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Current Approaches and Advances in the Treatment of Hemangiomas

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Abstract

The present study aimed to review current approaches and advances in the treatment of hemangiomas. Hemangiomas account for approximately 45.7% of all benign tumors in children, with up to one-quarter of newborns affected. The challenges in diagnosing and managing hemangiomas are compounded by the lack of a standardized classification system, which hinders effective communication among pediatricians, dermatologists, pediatric surgeons, and oncologists. One of the key issues in treatment remains the determination of clear indications for initiating therapy. Ulcerated hemangiomas, especially those complicated by infection and hemorrhage, pose a significant clinical concern. Patient management strategies must be individualized, with propranolol therapy and laser ablation recognized as the most effective, safe, and cosmetically favorable options. In addition, surgical excision and electrocoagulation have shown durable, relapse-free outcomes. This study involves a statistical analysis of 40 pediatric case records, presenting findings on the distribution of the disease by sex, age, anatomical location, and treatment modalities used.

Keywords: Propranolol therapy, Hemangioma, Surgical excision, Electrocoagulation, Vascular anomalies

Introduction

Hemangiomas represent the most common type of benign tumors in children, accounting for approximately 45.7% of all such neoplasms. Among newborns, the condition affects up to one-quarter of infants [1]. Complications arise in an estimated 40% of cases, with bleeding and ulceration reported in 7.5% and 21% of patients, respectively [2]. Although spontaneous regression of hemangiomas is a recognized phenomenon, the course of involution is highly unpredictable [3].

The exact etiology of hemangiomas remains a subject of debate. To date, only the mutational and placental hypotheses offer some degree of scientific support [4]. One of the key challenges in both diagnosis and treatment lies in the absence of a standardized classification system, which impedes interdisciplinary communication among pediatricians, dermatologists, pediatric surgeons, and oncologists.

Determining the appropriate timing for initiating treatment remains a central issue in clinical management. Particularly problematic are ulcerated hemangiomas, often complicated by secondary infections and bleeding [5]. Even minor trauma can trigger ulceration and subsequent infection, making the lesion refractory to standard therapies. The prolonged duration of treatment, associated physical discomfort, and significant financial

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burden contribute to the urgency of developing effective therapeutic strategies.

Vascular anomalies comprise a heterogeneous group of congenital vascular disorders, generally classified into two main categories: vascular tumors and vascular malformations, each with distinct structural, pathophysiological, and clinical characteristics [6]. Hemangiomas fall under the category of vascular tumors, whereas vascular malformations—such as lymphatic, capillary, venous, and arteriovenous malformations—constitute the majority of other vascular anomalies [7].

The most widely accepted system for classifying vascular anomalies is the ISSVA classification, first introduced in 1996 and grounded in the foundational work of Mulliken and Glowacki (1982), based on hemodynamic and histological criteria [8]. The cornerstone of this classification is the dichotomy between vascular tumors and malformations (**Table 1**). Hemangiomas are characterized by endothelial hyperplasia and are classified as benign tumors [3], while malformations are structural defects arising during embryonic development and vasculogenesis [9].

With the advent of new diagnostic and therapeutic techniques, the management of vascular anomalies—especially hemangiomas—has become increasingly multidisciplinary. Effective care now requires collaboration among pediatricians, dermatologists, otolaryngologists, hematologists, surgeons, orthopedists, and psychologists [4].

Table 1. Classification of vascular anomalies (adapted from ISSVA)

Vascular tumors	Vascular malformations
- Infantile hemangioma	1. Slow-flow malformations
- Congenital hemangioma	• *Capillary malformations:*
- Tufted hemangioma	– Port-wine stain
- Kaposiform hemangioendothelioma	– Telangiectasia
- Spindle cell hemangioendothelioma	– Angiokeratoma
- Other rare hemangioendotheliomas	• *Venous malformations:*
- Acquired vascular tumors (e.g., pyogenic granuloma, targetoid hemangioma, microvenular hemangioma)	– Isolated/sporadic lesions
	– Blue rubber bleb nevus syndrome (Bean's syndrome)
	– Familial mucocutaneous venous malformations
	– Glomangioma
	– Maffucci syndrome
	• *Lymphatic malformations*
	2. Fast-flow malformations
	– Arterial malformations
	– Arteriovenous malformations
	– Arteriovenous fistulas
	3. Combined and complex vascular malformations

