

CASE REPORT

Oral propranolol and topical timolol in the treatment of post-burn pyogenic granuloma: Two cases and a review of the literature

Zahra Ebrahimi¹ | Zeinab Mahdi² | Ali Asghar Khairi³ | Elham Behrangi^{2,4} |
Armaghan Gharehaghaji Zare⁵ | Abbas Dehghani² | Azadeh Goodarzi² 

¹Department of General Medicine, School of Medicine, Iran University of Medical Sciences, Tehran, Iran

²Department of Dermatology, Rasool Akram Medical Complex Clinical Research Development Center (RCRDC), School of Medicine, Iran University of Medical Science, Tehran, Iran

³Department of Plastic Surgery, Sina Hospital, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran

⁴Stem Cell Research Center, Tehran University of Medical Sciences, Tehran, Iran

⁵Department of Dermatology, Sina Hospital, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran

Correspondence

Azadeh Goodarzi, Department of Dermatology, Rasool Akram Medical Complex Clinical Research Development Center (RCRDC), School of Medicine, Iran University of Medical Sciences, Niayesh St., Sattarkhan Ave., Tehran 1445613131, Iran.

Email: azadeh_goodarzi1984@yahoo.com and goodarzi.a@iums.ac.ir

Abstract

Two cases of pyogenic granulomas in burned skin were presented, a 17-month-old boy and a 7-year-old girl, being given oral propranolol and topical timolol. Both cases showed lesions improvement with no adverse effects, suggesting that beta-blocker therapy may have a positive impact on the treatment of pyogenic granuloma after burns.

KEYWORDS

beta-blocker, burn, hemangioma, oral beta-blocker, post-burn hemangioma, post-burn pyogenic granuloma, propranolol, pyogenic granuloma, therapy, timolol, topical beta-blocker, treatment

1 | INTRODUCTION

A pyogenic granuloma (PG) or lobular capillary hemangioma is a benign vascular proliferation of the skin and mucous membranes. PG is a hyperproliferative vascular response to trauma, skin irritation, hormonal factors, viral pathogens, and growth factors that can develop on normal skin and cause tissue hypoxia and angiogenesis.¹ Pyogenic granuloma after a burn or scalded pyogenic granuloma is a variant of hemangioma that manifests within 2 to 4 weeks after a burn injury. As a result of the burn, intense

and rapid vascularization of the skin and mucosa occurs, resulting in hemangioma-like tissue.² Thermal, radiation, chemical, or electrical contact irritates the skin and causes burns of varying degrees, depending on the depth and severity of penetration.³

Several treatment options are available for PG, including surgical removal, curettage and cauterization, laser, and topical imiquimod; however, these treatments are invasive and may be associated with pain, scarring, as well as other local side effects.^{4,5} One of the treatments that may have fewer side effects for hemangiomas is beta-blocker therapy.

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In addition, beta-blockers have been shown to be an effective treatment for small PG, especially in children.⁶ In this study, we describe two cases with second-degree burns resulting hemangiomas. Both cases were treated with oral propranolol and topical timolol without any adverse effects.

2 | CASES PRESENTATION AND TREATMENT METHODS

2.1 | Case 1

A 17-month-old healthy boy was referred to the emergency department of Sina Hospital with a second-degree burn from boiling water in the area behind the ears, anterior and posterior to the right elbow, and anterior to the left shoulder (18% burn). The child was admitted to the burn ward and underwent fluid therapy with normal saline, intravenous ampicillin, and dressing. It was discharged after 5 days in good general condition with a wound dressing. One month later, the child and his mother presented to the outpatient department of Sina Hospital with multiple eruptive red lesions on the periphery of the burn sites behind the left ear and on the right elbow (Figure 1A–C). The child had no history of congenital etiology. Initially, the child was treated with oral amoxicillin and a mupirocin dressing, which was not effective. On physical examination, we found numerous asymptomatic angiomatous papulonodular lesions with crusted surface on a hyperpigmented background. The lesion behind the left

What's already known about this topic?

Pyogenic granuloma or lobular capillary hemangioma is a benign vascular tumor of the skin that is common in adolescents and may be a complication of a burn. Invasive treatments for cutaneous hemangiomas such as laser, curettage, and minor surgery can lead to adverse effects such as ulceration and scarring that are uncomfortable and distress patients.

