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Journal

Dermatology Online Journal, 20(3)

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Publication Date

2014

DOI

10.5070/D3203021726

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Peer reviewed

Volume 20 Number 3 March 2014

Case Report

Resolution of Recalcitrant Pyogenic Granuloma with Laser, Corticosteroid, and Timolol Therapy

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Dermatology Online Journal 20 (3): 4

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Abstract

A pyogenic granuloma (PG) is a rapidly growing benign vascular tumor that can be found on the skin or subcutaneous tissue. While some pyogenic granulomas may resolve spontaneously, most have a tendency to bleed easily and require treatment. Current therapeutic modalities include topical imiquimod, cryotherapy, electrodessication, curettage, excision, laser therapy, sclerotherapy, and microembolization. We report a recalcitrant case of chronic pyogenic granuloma occurring on the scalp of a healthy young male which was unresponsive to conventional surgical and non-surgical modalities. Ultimately, aggressive laser therapy, intralesional triamcinolone acetonide injections, and topical timolol application led to complete resolution and healing.

Introduction

Pyogenic granuloma (PG) is a rapidly growing benign vascular tumor on the skin or subcutaneous tissue (Table 1). Clinically, PGs present as red or purple smooth glistening papules that grow rapidly within a few days or weeks and occur most commonly on the lips and fingers. Also known as lobular capillary hemangiomas, PGs often bleed easily and commonly result after minor trauma, although they can develop spontaneously. Histologically, they appear as hyperplastic clusters of capillaries, separated by thin fibrous bands arranged in a lobular configuration. Approximately 60% of PG cases occur between the ages of 10 and 40, and they are more common in females. Approximately 60% of PG cases occur between the ages of 10 and 40, and they are more common in females.

PGs may resolve on their own; however, treatment is often required. Many therapeutic options are available including non-surgical and surgical options: topical imiquimod ⁵, cryotherapy, electrodessication, curettage or shave removal, surgical excision, a variety of laser therapies, microembolization⁶, and sclerotherapy. We report a challenging case of a healthy young male presenting with a chronic scalp wound with biopsies consistent with a pyogenic granuloma that ultimately healed with a multimodal approach of minimally invasive procedures and topical therapy.

Table 1: Overview of Pyogenic Granuloma.

Table 1. Overview of Pyogenic Granuloma		
Location	Commonly found on the neck, face, arms and hands	
	Can occur anywhere on the skin and mucosa	
	May be intravascular or subcutaneous	
Age	All age groups	
Sex	Mucosal variant more common in females	
Appearance	Red papule that grows rapidly and bleeds easily	
	Histologically resembles granulation tissue supplied with innumerable	
	capillary blood channels.	
Differential	Hemangioma	Amelanotic melanoma
Diagnosis	Kaposi sarcoma	Spitz nevus
	Nevus	Basal cell carcinoma
	Verruca	Squamous cell carcinoma
Treatment	Surgical Excision	
Options*	Most commonly used modality	
	Recurrence rate of 3-4%	
	Risk of scarring	
	Curettage or shave excision with cautery	
	Recurrence rate of ~10%	
	Risk of scarring	
	Laser Therapy	
	Treatment options include:	
	Neodymium-doped yttrium aluminum garnet (ND:YAG)	
	Flashlamp-pumped pulsed dye laser (PDL)	
	Postoperative complications are rare	
	Recommended for small lesions and cosmetically sensitive areas	
	Multiple treatments are typically required	
	Topical Imiquimod Cream	
	Multiple applications required	
	Intralesional Corticosteroid Injections	
	Commonly combined with other treatment modalities	
	Topical Timolol	
	The case described herein is the first reported use of timolol in the successful resolution of recalcitrant PG	
	*Spontaneous regression of PG lesions can occur, but most cases require	
	treatment due rapid growth and bleeding tendency	

Case Report

A 39-year-old Caucasian male presented to our clinic with a complaint of a chronic scalp lesion that was unresponsive to treatment over the past 1.5 years. He reported that it started as a red papule that progressively enlarged and bled frequently. The patient described the wound as "uncomfortable because of pressure," but denied pain, burning, crusting, or pruritus. He did not recall any preceding trauma to the area, history of surgery near or at the site, nor intracranial lesions. He denied manipulating or picking the site.