Clinical Manifestations of Hemangiomas

Hemangiomas of the skin commonly present as bright red, elevated lesions with a lobulated surface. In contrast, cavernous hemangiomas reside deeper in the subcutaneous tissue and appear as bluish, compressible, tumor-like masses. Combined hemangiomas include both cutaneous and subcutaneous components, while mixed-type hemangiomas may be associated with other tissue elements such as lymphatic tissue, fibrous tissue (fibroma), adipose tissue (lipoma), or keratinized elements (keratoma) [10].

These lesions may present as either well-defined (encapsulated) or diffuse masses. A characteristic sign is the temporary reduction in size upon palpation, followed by rapid re-expansion once pressure is released.

When located in the larynx, hemangiomas can cause airway obstruction and inspiratory stridor. Large hepatic hemangiomas may result in secondary cardiac failure, while facial lesions can lead to ulceration, necrosis, and disfigurement of facial structures such as the nose,

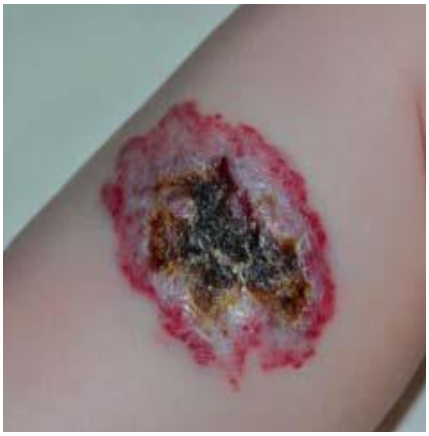
eyelids, lips, and ears. Periorbital and eyelid hemangiomas can impair visual development, potentially resulting in amblyopia [11]. Although rare, gastrointestinal hemangiomas may cause GI bleeding [12].

Hemangiomas typically manifest during the neonatal period, most often within the first two weeks of life. In 30–40% of cases, early signs such as skin discoloration may precede lesion development. The most common anatomical locations include the head and neck (60%), followed by the trunk (25%) and limbs (15%). In approximately 20% of patients, multiple lesions are observed [13].

The natural course of hemangiomas involves rapid proliferation during the first 6–8 months, reaching a growth plateau around 10–12 months. Involution begins around the end of the first year and may continue until 7 years of age, with complete regression generally occurring between 5 to 12 years [14]. Estimates of spontaneous regression vary: while some sources report rates of 5–15%, Robert M. Aresman suggests that 70–90% of hemangiomas regress naturally, excluding those in critical locations or with extensive involvement [15].

During involution, the lesion typically reduces in size becomes paler, and may develop atrophic skin changes. In roughly 50% of cases, normal skin reappears at the site of the regressed tumor. However, larger lesions may leave behind redundant skin with yellowish discoloration, or, if ulceration has occurred, scarring that may necessitate surgical intervention [16].

Complications can be categorized as systemic or local, with the latter occurring in approximately 5% of patients, most commonly involving ulceration and hemorrhage (**Figure 1**).



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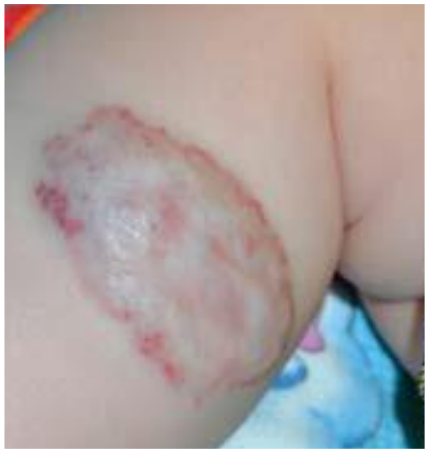


b)

Figure 1. Hemangioma of the right leg, complicated by ulceration (child aged 6 months): a) before treatment, and b) 12 days after the start of treatment.