What does this study add?

Beta-blockers affecting on cutaneous hemangiomas in oral and topical forms (oral propranolol and topical timolol in this study) could be consider as an effective treatment for post-burn pyogenic granulomas without particular complications.

ear and the lesion at the elbow were 2 and 1 cm in size, respectively (Figure 1A,B). Based on the biopsy performed, a possible diagnosis of post-burn pyogenic granuloma was made, propranolol was administered 5 mg orally twice a day and then the dosage was increased to 10 and 15 mg every 3 days. In addition, 0.5% timolol drop was administered twice a day during oral propranolol administration. The child's blood pressure and heart rate were closely monitored within 2 h from the start of medication and were normal.⁷ After 9 days, physical examination showed



FIGURE 1 (A–C): Multiple post-burn pyogenic granulomas specially behind the left ear and on the right elbow. (D): Significant improvement after a 9-day treatment with oral propranolol and topical timolol.

that the lesions had dramatically decreased (Figure 1D), so the treatments were discontinued.

2.2 | Case 2

A 7-year-old healthy girl suffered a burn from boiling water on her face and was referred to the skin clinic at Sina Hospital. The second-degree burn involved the left side of the face. Three weeks later, the mother brought the child with a swollen face and a 2-cm lesion (Figure 2A,B). Examination of the lesion revealed a red, oozing plaque with a crusty surface that bled easily. The patient received 15 mg of oral propranolol (under supervision) and 0.5% topical timolol drop, both of them twice a day. At the first administration, the patient's blood pressure and heart rate were monitored for 2h in the clinic,⁷ which were normal and medication was continued as an outpatient. Three days later, the patient was referred again, the propranolol dose was increased to 20 mg twice a day, and the patient's blood pressure and heart rate continued to be monitored. After 2 weeks of treatment, the lesion had significantly regressed (Figure 2C), and only an atrophic scar remained after 6 months of follow-up (Figure 2D).

3 | DISCUSSION

This study described two cases that occurred after trauma to the skin from a burn. Both cases were treated with oral

propranolol and topical timolol, which resulted in significant improvement.

The PG-like or hemangioma-like lesions after a burn can be triggered by hypoxia of the skin but can also occur in other situations such as chronic trauma or hormonal disorders.⁸ Lesions may bleed and cause psychological distress to patients, especially lesions on the face; therefore, treatment of these benign tumors is a high priority. Various treatments for cutaneous hemangiomas (which are described in Table 1) may be invasive or have various adverse effects such as ulceration or scarring. Surgery is a common treatment, but it is invasive and may cause distress or pain, scarring, and, in some cases, nonresponse or recurrence.⁹

In this study, we found that we can treat hemangiomas in children with a series of oral and topical beta-blockers, which appear to be an attractive option for disease management and maybe effective in treating wounds, ulcers, and proliferative vascular lesions based on their physiopathology and with a few side effects. In addition, recent studies have reported that beta-blocker therapy has a significant effect on wound healing and infantile hemangioma.^{10,11}

PG Lesions similar to infantile hemangioma have been discovered to express beta-adrenergic receptors.¹² Some studies have used oral and topical beta-blockers such as propranolol, timolol, and betaxolol to treat PG, which are described in Table 1. In a study by Khalifa E et al., oral propranolol was used for 2 weeks to treat post-burn pyogenic granulomas of two cases, which proved successful.¹³

