

Burn Hemangioma: Oral Propranolol is an Effective New Saving Therapy

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Abstract

Background: Burn hemangioma is new described variant of hemangioma that is commonly presented in winter time, that triggered by burning heat. It has many similarities to infantile hemangioma regarding the clinical course, histopathological picture. Its therapy is surgical resection.

Objective: To report new therapy for burn hemangioma by oral propranolol in large number of patients.

Methods: This is cross-sectional descriptive study with therapeutic trial where 14 cases of burn hemangioma were reported. Full demographic and clinical evaluation was performed. All patients were treated with oral propranolol in a dose of 1 mg/kg/day in 2 divided doses. In 3 (21.42%) cases of children, there was no improvement in 2 weeks after treatment, so the dose was increased to 2 mg/kg/day.

Results: A total of 14 cases were analyzed ,8(57.14%) females and 6 (42.85 %)males, their ages ranged from 6 months to 45 years. Two age groups were assessed: infants and children in 10(71.42%) cases with a mean age 5.75 years and 4(28.57%) in adults with a mean age 42.5 years. All patients had second degree burn apart from 2(14.28%) patients had combined 2nd and 3rd degree burn that followed contact with boiling liquids in 11(78.57%) cases, electric shock in 2(14.28%) cases and therapeutic cautery in one (7.14%) case. The hemangioma appeared after 1-2 weeks following burn injury. The therapeutic response was observed after few days but marked after 2 weeks but therapy continued for at maximum of six weeks until full resolution. No scarring was observed followed full resolution.

Conclusion: Burn hemangioma is commonly seen among children in winter cold months following burn with boiling liquid although occasionally can follow contact with any hot object like electric shock. Oral propranolol is a new an effective safe therapy leaving very good cosmetic appearance without scarring.

Keywords: Burn hemangioma, oral propranolol, pyogenic granuloma, treatment.

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Introduction

Pyogenic granuloma (PG) is a well-known and common acquired vascular proliferation with characteristic clinical and histopathological manifestations, usually presenting as a single tumor prone to bleeding.¹ It usually occurs in response to trauma, skin irritation, viral pathogens and hormonal factors, but can also occur spontaneously. In addition to the skin, mucous membranes can also be involved.² It can occur at any age

but most commonly affect infants and children.³

Scalded pyogenic granuloma (SPG) is a variant of PG that usually appears within 2 to 4 weeks after a burn injury and then multiply rapidly to form multiple angiomatous masses, which tend to coalesce into large lobulated red-gray masses. These vascular masses persist for several months and some cases resolve spontaneously.¹⁻³

Multiple angiomatous lesions have been reported

following exposure to boiling liquids, especially in children.⁴⁻⁷ As a result of burns, the skin and mucous membranes undergo intensive and rapid vascularization, resulting in the formation of hemangioma-like tissue.⁸

The histopathology of SPG tissue shows epidermal hyperkeratosis and acanthosis together with large dilated vascular spaces and new vascularization with edematous stroma infiltrated by lymphocytes and plasma cells in the dermis.^{7,9}

Due to major similarities in clinical and histopathological features between SPG and infantile hemangioma, Sharquie suggested more descriptive term for SPG called BH.^{7,9}

It has been reported that most of the published articles are isolated cases.^{4,5,10,11} Only four studies: two by Sharquie et al,^{7,9} and two by Zhao et al,^{12,13} presented a case series.

There are several therapeutic options for SPG, including laser, surgical excision, curettage and cautery, cryotherapy and topical imiquimod; however, these treatments are associated with variable results and many adverse effects.^{8,14}

In 2017, Sharquie introduced oral propranolol (non-selective β -adrenergic receptor blocker) in the treatment of few cases of burn hemangioma with promising results.⁹

So, the aim of the current work is to report therapy of BH by oral propranolol in a larger series of patients.

