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An Overview Of Infantile Hemangioma, Symptoms, Causes, Diagnosis And Various Types Of Treatment And Adverse Reaction Of Drugs Used In Treatment.

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ABSTRACT

Children's most prevalent tumors are called infantile hemangiomas (IHs). Rapid proliferation of endothelial cells in the early stages of infancy is indicative of these malignancies. primary care physicians should believe they will turn around on their own volition and without help or consequences. Pediatric hemangiomas can cause pain, functional disability, or irreversible damage if complications arise quickly. Children with IHs in potentially fatal places, local consequences such as bleeding, ulceration, and necrosis, and deformity that is either functional or cosmetic are represented in this group. Parents of patients as well as doctors may experience anxiety when choosing a course of treatment. Treatment techniques are very varied. The knowledge of this illness, its treatment, adverse drug reactions, and difficulties that arise in newborns following therapy will all be covered in this study.

KEYWORDS: Infantile hemangioma, symptoms, treatment, adverse drug reactions

INTRODUCTION

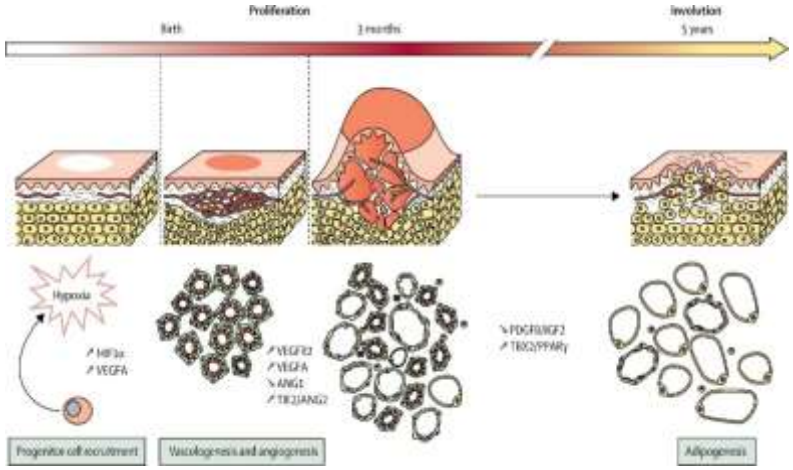
Hemangiomas are benign (non-cancerous) vascular tumors that originate from specific cell types found in blood vessels. It is known as infantile hemangioma (IHs) and is primarily observed in newborns. Childhood head and neck tumors are known as infantile hemangiomas. Known by another name, "strawberry mark," infantile hemangiomas are most commonly seen on the skin during the first week of life or at birth. **[1]** The depth of the hemangioma in the skin determines its hue. Although hemangiomas can develop anywhere on the body, they typically do so on the face, scalp, chest, or back. [**2**] As a youngster becomes older, they usually start to gradually shrink after growing for up to a year. **[1]** The location, size, age, and cosmetic consequences of a hemangioma determine its relevance. Rarely, internal hemangiomas can occur. **[2]**

I. PATHOGENESIS

There is much uncertainty regarding the pathophysiology of infantile hemangiomas. It is hypothesized that angiogenic factors-stimulated immature endothelial cell proliferation results in the formation of IH. **[3]** There is evidence to suggest that they originated cellularly from intrinsic endothelial progenitor cells (EPCs) or placental-originated angioblasts, but both intrinsic and extrinsic factors may have played a role in their development. Angiogenesis and vasculogenesis within the IH are examples of intrinsic factors. Disturbances in the developmental field and tissue hypoxia are examples of external influences. **[4]** Hypoxic stress as a trigger signal, along with overexpression of angiogenic molecules like VEGF through the HIFα pathway, is the most plausible scenario. Naturally occurring or recruited stem cells in fetal skin multiply and develop into immature endothelial cells in response to VEGF overexpression. **[5]**

