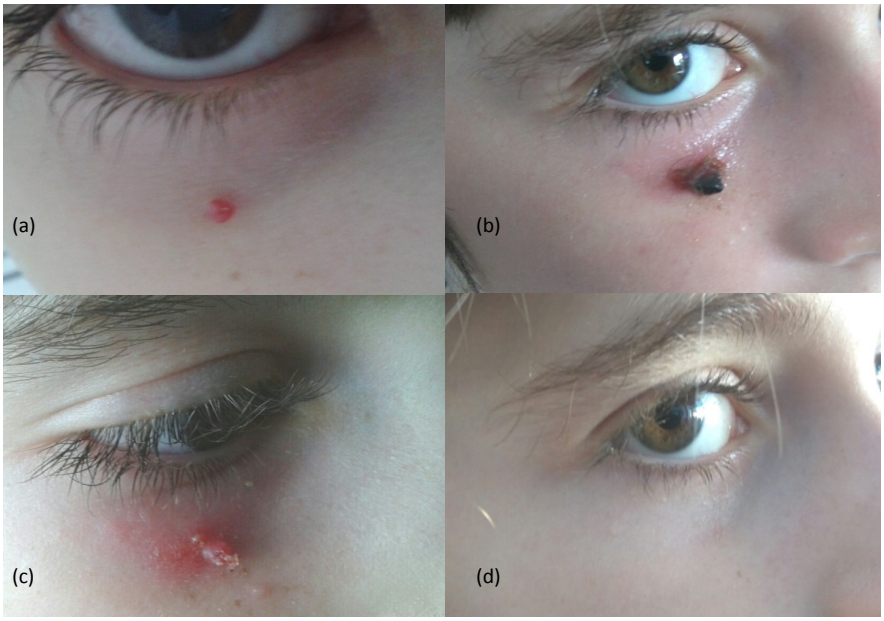

Figure 1. (a) Clinical aspect of the suborbital pyogenic granuloma prior to onset of therapy; (b) Hemorrhagic crust formation after 2 weeks of therapy; (c) Progressive shrinking of the lesion after 5 weeks of therapy; (d) Complete resolution of pyogenic granuloma after 8 weeks of topical treatment with imiquimod 5% cream once daily without occlusion.

and to exerting potent antiviral, antitumor, antiangiogenic and immunoregulatory effects [5] [6] [7]. These actions are accomplished, at least in part, through secretion of pro-inflammatory cytokines by monocytes, macrophages and dendritic cells, subsequent to drug's binding to Toll-like receptors [8].

Imiquimod is approved for the treatment of external genital and perianal warts in adults, basal cell carcinomas and actinic keratoses. It is also used for a variety of off-label indications including cutaneous viral infections and neoplasms [9]. Our team demonstrated for the first time that topical application of imiquimod induces systemic immunomodulation and significant alterations in peripheral blood lymphocyte subsets of healthy individuals [7]. We also successfully used imiquimod in the treatment of various skin disorders including pyogenic granuloma, herpes labialis, lichen striatus, granuloma annulare and molluscum contagiosum [10]-[15].

Although the pathogenetic mechanisms of PG are far from been fully understood, there is accumulating evidence suggesting an imbalance between angiogenesis enhancers(increased expression of vascular endothelial growth factor, basic fibroblast growth factor and decorin) and angiogenesis inhibitors (reduced expression of angiostatin) [16] [17]. A recent genetic study on vessels derived from cutaneous PG lesion identified a gene signature including genes of the nitric oxide pathway and those related to hypoxia-induced angiogenesis and vascular injury, like the tyrosine-kinase receptor FTL4 [18]. Thus, PG may be regarded as a reactive lesion resulting from tissue injury, followed by an impaired wound healing response, during which vascular growth is driven by FLT4 and the nitric oxide pathway.

Imiquimod, apart from its immunomodulatory effects, also exerts potent antiangiogenic activity [12] [19] [20] due to induction of antiangiogenic cytokines (interferons α, β and γ, and interleukins 10, 12 and 18), promotion of endothelial cell apoptosis, downregulation of proangiogenic factors (FGF-2 and matrix metalloproteinase-9) and upregulation of endogenous inhibitors of angiogenesis (thrombospondin-1 and tissue inhibitor of matrix metalloproteinase-1). These antiangiogenic effects could probably restore the upregulated neovascularization observed in PG and contribute to the therapeutic action of imiquimod.

In our case, a 9 year-old boy with a PG located 1.2 cm under his lower eyelid, topical treatment with imiquimod (once daily without occlusion) led to a complete remission of the lesion within 8 weeks and to an excellent cosmetic result. Besides the expected inflammatory reaction of the resolving lesion, moderate erythema was observed in the perilesional skin, whereas no systemic side-effects were seen. The patient is presently completing a 15-month follow-up and has revealed no relapse.

Successful treatment of PG with imiquimod in children has been previously reported [21] [22] [23] [24] [25]. However, only one paper on imiquimod treatment of PG lesion with suborbital localization has been published [21].

4. Conclusion

Our findings taken together with those of the literature suggest that imiquimod is a safe, effective and well-tolerated treatment for PG, even at difficult to treat areas like the suborbital region. This is of particular importance in pediatric patients whose parents usually refuse invasive treatment options for which general anesthesia is often required.

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