The patient was a healthy police officer. There was no history of chronic disease, cancer, physical trauma, or surgery. He also denied tobacco, alcohol, or recreational drug use. Review of systems was negative for any constitutional symptoms, including nausea, emesis, fever, chills, fatigue, weakness, or headaches.

Initially, he was evaluated at an outside facility where the lesion was excised and closed with sutures. Histopathology from this procedure was consistent with a diagnosis of pyogenic granuloma. Despite surgical removal, it recurred. At this point, he was subsequently treated with a variety of dressings, antibiotics, and silver nitrate over a 6-month period, but the wound persisted and grew larger. At presentation to our clinic, he had a 3.5 by 5 cm glistening red, well-circumscribed plaque on the left parietal scalp,

with slightly macerated borders with sparse hair adherent to the base (Figure 1). There was no evidence of infection or trauma. No other similar lesions were present on his body.



Figure 1. Initial presentation of scalp wound.

Given the clinical presentation and examination findings, our differential diagnosis included granulation tissue, hemangioma, bacillary angiomatosis, and pyogenic granuloma. A biopsy of the scalp lesion demonstrated histopathology that was consistent with pyogenic granuloma (Figure 2). Magnification at 20x showed complete ulceration of the epidermis with superficial fibrin deposition, proliferating blood vessels, and a mixed inflammatory infiltrate including conspicuous neutrophils. There were numerous adherent red blood cells on the surface. Special stains were negative for bacteria and fungi.

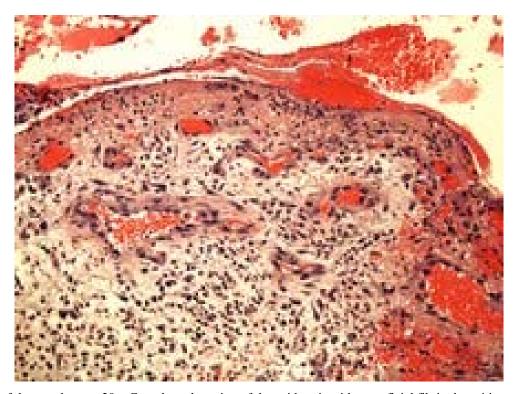


Figure 2. Biopsy of the neoplasm at 20x: Complete ulceration of the epidermis with superficial fibrin deposition, proliferating blood vessels, and a mixed inflammatory infiltrate including conspicuous neutrophils.

A trial of Acticoat® 7 silver-coated low-adherent primary wound dressing was attempted for 2 weeks without any improvement. He was then treated with a combination of topical imiquimod (5% cream applied nightly) and clindamycin (1% cream applied twice daily) as well as oral doxycycline (100 mg twice daily). In the office, the base of the wound was also hyfrecated to reduce bleeding. With this course of therapy, only mild improvement was observed, as the wound decreased in size to 2.5 cm x 3.2 cm, and the edges of the ulcer appeared less exophytic and raised. In addition, some hair regrowth was observed over the scalp. This treatment regimen was continued for 1 month. At his next follow up visit, the patient reported worsening symptoms including increased tenderness and bleeding.

At this point, a trial of pulsed dye laser was initiated. Two sessions of laser (595 nanometers (nm) with triple pulsing- spot size 7 millimeters (mm), 9 Joules of energy, 6 millisecond (msec) pulse duration) spaced over 4 weeks- were administered to the lesion.

