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 cautereization, 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.
In addition, beta-blockers have been shown to be an effective treatment for small PG, especially in children. 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 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. After 9 days, physical examination showed

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 considered as an effective treatment for post-burn pyogenic granulomas without particular complications.

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 2 h 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
| Reference | Article type | Age/sex | Causing agent | Degree of burn | Latency (days) | Location | Effective treatment |
|-----------|-------------|---------|---------------|----------------|---------------|----------|---------------------|
| De kaminsky et al. (1978) | Case report | 15 months/Female | Boiling milk | Second | 7 | Arm, trunk, face | Electrocoagulation |
| Momeni AZ et al. (1995) | Case series \((N = 3)\) | 1.5 years/Male | Boiling milk | Second | 14 | Trunk | Healed spontaneously after a period of 3 weeks. Two of the lesions were electrocoagulated and the remainder healed spontaneously in 3 weeks. |
| | | 5 years/Female | Boiling milk | Second | 14 | Back, abdomen, high | | |
| | | 35 years/Female | Boiling milk | Second | Nil | Face | Healed spontaneously after 4 weeks |
| Ceyhan et al. (1997) | Case report | 18 months/Female | Boiling milk | Second | 15 | Arm, trunk, face | Excision |
| Alligaoglu et al. (2006) | Case report | 5 years/Female | Unknown | Second | 15 | Arm | Total excision and primary closure. |
| Bozkurt M, et al. (2006) | Case report | 2 years/Male | Boiling milk | Second | 10 | Forearm | Excision |
| Liao et al. (2006) | Case series \((N = 2)\) | 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) | 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) | 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. |
| Ozbayoglu et al. (2011) | Case report | 8 years/Male | Flame | Second | 21 | Trunk | Excision |
| Shirol et al. (2012) | Case report | 42 years/Female | Unknown | Second | 30 | Chin | Surgical excision with split-thickness skin graft |
| Durgun et al. (2013) | 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) | Case report | 17 years/Male | Lightning injury | Second and third | 14 | Face, chest, limbs | Surgical excision |
| Dastgheib et al. (2016) | Case report | 12 months/Male | Boiling milk | Second | 14 | Lower limbs | Lost patient |
| Reference                     | Article type         | Age/sex                  | Causing agent   | Degree of burn | Latency (days) | Location                | Effective treatment                                                                 |
|------------------------------|----------------------|--------------------------|-----------------|----------------|----------------|-------------------------|-------------------------------------------------------------------------------------|
| Zhao et al. (2015)           | Case series (N = 5)  | 4 years/Male             | Scaling         | Second         | Nil             | Face, neck              | Conservative                                                                       |
|                              |                      | 15 months/Male           | Scaling         | Second         | Nil             | Arm, hand               | Conservative                                                                       |
|                              |                      | 3 years/Male             | Scaling         | Second         | Nil             | Arms                    | Conservative                                                                       |
|                              |                      | 26 months/Female         | Scaling         | Second         | Nil             | Back, buttocks          | Conservative                                                                       |
|                              |                      | 2 years/Female           | Scaling         | Second         | Nil             | Hand                    | Conservative                                                                       |
| Xu et al. (2016)             | 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)      | Case series (N = 6)  | 9 months/Male            | Boiling tea     | Second         | 10              | Abdomen                 | Lost patient                                                                       |
|                              |                      | 10 months/Male           | Boiling tea     | Second         | 12              | Foot                    | Oral propranol at a dose of 5 mg twice daily for 2 weeks                           |
|                              |                      | 25 years/Female          | Thermaldermabration | Nil        | Nil             | Cheek                   | Supportive therapy like topical and systemic ointment within 2 weeks.              |
|                              |                      | 3 years/Male             | Boiling tea     | Second         | Nil             | Lower limb              | Propranolol therapy for 2 weeks                                                    |
|                              |                      | 7 years/Female           | Boiling tea     | Second         | Nil             | Lower limbs             | Lost patient                                                                       |
|                              |                      | 2.5 years/Male           | Boiling soup    | Second         | 10              | Abdomen, lower limb     | Oral propranolol 10 mg with topical potassium permanganate solution given but lost follow-up. |
| Ashk Torab et al. (2018)     | Case report          | 15 months/Female         | Boiling water   | Second         | 10              | Trunk                   | Conservative (herbal treatment)                                                    |
| Staggers JR et al. (2019)    | 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)| Case report          | premature neonate/ Female| Transcutaneous CO₂ | First         | 24              | Thigh                   | Topical beta-blocker (Timolol gel)                                                  |
| Krieger Y et al. (2020)      | Case report          | 17 months/Male           | Boiling water   | Second         | 21              | Forearm and arm         | Excision and skin grafting                                                          |
| Iraji, et al. (2020)         | Case report          | 30 years/Female          | Oil             | Third          | 28              | Forearm                 | The excision of the lesions followed by electrosurgery of the base                  |
| Keshavarzi A et al. (2021)   | Case report          | 49 years/Female          | Boiling water   | Nil            | 14              | Hand                    | Full thickness skin excision and debridement and skin graft                         |
| Sharquie KE et al. (2022)    | 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. 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. 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.

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.

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