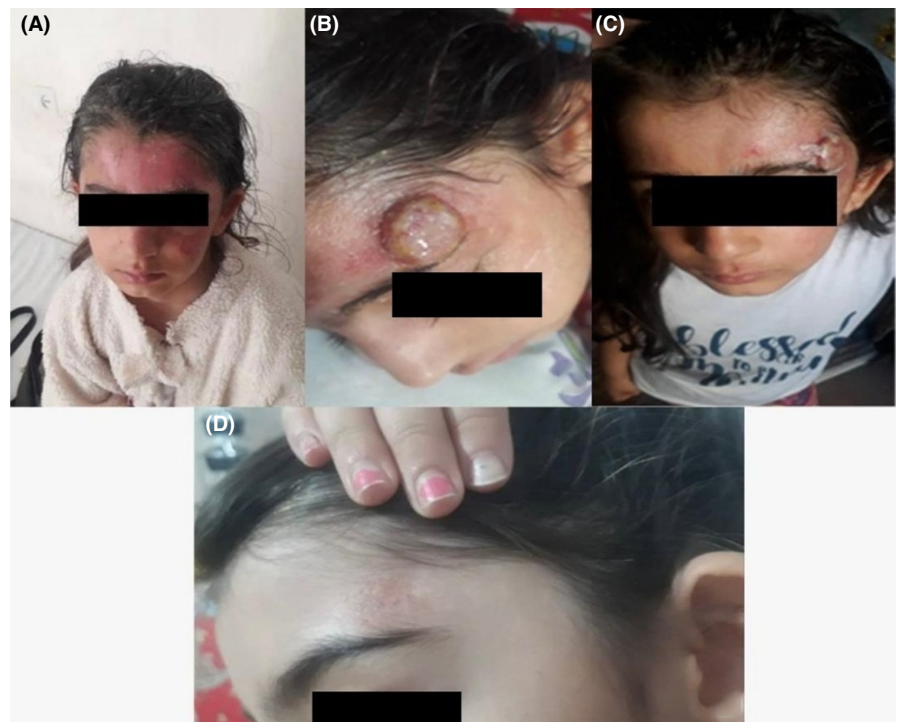


FIGURE 2 (A, B): A red, oozing pyogenic granuloma on the burned skin. (C): A dramatic reduction of the lesion after 2 weeks of treatment. (D): The lesion after treating with beta-blockers and a 6-month follow-up.

TABLE 1 Case reports and case series of post-burn pyogenic granuloma based on a literature review

Reference	Article type	Age/sex	Causing agent	Degree of burn	Latency (days)	Location	Effective treatment
De kaminsky et al. (1978) ¹⁷	Case report	15 months/Female	Boiling milk	Second	7	Arm, trunk, face	Electrocoagulation
Momeni AZet al. (1995) ¹⁸	Case series (N = 3)	1.5 years/Male	Boiling milk	Second	14	Trunk	Healed spontaneously after a period of 3 weeks.
		5 years/Female	Boiling milk	Second	14	Back, abdomen, high	Two of the lesions were electrocoagulated and the remainder healed spontaneously in 3 weeks
Ceyhan et al. (1997) ¹⁹	Case report	35 years/Female	Boiling milk	Second	Nil	Face	Healed spontaneously after 4 weeks
Aliagaoglu et al. (2006) ²⁰	Case report	18 months/Female	Boiling milk	Second	15	Arm, trunk, face	Excision
Bozkurt M, et al. (2006) ²¹	Case report	5 years/Female	Unknown	Second	15	Arm	Total excision and primary closure.
Liao et al. (2006) ²²	Case series (N = 2)	2 years/Male	Boiling milk	Second	10	Forearm	Excision
		41 years/Male	Scaling burn	Second	10	Forehead, cheek, lower jaw, forearm	Infusion of cefazolinum and topical application of mupirocin
		19 years/Male	Boiling water	Second	9	Back, face, upper limbs	Oral minocycline and topical application resulted in complete clearance
Diallo et al. (2006) ²³	Case series (N = 3)	8 months/Male	Thermal burn	Second	7–14	Face, limbs	Self-healing
		13 months/Male	Thermal burn	Second	7–14	Face, limbs	Self-healing
		13 years/Male	Thermal burn	Second	7–14	Face, limbs	Self-healing
Ceyhan AM et al. (2007) ²⁴	Case report	17 months/Male	Boiling water	Second	14	Arm	Oral erythromycin, 40 mg/kg four times daily, was given for 8 weeks. The lesions clearly improved after 12 weeks of the treatment.
Orzbayoglu et al. (2011) ²⁵	Case report	8 years/Male	Flame	Second	21	Trunk	Excision
Shirol et al. (2012) ²⁶	Case report	42 years/Female	Unknown	Second	30	Chin	Surgical excision with split-thickness skin graft
Durgun et al. (2013) ²⁷	Case series (N = 2)	2 years/Female	Unknown	Second	15	Face, neck	Excised and fixed with a full thickness skin graft
		7 years/Male	Boiling water	Second	14	Forearm	Excised and primarily sutured
Netchiporouk et al. (2014) ²⁸	Case report	17 years/Male	Lightning injury	Second and third	14	Face, chest, limbs	Surgical excision
Dasigheib et al. (2016) ²⁹	Case report	12 months/Male	Boiling milk	Second	14	Lower limbs	Lost patient