Clinical Classification of Hemangiomas

Clinically, hemangiomas are categorized into capillary, cavernous, and mixed types based on their morphological and anatomical characteristics.

Capillary hemangiomas are superficial vascular lesions primarily located within the dermis or subdermal layers. They can exhibit rapid growth, expanding outward across the skin or infiltrating deeper into subcutaneous and muscular tissues. The appearance of the lesion is influenced by the type and depth of the vasculature: lesions dominated by arterial-type vessels typically appear bright red, while those with a predominance of venous components tend to be darker in color. A hallmark feature is the “pressure sign,” where the lesion blanches or disappears upon stretching of the skin or mucosa.

A distinct subtype of capillary hemangioma is the vascular macule, commonly referred to as a “port-wine stain” due to its unique clinical presentation. These are congenital capillary malformations presenting as flat, red-to-purple patches, often intensifying in color under certain physiological conditions such as cold exposure, crying, or straining [17].

Cavernous hemangiomas present as soft, nodular masses with a dark red or bluish hue and poorly defined borders. Despite their benign nature, these lesions may exhibit rapid and aggressive growth during infancy, occasionally resulting in facial disfigurement. Cavernous hemangiomas may be localized or diffuse, with the latter involving deeper soft tissues beyond the cutaneous

layers. A defining diagnostic feature is the "filling sign"—blanching under pressure, followed by re-expansion when the head is lowered, often accompanied by pulsation.

Histologically, cavernous hemangiomas consist of large, thin-walled, blood-filled vascular spaces lined with flattened endothelial cells. These structures frequently anastomose, and in some cases, contain calcified thrombi (phleboliths**)** [18].

Diagnosis of Hemangiomas

Diagnosis of hemangiomas is primarily clinical, with external lesions being correctly identified in up to 90% of cases [19]. However, atypical presentations or deeper lesions may necessitate imaging and laboratory evaluation.

Differential diagnosis can be challenging, particularly in distinguishing hemangiomas from other vascular anomalies. In such cases, a combination of radiological assessments and biomarkers of angiogenesis may be employed to determine the lesion type and phase of progression.

- Plain radiography, Doppler ultrasonography, and magnetic resonance imaging (MRI) are commonly used to assess the extent, structure, and hemodynamic properties of the lesion.
- Color Doppler ultrasound effectively differentiates between low-flow and high-flow vascular anomalies. However, during the proliferative phase, hemangiomas exhibit bidirectional flow signals that may resemble those of arteriovenous malformations, making interpretation complex [20].
- MRI is considered the gold standard, offering superior soft tissue resolution and allowing comprehensive evaluation of lesion extent, depth, and vascular characteristics. While highly sensitive, MRI cannot reliably identify superficial capillary malformations such as port-wine stains [21].
- Contrast-enhanced computed tomography (CT), though limited by ionizing radiation, can precisely delineate venous, lymphatic, and lymphatic-venous malformations, and is particularly useful in assessing intraosseous involvement and secondary bone remodeling [22].
- Arteriography is the most invasive diagnostic tool, typically reserved for cases requiring both diagnosis and therapeutic intervention, such as super-selective embolization. Alternatively, digital subtraction angiography (DSA), especially intravenous DSA, provides a non-invasive option for differentiating hypervascular lesions from non-active ones, albeit with lower resolution than conventional arterial angiography [23].

In addition to imaging, qualitative and quantitative assessments of angiogenic markers contribute valuable insights into the biological behavior and developmental phase of the hemangioma.

Therapeutic Approaches for Hemangiomas

Despite ongoing interest and advancements in the management of hemangiomas, a unified and standardized therapeutic protocol has yet to be established. Clinical decision-making remains highly variable, with considerable heterogeneity in the choice of treatment strategies. This lack of consensus regarding optimal timing and modality often results in suboptimal therapeutic outcomes, particularly in terms of aesthetic and functional recovery.