II. PHASE OF GROWTH

IHs have a distinct life cycle. Proliferation and involution are two dynamic evolutionary phases that have been indicated by clinical data. Early infancy is the time of proliferation, and by the time a child is a year old, involution or regression has begun. a transitional phase known as the "plateau" phase that occurs between mid-to-late infancy and proliferation and involution. most likely denotes a brief time of equilibrium between individual cells going through apoptosis and involution and those that are multiplying. Up to 12 months of age is the proliferative phase. For most newborns with IH, the process of involution starts between the ages of 6 and 12 months, but it might take years to complete. **[4]**



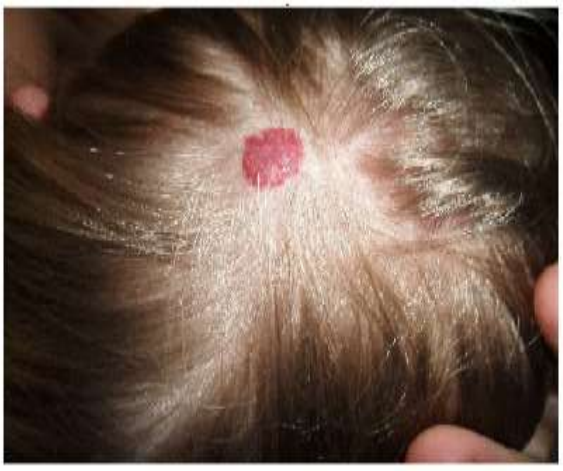
III. SIGNS AND SYMPTOMS

A hemangioma is an intensely red birthmark composed of additional blood vessels in the skin that resembles a rubbery hump or flat red area. The mark appears at birth or throughout the first month of life. Though it can appear anywhere on the skin, it usually appears on the face, scalp, chest, and back. **[6]**

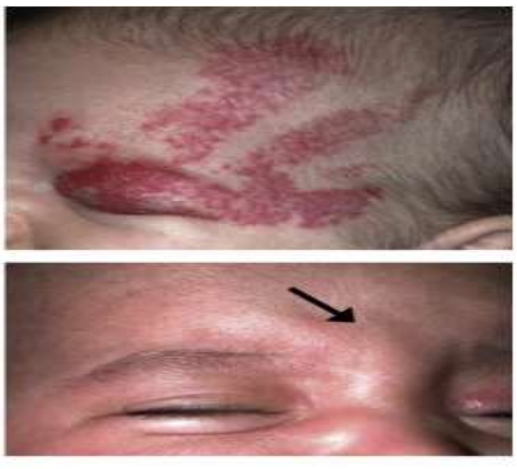
While a hemangioma can be seen from birth, it usually manifests itself in the first month of life. The red mark quickly develops into a spongy, rubbery-looking lump that protrudes from the skin throughout the first year of life. **[6]**

IV. CAUSES

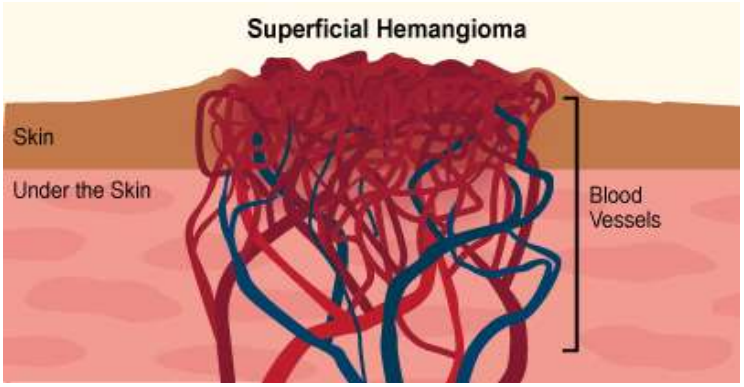
An accumulation of additional blood vessels that form a thick cluster is called a hemangioma. It is unknown what triggers the vessels to clump. The reason is unknown. **[6]**



Hemangioma on the scalp



Hemangioma on eye



V. COMPLICATIONS

1. Obstruction and functional impairment

Usually, during the early proliferation phase, visual blockage appears. Astigmatism, strabismus, and persistent amblyopia can result from hemangiomas that are situated on or near the eyelid. Inadequate eyelid closure and damage to the optic nerve are further issues. A life-threatening blockage of the upper airways can result from a hemangioma close to the jaw (beard area). **[5]**

