Original Article

Methods of Treatment of Hemangiomas

Abstract

The prevalence of hemangiomas in children reaches 45.7% of all benign childhood tumors, among newborns up to 1/4 of children are affected by the disease. The complexity of diagnosing and treating hemangiomas is exacerbated by the lack of a unified classification capable of providing mutual understanding between pediatricians, dermatologists, pediatric surgeons, and oncologists. One of the generally recognized problems in the treatment of hemangiomas is the definition of indications for the start of treatment. A serious problem is the treatment of ulcerated hemangiomas, accompanied by infection and bleeding. The tactics of managing a patient with hemangioma require an individual approach. For example, propranolol therapy and laser removal of hemangiomas are the most effective, safe, and cosmetically acceptable methods of removal. Surgical treatment and electrocoagulation show a persistent, relapse-free effect. As part of the scientific work, a statistical study of 40 case histories of children was carried out. The article presents data on the distribution of the disease by sex, and age, as well as by location and method of treatment.

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

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Introduction

The prevalence of hemangiomas in children reaches 45.7% among all benign childhood tumors, and among newborns, up to 1/4 of children are affected by the disease.[1] There is evidence that the frequency of complications of hemangiomas reaches 40%, among which 7.5% - are bleeding, and 21% - are ulceration.[2] The fact of spontaneous regression of hemangiomas has been proven, however, this process is unpredictable.[3] The etiological factors of hemangiomas are debatable, only mutational and placental theories have some validity.[4] The complexity of diagnosing and treating hemangiomas is exacerbated by the lack of a unified classification capable of providing mutual understanding between pediatricians, dermatologists, pediatric surgeons, and oncologists. One of the generally recognized problems in the treatment of hemangiomas is the definition of indications for the start of treatment. A serious problem is the treatment of ulcerated hemangiomas accompanied by infection and bleeding.[5] Sometimes, under the influence of minor injuries, hemangiomas are damaged, infected, and, having ulcerated, are difficult to respond to traditional methods of treatment. The treatment process always takes a lot of time, bringing great trouble to children and requiring large material costs. This is also one of the urgent problems that require the right solution.

Vascular anomalies represent a heterogeneous group of congenital vascular pathologies. They are divided into vascular tumors and malformations that differ in a specific structure, pathophysiology, clinical course, and treatment approaches.[6] Hemangioma is the most common vascular tumor. Lymphatic, capillary, venous, and arteriovenous malformations account for the majority of vascular malformations.[7]

Classification of vascular anomalies

Currently, the classification of ISSVA (International Society for the Study of Vascular Anomalies), adopted in 1996, is used to systematize vascular anomalies.[8] This classification is based on hemodynamic studies by Mulliken and Glowacki (1982).

The fundamental issue in this classification is the division of vascular anomalies into vascular tumors and malformations **(Table 1)**. Hemangioma is an endothelial hyperplasia and is a benign tumor.[3] Malformation is a defect in the structure of

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blood vessels that occurs during embryogenesis and vasculogenesis.[9]

Given that in recent years, new methods of treatment and correction of this vascular pathology have appeared, the management of such patients requires the involvement of specialists in various fields, namely pediatricians, otolaryngologists, dermatologists, hematologists, surgeons, orthopedists, and even psychologists.[4]

Table 1. Classification of vascular anomalies

Vascular tumors	Vascular malformations		
- infantile hemangioma; - congenital hemangioma; - bundle hemangioma; - kaposiform hemangioendothelioma; - spindle-shaped hemangioendothelioma; - other, rare hemangioendotheliomas; - acquired vascular tumors (pyogenic granuloma, target hemangioma, micro-venular hemangioma, etc.).	**1. Malformations with slow blood flow:** • **Capillary:** - "wine stain"; - telangiectasia; - angiokeratoma. • **Venous:** - ordinary sporadic; - Bean's syndrome; - family skin and mucous membranes; - glomangioma; - Mafucci syndrome. • **Lymphatic**	**2. Malformations with fast blood** flow: - arterial; - arteriovenous fistula; - arteriovenous.	**3. Combined complex** vascular malformations

Clinical manifestations of hemangiomas

Simple cutaneous hemangiomas are represented by formations of red color, often with a bumpy surface, rising above the surface of the skin. Cavernous hemangiomas are located in the subcutaneous tissue, their tissue is defined as a bluish tumor-like formation. Combined hemangiomas have cutaneous and subcutaneous parts. Mixed tumors are represented by combinations with lymphoma, fibroma, lipoma, keratoma, etc.[10]

The tumor may be encapsulated or diffuse. When pressed, a decrease in formation is noted, followed by rapid restoration of the previous dimensions after the removal of compression.