Current treatment strategies can be broadly categorized into systemic therapies targeting angiogenesis and localized interventions directed at tumor tissue. Systemic pharmacotherapy includes the administration of corticosteroids, interferon-alpha, cytostatic agents, and more recently, β-adrenergic blockers such as propranolol. Localized treatments encompass a range of options, including surgical excision, cryotherapy, electrocoagulation, sclerotherapy, laser ablation, radiotherapy, vascular embolization, and compression therapy [24].

Each method presents specific advantages and limitations. Therefore, the selection of a particular modality should be guided by considerations of procedural simplicity, availability, patient comfort, and the likelihood of achieving favorable cosmetic and functional results.

Electrocoagulation and Cryotherapy

Electrocoagulation and cryotherapy are widely used due to their technical simplicity, cost-effectiveness, and the fact that they do not typically require general anesthesia. However, these techniques are not without risks. Attempting to remove large hemangiomas using these methods can lead to significant complications, including primary or secondary hemorrhage and neurological damage, particularly when major nerve trunks (e.g., the facial nerve) are involved. Extensive tissue necrosis is

also a potential consequence, often resulting in delayed wound healing, infection, and poor aesthetic outcomes, even in the absence of major complications [25].

Propranolol Therapy

Propranolol has emerged as the first-line systemic therapy for infantile hemangiomas. This therapeutic shift followed a pivotal 2008 discovery that non-selective β-blockers inhibited hemangioma proliferation in infants undergoing cardiovascular treatment. Subsequent studies have consistently demonstrated rapid clinical improvement, with significant tumor regression observed within 1–2 weeks of initiating treatment [26].

Propranolol is particularly effective in managing hemangiomas for which surgical intervention is unsuitable or where observation poses a significant risk. Lesions in critical anatomical regions, such as the pharynx and periorbital area, as well as large or symptomatic hemangiomas, respond particularly well to this modality.

X-ray Therapy

Short-focus radiotherapy has historically been employed as an effective modality for superficial hemangiomas, particularly those involving the external integument in children. However, its utility is limited by the deleterious effects of ionizing radiation on pediatric tissues. X-ray exposure, especially with prolonged or repeated sessions, can negatively impact the epiphyseal growth plates of long bones, leading to growth disturbances and trophic bone alterations [27-30].

Additionally, radiotherapy is associated with a high risk of aesthetic and dermatological complications, including alopecia, skin atrophy, depigmentation, and persistent trophic ulcers, which compromise both the visual and functional outcomes of treatment.

Aim

The present study aimed to review current approaches and advances in the treatment of hemangiomas.

Materials and Methods

This research involved a retrospective statistical evaluation of clinical data from 40 pediatric patients diagnosed with hemangiomas. The primary goal was to assess the efficacy of current outpatient treatment methods for hemangiomas in children.

To achieve this, the study set out two main objectives:

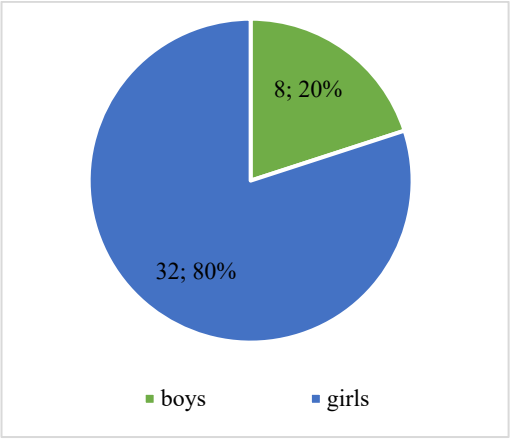
1. To evaluate the prevalence and clinical-morphological characteristics of hemangiomas in the pediatric population.
2. To review and describe contemporary therapeutic approaches used in treating these vascular anomalies.