2. Ulceration

One of the most frequent side effects of infantile hemangioma is ulceration, which is associated with pain and discomfort. The fourth and eighth months of life are when it is most common. Extended periods of wetness can exacerbate ulcers. **[5]**

3. Bleeding

It nearly only happens in lesions that are ulcerated. With pressure, most bleeding in non-ulcerated IHs can be controlled. The skin that covers the hemangioma tears, which results in bleeding. When pressure is applied to the area for five to fifteen minutes, the bleeding usually stops and is not life-threatening. **[4]**

4. Disfigurement

Infantile hemangiomas in the parotid or Centro facial region might cause disfigurement. Girls with large hemangiomas affecting the chest area. Subcutaneous hemangiomas in the vicinity of the parotid gland are frequently rather large. **[5]**

5. Congestive heart failure and Hypothyroidism

Infants with big IHs may experience high-output congestive heart failure, albeit it is uncommon, as a result of arteriovenous shunting of a significant blood volume through the lesion. There have been reports of this issue in newborns with massive cutaneous IHs. **[4]**

Severe consumptive hypothyroidism brought on by an overabundance of iodothyronine deiodinase synthesis can also be linked to diffuse liver lesions. **[4]**

VI. DIAGNOSIS AND ASSESSMENT

Clinical diagnosis is typically used to diagnose infantile hemangiomas. The diagnosis of infantile hemangioma requires imaging scans in addition to other procedures. A patient with infantile hemangioma who is at risk of complications should ideally be referred to a multidisciplinary team of doctors for assessment and particular diagnostic procedures (MRI, screening for hypothyroidism, abnormal coagulation, etc.), and treatment should be started after evaluating all of these. **[2]**

For clinical research, a number of severity scores, especially those for complications (such as the hemangioma severity scale and hemangioma dynamic complications scale), have been established. The proliferative activity of infantile hemangioma is evaluated using the Hemangioma Activity Score (HAS). **[5]**

In IH, ultrasonography reveals a high flow pattern and increased vascular density, which may aid in diagnosis. Well-defined lesions can be seen with magnetic resonance imaging (MRI). Because children in this

susceptible age group are exposed to radiation, MRIs are generally not advised. If CT is required, the radiation dose ought to be decreased to a level that is suitable for the patient's age and size. **[2]**

VII. TREATMENT

The majority of infantile hemangiomas tend to naturally regress, thus treatment is only necessary in more complex instances. Therapy for a Pediatric hemangioma that is obviously obstructed or ulcerated needs to start very away. When small infantile hemangiomas occur in important regions, watchful waiting, or intermittent attentive monitoring, can often be used to manage the condition. A tiny percentage of cases—children with IH who have local problems like bleeding, ulceration, necrosis, and functional disfigurements—require intervention. **[5]**

For many years, systemic corticosteroids have been the first-line treatment. Non-selective beta-blockers, like topical timolol and oral propranolol, have recently come to light as potentially safer treatments. Additional treatments for life-threatening hemangiomas that do not respond to traditional medications include vincristine and interferon alpha. **[7]**

Prior to the development of propranolol, infantile hemangiomas with ulcers and superficial lesions were said to respond rather well to pulsed dye laser treatment. In certain situations, early surgical excision of an obstructive infantile hemangioma remains a viable choice. This is especially true when propranolol is contraindicated. Surgical intervention has the benefit of a quick and long-lasting resolution. **[7]**

Drugs used in treatment of infantile hemangioma

1. Non selective β-adrenergic blockers:

The majority of clinicians who treat complex IH now use propranolol as their first line of treatment. The preferred course of treatment for complex infantile hemangiomas is now oral propranolol. It has been demonstrated that propranolol works well for both ulcerated infantile hemangioma and obstructive, potentially fatal airway infantile hemangioma. Although propranolol's precise mode of action is still unclear, it may control the growth of hemangioma cells by acting through the VEGF or catecholamine pathways. After therapy is stopped, some patients may experience recurrence. In infants at risk (those older than 12 months), recurrence is more likely to occur in segmental and deep infantile hemangiomas A paraben-free, sugar-free, and alcohol-free oral formulation designed for Pediatric use. **[4] [8]**