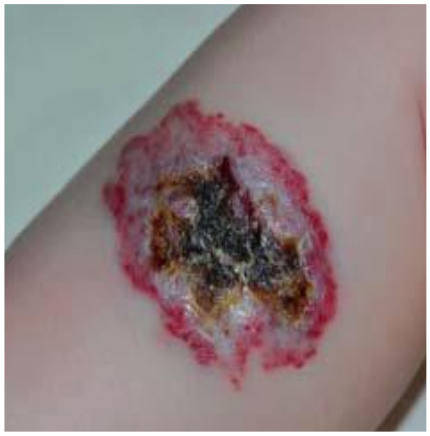
Localized in the larynx, hemangiomas cause stridor and airway obstruction. Volumetric liver hemangiomas can lead to the development of secondary heart failure, facial hemangiomas - to tissue necrosis with cosmetic defects of the eyelids, nose, lips, and ears. Periorbital tumors and eyelid lesions contribute to visual impairment and the development of amblyopia.[11] Gastrointestinal localizations are very rare but can cause gastrointestinal bleeding.[12]

Hemangiomas appear in the neonatal period, usually in the first two weeks of life. Preceding skin symptoms are detected in 30–40% of patients. The most frequent localizations are the head and neck (60%), various parts of the body (25%), and limbs (15%). In 20% of cases, multiple hemangiomas are observed.[13]

Hemangiomas are characterized by rapid growth at the age of 6-8 months. followed by a plateau at 10-12 months. Involutive changes in the tumor appear at the age of about 1 year and can last up to 7 years; complete regression occurs in 5–12 years.[14] Data on the frequency of spontaneous regression range from 5-10% to 15%. According to Robert M. Aresman, about 70–90% of hemangiomas can regress on their own, except for common tumors and tumors of critical locations.[15]

In the involution phase, the tumor decreases in size turn pale, and patches of skin appear on its surface. In the future, in 50% of patients, normal skin is determined at the site of the regressed hemangioma. In children with voluminous tumors, there may be excess skin with icteric coloration, and with ulceration, scars that require surgical correction.[16]

Allocate general and local complications. The latter occurs in approximately 5% of patients and is more often represented by ulceration and bleeding **(Figure 1)**.



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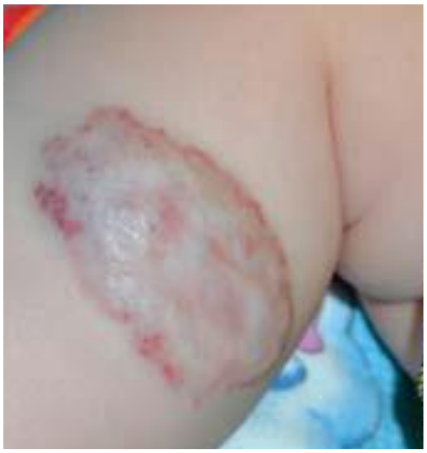


b)

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

According to clinical signs, there are: capillary hemangiomas, cavernous, and mixed.

Capillary hemangioma is located under the epidermis in the dermal or subdermal layers with the possibility of rapid growth over the surface of the skin or deep into the subcutaneous tissue, muscle structures, etc. The color of the tumor depends on the nature of the vessels, their lumen, and depth of occurrence: the prevalence of arterial type vessels causes a bright red color of the formation, and with the predominance of the venous network, its color is darker. When the skin or mucosa is stretched, the GA brightens or disappears ("pressure symptom").

As a kind of capillary hemangioma, specialists distinguish a vascular spot - a malformation of skin vessels, which, due to a specific clinical picture (a red formation with varying degrees of manifestation), is called a "port wine stain". The color of such a formation intensifies in the cold, during crying, with tension, etc.[17]

Cavernous hemangioma is a nodular tumor of a dark red or bluish color, soft consistency without clear boundaries. Despite its benign nature, its rapid progressive growth can be observed, especially in early childhood, which is accompanied by the facial deformity.

Depending on the clinical manifestations, cavernous hemangiomas are limited and diffuse, affecting not only the skin but also the underlying soft tissues.

A specific sign of cavernous hemangioma is a "filling symptom" (it turns pale when pressed, and when the head is tilted, it increases in size and pulsates).

Microscopically, cavernous hemangiomas consist of thin-walled blood-filled cavities lined with a flattened endothelium, anastomosing with each other, in which calcified thrombi or phleboliths were observed in some cases.[18]

Diagnosis of hemangiomas

In most cases, the diagnosis of hemangioma is made clinically, but in some cases, it should be supported by additional instrumental research methods (X-ray, Dopplerography, MRI).