TABLE 1 (Continued)

Reference	Article type	Age/sex	Causing agent	Degree of burn	Latency (days)	Location	Effective treatment
Zhao et al. (2015) ³⁰	Case series (N = 5)	4 years/Male 15 months/Male 3 years/Male 26 months/Female 2 years/Female	Scaling Scaling Scaling Scaling Scaling	Second Second Second Second Second	Nil Nil Nil Nil Nil	Face, neck Arm, hand Arms Back, buttocks Hand	Conservative Conservative Conservative Conservative Conservative
Xu et al. (2016) ³¹	Case report	4 years/Female	Boiling soup	Second	13	Arm	Sodium fusidic ointment and compound Huangbo solution (Chinese herbal medicine) were applied topically twice daily for 4 weeks
Khalifa E et al. (2017) ¹³	Case series (N = 6)	9 months/Male 10 months/Male 25 years/Female	Boiling tea Boiling tea Thermaldermabrasion	Second Second Nil	10 12 Nil	Abdomen Foot Cheek	Lost patient Oral propranolol at a dose of 5 mg twice daily for 2 weeks Supportive therapy like topical and systemic ointment within 2 weeks.
Ashk Torab et al. (2018) ³²	Case report	15 months/Female	Boiling water	Second	10	Trunk	Conservative (herbal treatment)
Staggers JR et al. (2019) ³³	Case report	29 years/Male	Unknown	Nil	14	Finger	Silver nitrate therapy was ineffective, though surgical excision resulted in complete resolution of the mass.
Rosa-Mangeret F et al. (2020) ³⁴	Case report	premature neonate/ Female	Transcutaneous CO ₂	First	24	Thigh	Topical beta-blocker (Timolol gel)
Krieger Y et al. (2020) ³⁵	Case report	17 months/Male	Boiling water	Second	21	Forearm and arm	Excision and skin grafting
Iraji, et al. (2020) ³⁶	Case report	30 years/Female	Oil	Third	28	Forearm	The excision of the lesions followed by electrocautery of the base
Keshavarzi A et al. (2021) ³⁷	Case report	49 years/Female	Boiling water	Nil	14	Hand	Full thickness skin excision and debridement and skin graft
Sharquie KE et al. (2022) ³⁸	Case series (N = 34)	mean age: 17.6 years and median age: 3.5 years/16 Female, 18 Male	Boiling liquids, Fire flame	Second- and combined second- and third-degree	7–14	Scalp in two cases, trunk in six cases, upper limbs in eight cases, and lower limbs in 15 cases	Nil

Consensus guidelines exist for initiating and monitoring treatment with propranolol but are extremely variable.⁷ The mechanism of action of beta-blockers, particularly propranolol and timolol, is not fully understood. However, inhibition of angiogenesis, blockade of beta-2-adrenergic vasodilator nerves of the skin, and induction of apoptosis of capillary endothelial cells have been proposed as mechanisms.^{14–16} Contraindications to oral propranolol for burn hemangioma are similar to those for infantile hemangioma and include the following: cardiogenic shock, sinus bradycardia, hypotension, greater than first-degree heart block, heart failure, bronchial asthma, and hypersensitivity to propranolol.⁷

We also reviewed 23 studies that included 71 cases of post-burn PG (Table 1). More than 60 patients from previous studies suggest that the lesion is more likely to develop in children, so it logically needs to be approached more conservatively with noninvasive, effective, and safe treatments, making beta-blockers a good choice, and current ones are particularly interesting in this regard.

4 | CONCLUSION

Beta-blockers in systemic and local forms could be considered as an effective treatment options for scalded PG, and with minimal complications, they may replace invasive procedures such as surgical excision in the future.

AUTHOR CONTRIBUTIONS

ZE and AG designed the research, wrote and edited the paper, and edited the manuscript. ZM, AAK, EB, and AGZ identified and treated the cases. ZE, AD and AG supervised the study, and wrote the manuscript. All authors have read and approved the content of the article.

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CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

CONSENT

Written informed consent was obtained from the patients' legal guardians to publish this report in accordance with the journal's patient consent policy.

ORCID

Azadeh Goodarzi  <https://orcid.org/0000-0002-1249-4429>

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