Methods

This is cross-sectional descriptive study with therapeutic trial that was conducted during the period from 2017-2023 years where 14 cases of BH were reported. Full demographic and clinical evaluation were performed. Informed consent was obtained from every patient or his/her parent and this work followed the Declaration of Helsinki Principles. The study was approved by the Ethics Committee of Al-Anbar Health Directorate, Fallujah Teaching Hospital (number: 625; date: 4/ 1/2023).

Complete medical history includes gender, age, weight of the patient, type and cause of burn,

time interval between burn and onset of lesions, and season of burn. Clinical examination was performed including assessment of the morphology and number of lesions, as well as assessment of the size, location, degree, and extent of burns. History of contact with hot object was registered in all cases while the diagnosis of BH was based on history, clinical manifestations and confirmed by histopathological results.

Before treatment initiation, the patients underwent many laboratory examinations such as: blood glucose, complete blood picture, and renal and liver functions. Also, pictures of lesions were taken before therapy and during treatment course and follow-up. Any patient with history of bronchial asthma, history of heart diseases, diabetes, heart block, heart failure, hypotension, sinus bradycardia and hypersensitivity to propranolol, was excluded from the study. Biopsies for histopathological assessment were done for selected cases.

All patients were treated with oral propranolol in a dose of 1 mg/kg/day in 2 divided doses. In 3 (21.42%) cases of children, there was no marked improvement 2 weeks after treatment, so the dose was increased to 2 mg/kg/day.

The duration of therapy was until full resolution of lesions and was maximum for 6 weeks. In infants and children, propranolol tablet was dissolved in sugary water and taken with food in order to decrease the possibility of hypoglycemia. Topical and oral antibiotics were given when necessary.

The follow-up was achieved every 2 weeks until complete clearance of the lesions. During this period, the patients were assessed carefully to record any complications or side effects.

Results

A total of 14 patients were analyzed, 8 (57.14%) females and 6 (42.85 %) males, their ages ranged from 6 months to 45 years with a mean of 5.75 years in infants and children and 42.5 years in adults. Two age groups were assessed (Table 1): infants and children 10 (71.42%) cases and 4 (28.57%) adults. All patients had second degree

burn apart from 2 (14.28%) cases had combined 2nd and 3rd degree burn. These cases followed contact with boiling liquids in 11 (78.57%) cases, electric shock in 2 (14.28%) cases and therapeutic cautery in one (7.14%) case.

Table 1: The demographic features of 14 included cases.

	Group A	Group B
Number(n)	10	4
Age/years	0.5-12	40-45
Gender	6 female/4 male	2 females/2 males
Etiology, n:		
Boiling liquids	5	6
Electric shock	1	1
Therapeutic cautery	1	1

The lesions were multiple eruptive angiomatous compressible painless nodules and masses red grayish in color on the site of healed 2nd degree burn (Figure 1). These lesions affected different sites of the body including lower limbs in 6 (42.85%) cases, upper limbs in 4(28.57%) cases, trunk in 2 (14.28%) cases and face in 2(14.28%) cases. More than one site affected was seen in some cases. The hemangioma appeared 1-2 weeks after burn injury and the lesions evolved to large lesions within weeks. Few or single lesions were seen in the adults, while multiple lesions were recorded in children and infants. The adults had their lesions mostly on the limbs, while in the infants and children the lesions were on the scalp, extremities and trunk.

The size of the angiomatous lesions was variable and ranged from 1 × 0.5 cm to 10×10 cm.

The histopathological results showed epidermal hyperplasia and acanthosis while the dermis especially the upper part showed large dilated vascular spaces with new vascularization that lined by a single layer of endothelial cells. In addition, severe dermal edema infiltrated by inflammatory cells mainly lymphocytes admixed with few plasma cells and eosinophils were noticed (Figure 2).



Figure 1: Child with boiling liquid burn hemangioma of left leg and foot.