As adjuvant therapy, the patient was also instructed to apply timolol 0.5% ophthalmic solution once daily to the site and continue taking oral doxycycline. At his follow-up visit, he stated that the lesion improved but still bled intermittently. To address vessels at the base of the lesion, a more deeply penetrating vascular laser was selected. The patient received two sessions of neodymium-doped yttrium aluminum garnet (Nd-YAG) laser (1064 nm with single pulsing- spot size 3 mm, 240 Joules of energy, 50 msec pulse duration). Silver nitrate was also focally applied. These laser sessions were also accompanied by 2 sets of intralesional injections of triamcinolone acetonide (10 milligrams/milliliter (mg/mL).

Finally, two years after initial presentation, the lesion resolved following 3 months of combination therapy: minimally invasive procedures (vascular lasers and intralesional steroids) and topical treatment with timolol. The patient reported no further ulceration or bleeding and nearly complete regrowth of hair (Figure 3). He denied any other associated symptoms and was able to return to full duties at work. For maintenance therapy, he reported that he continued to use topical timolol once daily to the original site and has remained clear for 6 months.



Figure 3. Scalp wound 2 months after discontinuing laser therapy and initiating timolol treatment.

Discussion

Contrary to its name, PG is not of granulomatous or infectious origin. It is more accurately referred to as lobular capillary hemangioma due to its characteristic histological appearance. ^{8; 9} The benign lesion is believed to form from rapidly growing capillary blood vessels, presenting clinically as a red shiny papule that bleeds easily.

At present, there is no known definitive cause for PGs; however, several factors have been identified that may be associated with their development: i) hormonal changes during pregnancy^{10; 11}, ii) trauma¹², iii) drug-induced by retinoids or anti-neoplastics ^{13; 14}. In many cases; however, the etiology remains undefined, leading some investigators to suggest that some PGs arise de novo. ¹⁵

In the literature, the disease can be found most frequently on the neck, face, arms, and hands, but it can also occur anywhere on the skin and mucosa. ^{10; 12} In rare cases, PGs can present intravascularly or subcutaneously. ^{18; 19} Demographically, the disease

has been observed to affect people of all age groups²⁰, and it is quite common in children and young adults. The literature remains divided on the male to female ratio for the disease ^{10; 15; 20; 21}, but the mucosal variant shows a clear predilection for the oral cavity and adult women. ^{10; 22}

Common warning signs of a PG include a history of a small vascular papule or polyp (ranging from millimeters to centimeters) that bleeds easily and develops quickly. ^{10; 20} The appearance of a PG can be smooth or lobulated. Occasionally, a PG can be difficult to distinguish from other lesions such as amelanotic malignant melanoma²³, hemangiomas²¹, Kaposi sarcoma²⁴, common moles and warts¹⁵, among others. Biopsy is routinely used to confirm suspicion of a PG. Histology typically shows granulation tissue supplied with innumerable capillary blood channels. The lateral edges are commonly described as lobular, and an epidermal collarette is often seen at the peripheries. ²⁰

In some cases, PGs may eventually regress spontaneously. PG in pregnant women, referred to as granuloma gravidarum, has been observed to disappear postpartum¹¹. More often, PGs persist as older lesions become increasingly fibrotic¹¹. Due to their tendency to bleed easily and profusely, treatment is usually preferred. There are several treatment options; however, some procedures have a higher association with scarring or recurrences than others.²⁰ While there is an increased chance of recurrence if the lesion is not removed in its entirety, complete excision may not always be feasible because associated blood vessels may extend deep into the dermis and even into the subcutaneous fat layer.²⁵

There is no consensus among investigators on the optimal treatment for PGs due to the lack of prospective randomized controlled trials and the large variability in patient demographics of case reports and retrospective studies. Additionally, further consideration is needed regarding the anatomic site of the lesion (mucosa vs. cutaneous) and cosmetically sensitive areas. The most common treatment modality is surgery-excision was performed in 80% of 408 PG cases in one retrospective study ²⁰ and 64.8% in a series of 1196 cutaneous PG cases. ²⁶ The incidence of recurrences following surgical excision was approximately 3 to 4%. ^{20; 22; 26} Curettage/shave excision with or without cautery is another viable option; however, investigators note it has a higher recurrence rate of approximately 10%. ^{20; 26} Standard therapy may be complete excision of the lesion and surgical closure; however, investigators note that post-operative scarring may be more frequently observed than with non-surgical treatment modalities such as topical imiquimod 5% or laser therapy: Nd:YAG and flashlamp-pumped pulsed dye laser (PDL). ^{20; 27}