2. Topical β-blockers:

In an attempt to reduce the systemic adverse effects of oral propranolol, topical beta-blockers have been studied. Topical beta-blockers like timolol are employed. It has been demonstrated that non-selective topical beta-blockers are preferable to highly strong topical steroids. The primary goal of topical medicine delivery is to treat lesions effectively while minimizing negative effects. Topical beta blocking medications are usually sufficient for the treatment of ulcerated hemangiomas and small, superficial, uncomplicated IHs. **[9] [8]**

Timolol is a topical medication that can hasten the natural shrinking process of hemangiomas and assist prevent them from developing. It is said to lower blood flow by inhibiting β-adrenergic receptors, which causes blood vessels to constrict, though the precise process is unclear. Topical beta-blockers may irritate skin or produce localized redness where they are applied. **[10]**

3. Corticosteroid therapy:

Over the past few decades, steroids have played a crucial role in the management of IHs; nonetheless, when used properly and under close observation, they continue to be a useful way of care. For big and difficult IHs, systemic therapy with corticosteroids has been substituted with systemic β-blockers. **[4]**

A different option for people who cannot take propranolol or whose reaction to it is insufficient is corticosteroid therapy. In certain instances, hemangioma injections or oral corticosteroids may be used to aid in tumor shrinkage. It is possible to inject corticosteroids intralesionally or orally, such as prednisolone or dexamethasone. In addition to managing related consequences such ulceration or obstruction of breathing or vision, this therapy aids in the reduction of the hemangiomas size and growth.

Although the exact mechanism of action of steroids is unknown, it is believed that they block the stem cells in hemangiomas from producing vascular endothelial growth factor A (VEGF-A). During the early

proliferative phase, steroids are most effective. Long-term corticosteroid medication can have a variety of negative effects. **[9]**

4. **Topical steroids:**

Sometimes, topical steroids are used to treat infantile hemangiomas. The effects of topical steroids, like Temovate (clobetasol propionate 0.05%), have also been studied and are deemed to be modest. IH flat or slightly elevated vascular plaques have been treated with strong steroids. **[2]**

5. **Interferon-alpha:**

Interferon alpha has also been studied as a potential steroid-sparing drug. Interferon-α possesses anti-angiogenic qualities. In some situations, interferon alpha may be helpful, but it should only be administered sparingly and under a Pediatric specialist's supervision. Its use had major side effects, such as neutropenia, and an unacceptable risk of neurotoxicity that led to the discontinuation of treatment. **[2]**

6. **Vincristine:**

Vincristine is an alkaloid treatment for cancer that has been utilized as a steroid sparing drug for IH. It induces apoptosis by mitotic spindle microtubule interference. **[2]** Because of the possible adverse effects and risks involved with using vincristine, a chemotherapy agent, in babies with hemangioma, it is normally not the first choice for treatment. **[11]**

Some other treatment methods

1. **Surgery:**

Early surgical removal of an obstructive infantile hemangioma is still an option for special cases, especially in the presence of contraindications to propranolol. If the patient has a significantly large scalp tumor, surgical excision should be considered as first-line therapy. Surgical intervention has the advantage of a rapid, permanent solution, but carries the disadvantage of requiring general anaesthesia and leaving a permanent scar. **[5]**

2. **Laser therapy:**

One treatment option for lesions left over from hemangioma involution is laser therapy. The hemangiomas appearance is frequently improved by pulse dye laser treatment, which targets the blood vessels in the lesion selectively. Prior to the development of propranolol, infantile hemangiomas with ulcers and superficial lesions were said to respond rather well to pulsed dye laser treatment. Remaining lesions are still primarily treated with pulsed dye laser. **[12]**

