BRIEF ARTICLES

Timolol for Treatment of Recalcitrant Pyogenic Granulomas: a Case Report and Review of the Literature

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ABSTRACT

Importance: Pyogenic Granuloma (PG) is a benign vascular tumor that forms commonly on the face, oral mucosa, or a site of previous injury. Though some PGs resolve spontaneously, most require some-to-multiple form(s) of treatment to prevent bleeding, ulceration, and scarring. Current treatment options for PGs include cryotherapy, laser, electrodessication, curettage or shave excision, sclerotherapy, corticosteroid injections, and imiquimod 5% cream. Timolol 0.5% ophthalmic solution has been used as a noninvasive topical treatment for PG in the pediatric population.

Objective: To present a case of successful treatment of a recalcitrant PG with topical timolol, and to report on the current literature for similar cases.

Case Presentation: We present a case of a 40-year-old healthy female who developed a biopsy-proven PG on her index finger. This is the first reported case to successfully use tangential biopsy and electrodessication followed by twice daily topical Timolol to treat recalcitrant PG.

Conclusions: This case supports the use of 0.5% Timolol ophthalmic solution and demonstrates that it is a safe and economical therapy for adult patients with recurrent PGs. A review of the current literature is discussed and supports timolol as an easy and economical therapy option.

INTRODUCTION

Pyogenic Granuloma (PG) is a benign vascular tumor also known as a lobular capillary hemangioma. It grows rapidly on the skin or mucosal surfaces, commonly affecting the face, oral mucosa, and sites of previous injury. PGs appear as a solitary, pedunculated lesion with a friable surface that bleeds easily.[1] Though some PGs resolve spontaneously, treatment is often warranted to prevent bleeding, ulceration, and scarring. Current treatment techniques include cryotherapy, laser, electrodessication, curettage or shave excision, sclerotherapy, corticosteroid

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injections, and imiquimod 5% cream either alone or in combination.[2] Unfortunately, these treatment options have been associated with pain, scarring, or other side effects.[3] This poses a challenge when dealing with pediatric patients or when treating on sensitive areas like the face. Beta blockers, such as propranolol, have shown great success in reducing the size of vascular tumors like hemangiomas.[4] The exact mechanism of growth inhibition on capillary tumors by Beta blockers is unknown. It is thought that they inhibit growth through four main mechanisms: vasoconstriction, inhibition of angiogenesis, induction of apoptosis, and recruitment of endothelial progenitor cells.[5,6] Timolol 0.5% ophthalmic solution is thought to work similarly on pyogenic granulomas and has been reported as an effective noninvasive treatment option for multiple cases.[6] We report a challenging case of a woman with recalcitrant PG that was successfully treated with topical Timolol.

CASE PRESENTATION

A 40-year-old Caucasian female presented to the dermatology clinic in November 2015 for the evaluation of a bump on her right index finger (Figure 1A, B). She denied any previous injury to the site. A tangential biopsy was performed and histopathology of the lesion was consistent with pyogenic granuloma. Hemostasis was obtained with aluminum chloride, and electrodessication was performed. When the patient returned to clinic 1 month later, the lesion had regrown and was treated with a second tangential excision, repeat electrodessication, and a 5 mg/mL intralesional kenalog injection into the base of the lesion. Three months later, the patient reported regrowth of the lesion and returned to clinic. After reviewing the literature, a trial of Timolol 0.5% ophthalmic solution twice daily was started. The lesion did not improve with Timolol 0.5% twice daily alone, and the patient returned to clinic 2 weeks later with continued bleeding and pain. The recurrent lesion was treated with a third tangential excision with electrodessication, and the patient was instructed to apply one drop of Timolol 0.5% ophthalmic solution to the base of the lesion twice daily. One month follow up via telephone revealed the lesion had not recurred and the patient reduced her Timolol applications to once daily. Per our request during the one month telephone follow up, the patient sent photos of the nearly resolved lesion to the clinic. (Figure 2A, B)

A.

B.

FIGURE 1: Recurrent pyogenic granuloma after two shave excisions

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A.

B.

FIGURE 2: Patient-provided follow-up images of resolution of pyogenic granuloma

DISCUSSION

Pyogenic Granuloma (PG) can be difficult to treat and often recurs. Treatment options generally include one or more of the following options: cautery, laser, excision, curettage, sclerotherapy, or cryotherapy. Imiquimod 5% cream is a less invasive option for treating PG, but it can be limited by its adverse effects of crusting, superficial scarring, and dyspigmentation.[7] Based on our review of the literature, Timolol 0.5% ophthalmic solution has been utilized as either a primary or adjunctive therapy for PGs. Timolol is a beta-adrenergic receptor blocker, which is hypothesized to work similarly to propranolol, which can be used to treat cutaneous vascular tumors such as hemangiomas.[4] It is thought to work through local blockade of the vascular beta receptors, resulting in vasoconstriction, decreased vascular growth factors, and decreased blood flow into the vascular tumor which inhibits growth and proliferation.[5,6] Noninvasive topical Timolol is an important alternative for the treatment of PGs in pediatric patients who cannot undergo invasive procedures for PGs located on sensitive areas such as the face. Topical application of Timolol is not associated with systemic side effects of beta adrenergic blockers and does not require any monitoring.[8] Treatment is often painless, noninvasive, and cheap compared to alternate therapies. We present the first reported case to successfully treat PGs using tangential biopsy and electrodessication followed by twice daily topical Timolol. There are currently 19 cases, 5 adult and 14 pediatric, in the literature that have shown improvement or complete resolution of PG with either timolol alone or as adjuvant therapy (Table 1). Our case and review of the current literature suggests that topical Timolol 0.5% Ophthalmic Solution may be an effective single agent or adjunctive therapy for primary and recurrent pyogenic granuloma in both children and adults. More studies are needed in this area of research to provide additional evidence that supports this treatment.