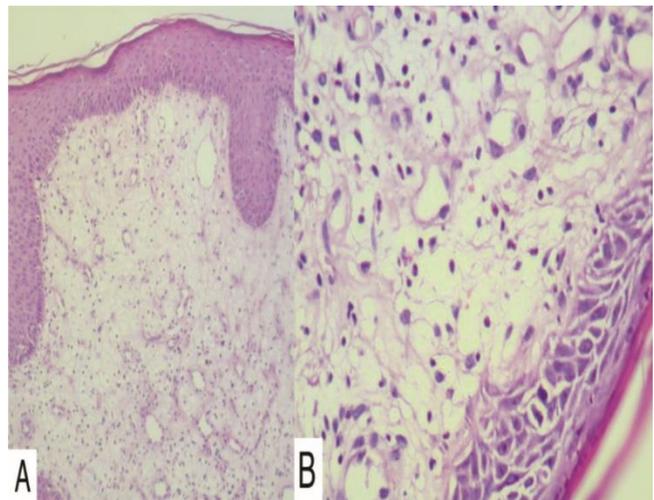


Figure 2: Histopathology of burn hemangioma showing mainly pseudoepitheliomatous hyperplasia, acanthosis with new vascularization and dermal infiltrate (A). (HE stains × 10). While section (B) showing numerous blood vessels with dermal edema infiltrated by inflammatory cells mainly lymphocytes, plasma cells and eosinophil. (HE stains × 40).

The therapeutic response was observed after few days but marked after 2 weeks and therapy continued for at least 4 weeks until full resolution and no scars were recorded at the sites of angiomatous lesions (Figures 3 and 4). While the neighboring deep burns also showed partial resp-

onse but left scars. The response to therapy characterized by decrease in the size and color of the angiomatous lesions.

No side effects were recorded in any patients and all infants and children showed normal growth. Neither appearance of new lesions during therapeutic course nor recurrence of the old lesions during follow-up during 3-6 months. One child that seen accidentally after 2 years for another cause showed complete clearance with no recurrence (Figure 3C).

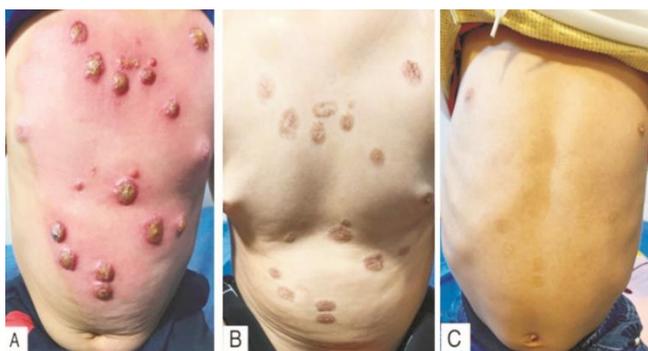


Figure 3: 4-years-old male child patient with multiple burn hemangioma affecting abdomen (A) before treatment, (B) 6 weeks after treatment and (C) 2 years after treatment stopped.



Figure 4: 2-years-old female child patient showing multiple burn hemangioma affecting left leg and foot, (A) before treatment, (B) one month after treatment and (C) 6 weeks after treatment.

Discussion

Burn hemangioma is newly described a variant of hemangioma with distinctive clinical features that make it more characteristic and informative than the name scalded PG.^{7,9} The course of the disease and the histopathology was comparable with infantile hemangioma. This encouraged us

to conduct the present work using propranolol in therapy of BH.

To the best of our knowledge, this is the largest prospective therapeutic trial study worldwide in which fourteen cases of BH from one country were enrolled.

In the current work, we included cases that had typical features of BH after burn with different types of boiling liquids in 11 (78.57%) cases, electric shock in 2 (14.28%) cases and therapeutic cautery in 1 (7.14%) case. These results are comparable to other Iraqi studies^{7,9} while differ from other international studies where boiling milk was main causative agent for BH.^{15,16} Furthermore, this result refutes previous studies that suggested an exogenous protein present in the milk may play an important role in the pathogenesis of BH but other factors and mechanisms may be responsible for BH formation.

