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Topical timolol for treatment of persistent granulation tissue in the setting of severe hidradenitis suppurativa

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Abstract

Hidradenitis suppurativa (HS) is a potentially debilitating dermatological disease that negatively impacts patients' quality of life. Severe cases can be further complicated by persistent granulation tissue at the ostia of sinus tracts, which may prove recalcitrant to standard interventions. Herein we report such a case in which a patient experienced significant improvement from severe HS but was left with persistent granulation tissue that complicated his course of recovery. When standard interventions failed, we elected to begin treatment with topical timolol. After three months, the majority of the granulation tissue had regressed and has remained quiescent after 12 months of follow up. The patient has tolerated the treatment well and continues to use topical timolol daily as needed for flares. We believe that topical timolol can provide a practical and painless alternative to current invasive and expensive therapies for persistent granulation tissue associated with severe HS.

Keywords: timolol, granulation tissue, hidradenitis suppurativa

Introduction

Hidradenitis suppurativa (HS) is a chronic dermatosis with painful, deep-seated, inflamed

nodules and sinus tracts that occur in skin bearing apocrine glands [1]. Mild to moderate cases are managed with topical antibiotics and antiseptics as well as intralesional corticosteroids and oral antibiotics [2, 3]. In severe cases, systemic immunosuppressive agents and surgical interventions are indicated. In the authors' experience, dramatic improvement may occur when severe cases are treated with anti-tumor necrosis factor agents only to be complicated by residual granulation tissue at sites of chronically draining sinus tracts. We present a case in which large areas of granulation tissue proved recalcitrant to intralesional steroids and curettage but responded dramatically to topical timolol.

Case Synopsis

A 26-year-old man with diabetes mellitus and asthma presented with a 12-month history of debilitating HS associated with persistent tachycardia and a 60-pound unintentional weight loss. The patient had recently been admitted to another hospital out of concern for sepsis. Upon admission, the patient's HS was managed with adalimumab, which was promptly discontinued owing to concern for sepsis. He was managed with serial debridement and broad-spectrum antibiotics without improvement. Blood and tissue cultures throughout his admission were negative.

The patient reported painful actively draining nodules and sinus tracts in several areas. He had previously failed numerous oral antibiotics, topical clindamycin, and dilute bleach soaks. Physical examination revealed a cachectic appearing man in mild distress. The patient was tachycardic with a pulse rate of 150. Skin examination was notable for inflamed nodules and actively draining sinus tracts in bilateral axillae, gluteal cleft, perineum, and inguinal folds. Laboratory tests were remarkable for microcytic anemia (hemoglobin level 9.3g/dL, mean corpuscular volume $76\mu\text{m}^3$), leukocytosis ($19400/\mu\text{L}$), and thrombocytosis ($576000/\mu\text{L}$). Thyroid stimulating hormone level was normal.

After reviewing his admission records, we suspected that the patient was never septic but was experiencing an HS flare despite treatment with adalimumab. We started the patient on clindamycin 1% lotion, minocycline 100mg twice daily, and infliximab 5mg/kg every 8 weeks. This resulted in resolution of his chronic tachycardia, anemia, and thrombocytosis. In addition, he experienced an 80-pound weight gain and dramatic improvement in his HS with resolution of active drainage from all previously involved areas. As the inflammation subsided, the patient was left with several areas of granulation tissue at sites of prior draining sinus tracts (**Figure 1A**).



Figure 1. A) In October 2018, left axilla after treatment with intralesional steroids and curettage but before treatment with topical timolol. Note the lack of actively draining sinus tracts or inflammation, but extensive scarring and persistent exuberant granulation tissue. **B)** In January 2019, left axilla after three months of timolol treatment. Note continued control of inflammation and drainage with infliximab and dramatic regression of granulation tissue after treatment with topical timolol.

These areas of granulation tissue bled readily and were quite bothersome to the patient. No improvement was noted with injections of triamcinolone 40mg/ml solution. The granulation tissue was also extirpated with curettage but quickly recurred. Having read previous reports regarding treatment of lobular capillary hemangiomas (pyogenic granulomas) with topical timolol, we instructed the patient to apply several drops of timolol 0.5% ophthalmic gel-forming solution to all involved areas once daily [4, 5]. In three months, the areas of granulation tissue had regressed dramatically (**Figure 1B**).

Case Discussion

As granulation tissue and lobular capillary hemangiomas are histologically similar, we hypothesized that both conditions might respond to similar interventions. Because our patient failed more invasive interventions, we elected to treat him empirically with topical timolol, which was highly effective and painless [4, 5].

Timolol is a nonselective β -adrenergic antagonist that can induce vasoconstriction and thus, affect angiogenic events to promote endothelial cell

apoptosis. It is an effective first-line treatment for lobular capillary hemangiomas and infantile hemangioma and has been reported to promote healing of chronic wounds [6]. Since granulation tissue is highly vascular, we suspect that timolol-induced endothelial cell apoptosis was likely the driving mechanism behind the regression of granulation tissue in this case.

Conclusion

Hidradenitis suppurativa (HS) is a chronic dermatosis the treatment of which can be complicated by residual granulation tissue recalcitrant to conventional therapies at sites of chronically draining sinus tracts. In our case, we found that topical timolol can provide a highly effective and painless treatment in patients with recalcitrant granulation tissue that can complicate treatment of severe cases of HS. Our unique case may contribute to the ever-expanding list of indications of topical beta blockers for the treatment of various cutaneous diseases.

Potential conflicts of interest

The authors declare no conflicts of interests.

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