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Table 1. Previously reported cases of pyogenic granulomas treated with timolol

Author / year	Age (yrs)	Sex	Location	Diameter (mm)	Treatment	Treatment Duration	Treatment response
Wine L, et a.l 2013 (6)	32 mos	F	Cheek	N/A	Curettage + 0.5% Timolol GFS (BID)	6 months	Complete Resolution
	4	F	Cheek	N/A	2% Timolol GFS (BID)	2 months	Partial response at 2 months, Resolution at 3 months
	6	M	Lower eyelid	N/A	2% Timolol GFS (TID)	2 months	Partial response at 2 months, Near resolution at 4 months
	7	F	Medial canthus	N/A	2% Timolol GFS (TID)	6 weeks	Partial Response
	8	M	Scalp	N/A	0.5% Timolol GFS (TID)	12 weeks	Partial response at 6 weeks, Complete Resolution
	5	F	Forearm	N/A	Electrocautery →		
					2% Timolol GFS (TID)	8 weeks	Partial response
	6	M	Buccal mucosa	N/A	Excision x4, intralesional triamcinolone, potassium titanyl phosphate laser →		Resolution
					Propranolol 2mg/kg/day (BID)	6 months	
Khorsand K, et a. 2014 (11)	5 mos	F	Cheek	7mm	0.5% Timolol GFS	1 month	Mild improvement
					0.5% Timolol GFS	8 months	Complete resolution
Malik M, et al. 2014 (13)	14	N/A	Finger	N/A	0.5% Timolol GFS (BID)	3 weeks	Complete resolution after 7 months
Milsop JW, et al. 2014 (2)	39	M	Scalp	50mm	Acticoat 7-silver coated low adherent primary wound dressing →	2 weeks	No improvement
					5% topical imiquimod (QHS), 1% topical clindamycin (BID), oral doxycycline 100mg (BID) →	1 month	Mild improvement
					Pulsed dye laser + 0.5% timolol GFS + oral doxycycline 100mg (BID) →	4 weeks	Improvement + intermittent bleeding
					Vascular laser + silver nitrate + intralesional injections of triamcinolone acetonide (10mg/ml) →	3 months	Complete resolution
					Vascular lasers + intralesional steroids + 0.5% Timolol GFS		
Resenstein R, et al. 2015 (14)	39	F	Periungual	N/A	0.5% Timolol GFS (1-2x daily) + Mupirocin (PRN)	1 month	Complete Resolution

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Table 1 (continued). Previously reported cases of pyogenic granulomas treated with timolol

Author / year	Age (yrs)	Sex	Location	Diameter (mm)	Treatment	Treatment Duration	Treatment response
Gupta D, et al. 2016 (10)	26	M	Finger	7mm	0.5% Timolol maleate (ii gtt QID)	3 days	Complete resolution
	20	F	Lip	6mm	0.5% Timolol maleate (ii gtt QID)	2.5 months	Partial response
	16	M	Scalp	13mm	0.5% Timolol maleate (ii gtt QID)	22 days	Complete resolution
	16	M	Arm	30mm	0.5% Timolol maleate (ii gtt QID)	24 days	Complete resolution
	50	M	Scalp (multiple)	1-4mm	0.5% Timolol maleate (ii gtt QID)	16 days	Complete resolution of smaller papules. No response of other lesions
	15	M	Abdomen	4mm	0.5% Timolol maleate (ii gtt QID)	12 days	Partial response
Chiriac A, et al. 2016 (9)	2	M	Palpebral area	N/A	0.1% Timolol in occlusive dressing (BID) + 2 applications of 70% Trichloroacetic Acid (1 every 7 days)	2 weeks	Complete resolution
	13 mos	F	Face	N/A	0.1% Timolol in occlusive dressing (BID) + 1 application of 70% Trichloroacetic Acid	2 weeks	Complete resolution
Knöpfel M, et al. 2016 (12)	2	M	Scalp	N/A	0.5% Timolol GFS (BID)	1 month	Almost complete resolution
Hoyer P, et al. 2017	40	F	Finger	N/A	Electrodessication →	1 month	Regrowth of lesion
					Electrodessication + Kenalog 5mg/ml →	1 month	Regrowth of lesion
					0.5% Timolol GFS (BID) →	2 weeks	Bleeding and pain
					Electrodessication + 0.5% timolol GFS (BID)	1 month	Complete resolution

CONCLUSION

Topical Timolol was an effective treatment for our case of Pyogenic Granuloma. No side effects were associated with the treatment and a complete resolution of the lesion was observed. Our case report supports the use of 0.5% Timolol ophthalmic solution as a safe and cost effective adjunctive option for PG therapy. Our review of the literature suggests that topical Timolol may be effective as a single agent or as adjunctive treatment for primary and recurrent PGs in both pediatric and adult populations. More studies are needed in this area of research to provide additional evidence that supports this treatment.

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