The clinical manifestations and histopathological results of burn and infantile hemangiomas revealed very similar features as there are rapid growth, static phase, and spontaneous regression in both conditions. Infantile hemangioma usually appears after birth, grows rapidly over a few months, then reaches a plateau state and resolves over a few years. While BH grows rapidly within 1 to 2 weeks after 2nd degree burn and resolves rapidly within weeks or months.^{7,9} Vascular endothelial growth factor-A (VEGF-A) is a primary regulator of vasculogenesis and angiogenesis. It has been supposed that this factor leads to the development of these tumors.¹⁷ CD34 is positive in BH while CD133, CD34 and CD31 in infantile hemangioma.¹⁸ Histopathologically, both showed angiomatous pathology with marked active proliferation of endothelial cells. While in previous studies, it was difficult to distinguish between these two conditions with conventional histopathological staining, while only few differences were found when stained with Periodic acid-Schiff (PAS).

These major resemblances in clinical and pathological manifestations between BH and infantile hemangioma lead us to conclude that BH should be considered as hemangioma rather than PG,

hence we emphasized the name BH, as previously suggested by Sharquie.^{7,9}

Burn degree may be the most essential determinant in pathogenesis of BH. This study, like most previous studies,^{19,20} showed that the second-degree burned areas were affected in all enrolled patients, while the third-degree burn areas were spared to develop hemangioma.

For unexplained causes, Sharquie mentioned an upsurge in the cases of BH in the last decade.⁹ Hence, this increment in BH cases encouraged us to collect these cases and look for simple, safe, effective treatment and suitable for all ages.

In this study and other reviewed studies,^{7,9} infants and children were the most commonly affected age group. Logically, this age group needs to be treated conservatively with safe, simple, effective, non-invasive and low cost treatment, making propranolol a good choice as it has all these properties.

Before Sharquie⁹ introduced oral propranolol for BH treatment, conservative therapy including wound management and antibiotics was the first line. Surgery could be a 2nd line treatment especially when conservative treatment is ineffective which includes cryotherapy, cautery, and full-thickness surgical excision.²¹ But it is invasive and may cause pain, infection, ulceration, scarring and recurrence in some cases.²²

Oral propranolol has been used for the treatment of different vascular skin diseases^{23,24} but Sharquie⁹ is the first one to try it for the treatment of BH and proved successful but in few cases while the present work consisted of large series of patients. The response to therapy was quick as noticed by patients after few days but was marked after 2-3 weeks and complete clearance after a month and left no scarring but slight pigmentation and the effectiveness was the same regardless the mechanism of burn. In addition, even the deep burns showed some response will residual scarring.

The mechanism of action of propranolol is not well known. Nevertheless, inhibition of angiogenesis, induction of apoptosis of capillary endo-

thelial cells and blockade of beta-2-adrenergic vasodilator nerves of the skin have been suggested as mechanisms.²⁴

Based on the results yielded in this study, the use of oral propranolol may be the best hope for treating this disease. Most recently, Sharquie used triple therapy in treatment of infantile hemangioma consisting of oral propranolol, oral corticosteroids and topical timolol drops which is more rapid and effective than propranolol alone.²⁵ This new regime could be also advised in management of BH to have more quick response.

Conclusion

Propranolol is an effective safe therapy leaving very good cosmetic appearance without scarring. Triple therapy like for infantile hemangioma could be advised as more rapid and effective. The invasive surgical excisional management must be no more advised.

Ethical Approval: The study was approved by the Ethics Committee of Al-Anbar Health Directorate, Fallujah Teaching Hospital (number: 625; date: 4/ 1/2023).

Conflict of Interest: There was no conflict of interest to be declared by any author.

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Author's Contribution

KES: Conception & design, acquisition of data, drafting of article, analysis & interpretation, critical revision of the article, final approval of the version to be published.

RIJ: Conception & design, acquisition of data, analysis & interpretation, final approval of the version to be published.

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