Medical records of children between the ages of 1 month and 18 years, who received treatment at the Regional Children's Clinical Hospital in Stavropol during 2017, were analyzed. Statistical data processing was carried out using Microsoft Excel 2010 and OpenOffice, which facilitated tabulation, calculations, and graphical presentation of the results.

Results and Discussion

Analysis of the collected data highlighted several notable trends regarding the demographics and clinical distribution of hemangiomas:

3. Gender disparity: A significant predominance of hemangiomas was observed in female patients. Out of the 40 cases examined, 32 were girls and 8 were boys, indicating a 4:1 female-to-male ratio (see **Figure 2a**).
4. Age distribution: The highest incidence of hemangiomas was seen in infants under the age of one. 18 of the 40 children were under 12 months old, showing that early infancy is the most affected period. In comparison, 16 patients were between 3 and 18 years of age (**Figure 2b**).
5. Anatomical localization: The torso emerged as the most frequent site for hemangiomas, with 21 out of 40 cases located in this region. Additionally, 13 patients had hemangiomas on their limbs, suggesting these as the second most common location (**Figure 2c**).



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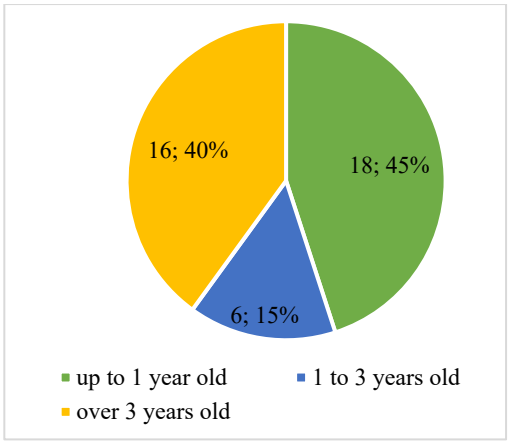

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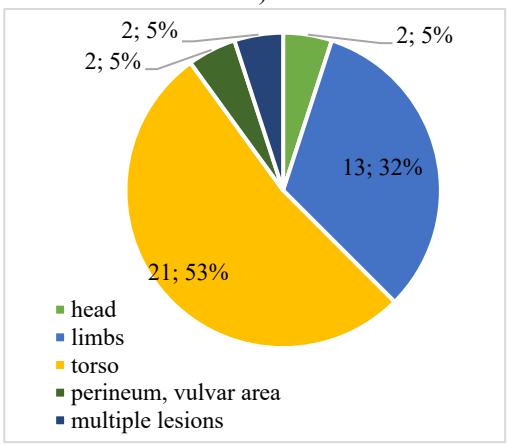

c)

Figure 2. Distribution of hemangiomas in children: a) by sex, b) by age, and c) by localization

Additionally, the study revealed that cavernous hemangiomas accounted for 65% of the cases (26 children), while mixed hemangiomas were observed in 35% (14 children).

80% of the children (32 out of 40) presented to medical facilities due to complications related to their hemangiomas. The complications were as follows:

- Ulceration: Found in 65% of cases (26 children).
- Bleeding: Occurred in 10% (4 children).
- Inflammation: Noted in 5% (2 children).

The preferred and most commonly sought-after treatment method for hemangiomas is surgical excision, as it generally offers a stable outcome with a lower risk of complications. Specifically, 85% of the children (34 cases) underwent surgical removal of the hemangioma, while 2 patients were treated with electrocoagulation, and 4 patients received propranolol therapy.

Conclusion

Management of hemangiomas requires a tailored, patient-specific approach. A clear framework for determining when to begin treatment is crucial, especially during the period of active tumor growth.

The most effective and cosmetically acceptable methods for treating hemangiomas are propranolol therapy and laser removal, both of which are safe and have proven to be highly successful.

On the other hand, surgical treatment and electrocoagulation offer long-lasting, relapse-free outcomes and remain reliable treatment options for more complex or persistent cases.

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Ethics Statement: None

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