Diagnosis with external localization of hemangioma is usually not difficult and is possible in 90% of cases.[19]

Certain difficulties arise in differentiation with other vascular tumors and malformations. In these cases, radiological studies and determination of the level of angiogenic factors are diagnostically significant to verify the phase of hemangioma development.

Radiation methods make it possible to determine the rheological features and prevalence of formations.

Color Doppler ultrasonography differentiates between fast and slow flow anomalies. However, in the proliferative phase, the hemangioma gives a special directed and reverse signal, which is difficult to distinguish even for an experienced specialist from the signal in arteriovenous malformations.[20]

The most informative is magnetic resonance imaging (MRI), which can be used to determine the prevalence of education and its rheological features. Magnetic resonance imaging makes it possible to differentiate almost all types of vascular malformations, except for skin capillary spots.[21]

Contrast-enhanced computed tomography (CT) is less commonly used due to radiation exposure. However, this method allows more accurate differentiation of lymphatic, venous, and lymphatic-venous malformations. Computed tomography provides more accurate information in the study of intraosseous vascular malformations and secondary bone changes.[22]

Arteriography, as the most invasive technique, is used exclusively for the diagnosis of vascular anomalies in combination with therapeutic super-selective embolization. Intravenous digital subtraction angiography is a relatively non-invasive method that allows to differentiation of highly vascular masses from inactive ones but does not have the resolving capabilities of standard angiography and arterial digital angiography. Angiography provides information on the size of the lesion and the vessels that feed it, and also makes it possible to differentiate hemangiomas from vascular malformations.[23]

Thus, in addition to radiation research methods, qualitative and quantitative indicators of angiogenic factors are significant in determining the phase of development of hemangiomas.

Therapeutic tactics for hemangiomas

Despite the long-term increased interest of surgeons in the treatment of hemangiomas, a unified medical doctrine has not yet been created. In specific clinical situations, doctors make

very ambiguous tactical decisions. There is still no generally accepted opinion regarding the optimal timing and methods of therapy. Inadequate choice of treatment and the development of complications lead to unsatisfactory cosmetic results.

The main directions of treatment are systemic effects on angiogenesis and local effects on tumor tissue. Systemic pharmacological therapy is carried out with corticosteroids, recombinant interferon, cytostatics, and β-blockers. Local methods include surgical removal, cryotherapy, electrocoagulation, sclerosing therapy, laser destruction, X-ray therapy, embolization of feeding vessels, and compression therapy.[24]

Each of the methods has certain advantages, and the only question is which of them is the most rational in terms of simplicity, accessibility, convenience for the patient, and effectiveness in terms of cosmetic and functional results.

Electrocoagulation and cryotherapy

These techniques are easy to perform and do not require expensive equipment, there is no need for deep general anesthesia. At the same time, attempts to remove large hemangiomas can lead to the development of both primary and secondary bleeding, and damage to large nerve trunks, such as the facial nerve. Massive tissue necrosis after these procedures leads to prolonged healing, often with infection of the wound surface. Even with a good postoperative course, healing ends very mediocrely in terms of aesthetics.[25]

Propranolol therapy for hemangiomas

The current 1st line of systemic treatment is propranolol. In 2008, it was found that the use of non-selective B-blockers in newborns with cardiovascular disease and concomitant infantile hemangioma inhibits the proliferation of hemangioma. This observation has been confirmed by multiple studies that have demonstrated a marked reduction in tumor size within 1-2 weeks after the start of treatment with propranolol.[26] Propranolol is recommended for the treatment of problematic hemangiomas for which surgery or expectant management is unacceptable. The most effective treatment of pharyngeal, periorbital, and other volumetric hemangiomas.

X-ray therapy

Short-focus X-ray therapy, according to many authors, is a highly effective method for the treatment of hemangiomas of the external integument in children. However, X-rays with vigorous or prolonged use harm the body, especially growth. They harm the growth zone of the meta epiphyses of tubular bones, inhibiting their growth and causing trophic changes in the bone tissue. In addition, there are often unsatisfactory cosmetic results - baldness on the scalp, atrophy of the skin with deprivation of their natural pigmentation, and the development of non-healing trophic ulcers.[27]

Materials and Methods

As part of this scientific work, a statistical study was conducted based on the study of the case histories of 40 children. The study aimed to analyze modern methods of treating hemangiomas in an outpatient setting and their effectiveness. To achieve the goal, the following tasks were set:

1. To study the frequency of occurrence and clinical and morphological features of hemangiomas in children.
2. To characterize modern methods of treatment of hemangiomas in children.