VIII. ADVERSE DRUG REACTION

Harmful, unintended reactions to medicines that occur at doses normally used for treatment are called adverse drug reactions (ADRs). **[13]**

The treatment of infantile hemangioma can have potential adverse drug reactions depending on the medications used. Adverse drug reactions of drugs used in treatment of infantile hemangiomas are as follows:

a. Adverse drug reaction of non-selective β-blockers:

Diarrhoea, sleep disturbance cold peripheries and agitation were common ADRs with propranolol treatment in infantile hemangioma. Diarrhoea and weight loss emerged as severe ADRs which mandated permanent withdrawal of propranolol. **[14]**

1. **Hypotension:**

Propranolol can cause low blood pressure, especially in infants, which may lead to dizziness or fainting.

2. **Bradycardia:**

Propranolol can slow down the heart rate, so monitoring heart rate is essential during treatment.

3. Hypoglycemia:

Propranolol can lower blood sugar levels, so infants may be at risk for Hypoglycemia. Low blood sugar level can cause drowsiness or rarely seizures. Low blood sugar level with propranolol is more likely to occur when a child is not eating properly or has gone for several hours without eating.

4. Respiratory issues:

Infants on propranolol may experience bronchospasm, which can affect breathing. It also causes wheezing which is frequently associated with colds.

5. Gastrointestinal problems:

Nausea, vomiting and diarrhoea are possible side effects of propranolol. **[15]**

b. Adverse drug reaction of corticosteroids:

Potential systemic adverse effects of corticosteroids used in the treatment of infantile hemangioma are:

1. HPA axis suppression:

Suppression of the hypothalamic-pituitary-adrenal axis has been observed. A child with unknown HPA axis suppression who can undergoes significant stress. Additionally, if the HPA axis response is severely limited there is risk of coma and death.

2. Growth deceleration:

In some cases, growth deceleration has been observed. It means the growth of the child is slow.

3. Hypertension:

Corticosteroid can cause increase in blood pressure in infants which is severe and can harm to child's health.

4. Osteopenia:

It is a well-known adverse effect of long-term systemic corticosteroid therapy but it is rarely observed. Osteopenia means bone loss. Due to osteopenia, there is increased risk of fracture and poor skeletal support.

5. Immune suppression:

Corticosteroid therapy have immune suppressive effect. These include increased infection risk, reduced B- and T-lymphocytes counts and poor response to vaccines.

6. Ocular adverse effect:

It is an adverse effect of long-term therapy of corticosteroid, which include cataracts and increased intraocular pressure. The serious adverse effect is vision loss due glaucoma. Mild behavioural changes have been seen in infants who receiving corticosteroid therapy. These include irritability, fussiness and insomnia. **[16]**

c. Adverse drug reaction of topical β-blockers:

Topical beta-blockers may cause skin irritation or localized redness at application site. The skin itching, redness of skin and swelling of localized site may be occurred. **[17]**

d. Adverse drug reaction of topical steroids:

Topical steroids also have common adverse effect like atrophy and hypopigmentation. Glaucoma, and cataract formation when used over time. **[18] [2]**

e. Adverse drug reaction of interferon-α:

Serious ADRs of interferon-alpha include neutropenia and it has also a risk of neurotoxicity was unacceptably high and treatment was abandoned. **[2]**

f. Adverse drug reaction of vincristine:

It carries many side effects, including peripheral neuropathy, constipation, jaw pain, and hematologic toxicity. these side effect made it a third-line treatment for refractory cases. **[2]**

CONCLUSION

Among benign vascular tumors, infantile hemangiomas are most prevalent. From a therapeutic perspective, they must be carefully evaluated. Pharmacological and non-pharmacological therapeutic approaches come in a variety. Using medicine to treat infantile hemangioma carries the risk of adverse drug responses. In especially when caring for the fragile newborn population, healthcare providers need to consider the benefits of a treatment plan against its risks. Continued pharmacovigilance and further research are required to advance our understanding of potential adverse effects and the safety profile of drugs used to treat infantile hemangiomas.

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