Laser therapy is capable of selectively treating cutaneous vascular lesions and has several advantages over surgical means: lack of post-procedural discomfort²⁸; often no anesthesia is required²⁹; and minimal to no postoperative complications.^{25; 28} Nonetheless, due to the limited tissue penetration, several laser treatments may be required over time. In a series of 20 pediatric patients, the vascular-specific (585 nm) flashlamp-pumped PDL was used to treat PGs with a 91% success rate, and 25% of the patients required only 1 treatment.³⁰ Similarly, in 1 case series, 16 out of 18 patients treated with PDL had excellent clearing of the lesions²⁸, and post-treatment care was minimal and limited to the application of topical antibiotics. It was expected among investigators that lasers with wavelengths that target oxyhemoglobin chromophore would also be effective for vascularized PG lesions. Thicker PG lesions are often less responsive to laser due to limited penetration depth. Small PG lesions can often be effectively treated with multiple rounds of PDL therapy; however, larger lesions are more resistant and may warrant a different approach.³¹

Superficial lesions that are limited to the papillary dermis will respond to traditionally used wavelengths of 577 and 585 nm but the deeper vessels often require lasers with longer wavelengths. ²⁹ A suitable alternative to treating deeper and larger lesions is Nd:YAG (1064 nm), which has been reported as a successful modality for resolving PGs. ^{25; 32} Additionally, in sensitive sites such as the nail matrix and gingiva where cryotherapy and electrocoagulation produce modest results, PGs have been reported to respond more favorably to Nd:YAG treatment. ²⁵

Although laser treatments are well-known therapeutic options, there is no case report in the literature that describes the use of timolol, a nonselective beta-adrenergic receptor antagonist, for treatment of PG. However, the efficacy and safety of topical timolol has been recently described in the treatment of infantile hemangioma³³⁻³⁵, a vascular tumor similar to PG. The effects of beta-blockers on endothelial growth are variable, but there is evidence that they have anti-angiogenic, pro-apoptotic, and vasoconstrictive properties.³⁶ {Aguila, 2003 #64} The induction of pro-apoptotic signals in proliferating endothelial cells may explain their efficacy in treating rapidly proliferating vascular tumors. Additionally, timolol was found to enhance cutaneous wound healing by increasing the rate of keratinocyte galvanotaxis and single cell migration³⁷, which ultimately accelerated skin re-epithelialization of a chronic refractory wound.³⁸ The effects of timolol on keratinocyte and endothelial cells are linked to the presence of beta 2-adrenergeric receptors on these cells.

Another treatment modality seldom mentioned in the literature is corticosteroid injections of triamcinolone acetonide solution. While triamcinolone acetonide is widely used to regulate inflammatory immune response in a variety of dermatologic diseases, its mode of action for treating PGs, as reported in a handful of cases, has not been identified.^{39; 40} It is probable that the synergistic

effects of destruction of lesional vessels (via laser therapy), promotion of wound healing balanced with antiangiogenesis (via timolol), and suppression of inflammatory response (via corticosteroid) could explain the successful treatment of the recalcitrant PG in our patient. Further investigations are necessary to determine the efficacy and underlying principles of this multimodal approach.

Conclusion

We report a severe case of chronic pyogenic granuloma of the scalp in a healthy adult male resistant to a variety of common therapies including surgical excision, imiquimod application, antibiotics, and dressings. Ultimately, aggressive laser therapy, corticosteroid injections, and topical timolol application to the wound effectively treated the condition. Further work is needed to determine the efficacy of timolol as monotherapy or as an adjuvant treatment in combination with other therapies, such as laser treatment.

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