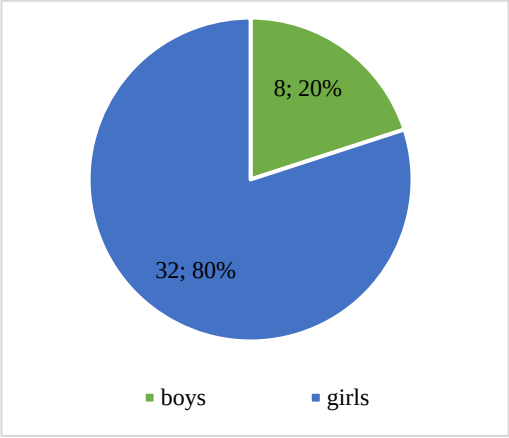
A retrospective analysis of 40 case histories of children with hemangiomas aged from 30 days to 18 years who were treated at the Regional Children's Clinical Hospital of the city of Stavropol in 2017 was carried out.

Statistical processing of the obtained results was carried out using Microsoft Excel 2010 and OpenOffice.

Results and Discussion

The results of the study showed the presence of the following patterns:

1. Hemangiomas in girls occur 4 times more often than in boys **(Figure 2a)**. Among the 40 case histories studied, 32 cases belonged to girls and only 8 to boys.
2. Hemangiomas are most common among newborns **(Figure 2b)**. So, among 40 patients, 18 were less than one year old. 16 children were aged from 3 to 18 years.
3. Hemangiomas are most common on the torso (21 out of 40 children) and also on the extremities (13 out of 40 children), **(Figure 2c)**.



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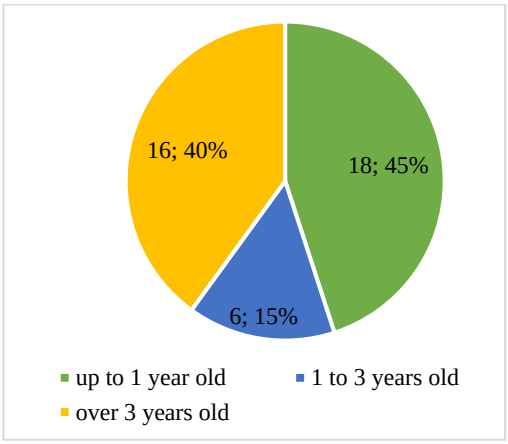

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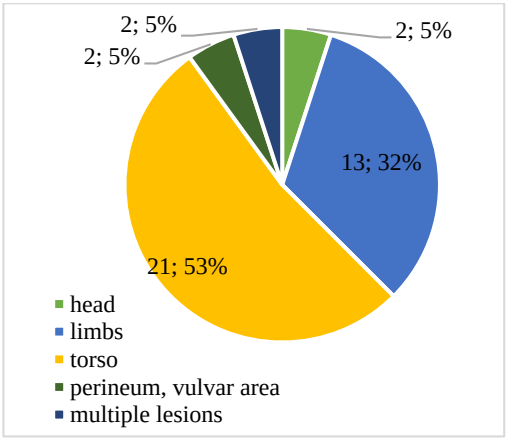

c)

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

In addition, it should be noted that cavernous hemangiomas accounted for 65% (in 26 children), and mixed - 35% (in 14 children).

80% of all children (32 people) sought medical help with various complications:

- in the form of ulcers - in 65% of cases (26 people);
- in the form of bleeding - in 10% of cases (4 people);
- in the form of inflammation - in 5% of cases (2 people).

The most popular and sought-after methods of treating hemangiomas are surgical since they give a stable result with a minimal likelihood of complications.[28-30] In 85% of children (34 cases), the method of treatment was excision of the hemangioma, in two people - electrocoagulation, and four people - propranolol therapy.

Conclusion

The tactics of managing a patient with hemangioma require an individual approach. The method for determining indications for the treatment of hemangiomas allows us to objectively determine the timing of the start of treatment of hemangiomas with their active growth.

Propranolol therapy and laser removal of hemangiomas are the most effective, safe, and cosmetically acceptable methods of removal.

Surgical treatment and electrocoagulation show a persistent, relapse-free effect.

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Conflict of interest

None.

Financial support

None.

Ethics statement

A retrospective analysis of 40 case histories of children with hemangiomas aged from 30 days to 18 years who were treated at the Regional Children's Clinical Hospital of the city of Stavropol in 2017 was carried out. For all cases, permissive agreements were obtained from parents.

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