Shahzad F, et al., J Surg Curr Trend Innov 2018, 2: 007
DOI: 10.24966/SCTI-7284/100007

HSOA Journal of Surgery: Current Trends & Innovations

Case Report

Current Management of Hemangiomas

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Abstract

Vascular anomalies are the most common congenital malformations. They are classified into two broad categories based on their endothelial characteristics: Vascular tumors and vascular malformations. Vascular tumors are characterized by endothelial proliferation. The most common vascular tumors are hemangiomas. Current management of infantile and congenital hemangiomas is presented in this review.

Introduction

Vascular anomalies are the most common pediatric congenital malformations. The management of vascular anomalies has historically been plagued with inconsistencies in terminology, which has led to incorrect diagnosis and treatment. A major step in streamlining terminology was the classification of vascular anomalies into two groups: Tumors and malformations [1]. The International Society for Study of Vascular Anomalies (ISSV) has further refined this classification over the years as our understanding of vascular malformations has improved and new entities have been described [2].

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Citation: Shahzad F, Gangopadhyay N, Zuberi J (2018) Current Management of Hemangiomas. J Surg Curr Trend Innov 2: 007.

Received: February 06, 2018; **Accepted:** May 25, 2018; **Published:** June 08, 2018

Most vascular anomalies can be diagnosed on the basis of history and exam. If diagnosis is still in question, color Doppler and ultrasound can be performed. The gold standard imaging modality is MRI, which gives information about the extent and characteristics of the lesion. If the diagnosis is still unclear, biopsy should be performed to clarify the diagnosis and exclude a malignant process. Pathologic analysis should include immunohistochemical staining for Glucose Transporter 1 (GLUT1), which is positive in infantile hemangioma and negative in vascular malformations [3].

Vascular anomalies are best managed by multidisciplinary teams. These teams consist of experts from many specialties including plastic surgery, dermatology, interventional radiology, hematology, physiatry, physical therapy, psychology and nursing. Other specialties - e.g., otolaryngology, orthopedics, urology, neurosurgery, pediatric general surgery etc., - are called upon when their services are needed. This ensures accurate diagnosis and optimal treatment plans for these challenging problems. Hemangiomas are of two types: Infantile and congenital. This review will focus on the current management of hemangiomas.

Infantile Hemangiomas

Incidence

Infantile Hemangiomas (IH) are the most common vascular anomalies, with an incidence of 4.5% in Caucasian children [4]. The incidence is lower in African Americans. In preterm babies <1200 g, the incidence is 23% [5].

Clinical features

Hemangiomas may not be clinically apparent at birth. They may appear as apale area, red or blue macule or papule. IH are characterized by three distinct clinical phases. The initial proliferative phase is the period of rapid growth, which lasts up to 6 to 12 months of age. The malformation grows out of proportion to the rate of growth of the child. The appearance of the lesion depends on its depth, with superficial lesions having a more reddish color and deeper lesions having a more purplish color. The growth of the lesion then stabilizes in the plateau phase (Figure 1). After a variable period of time the lesion enters the involution phase where the tumor starts to regress. The median age of involution is 4 years [6]. After involution (involuted phase), approximately half of the lesions leave behind local tissue changes like anetoderma, fibro fatty residuum and telangiectasias. Hemangiomas are morphologically classified as localized, segmental or multifocal. The segmental and multifocal varieties can be associated with other malformations and further investigation may be warranted (Table 1).

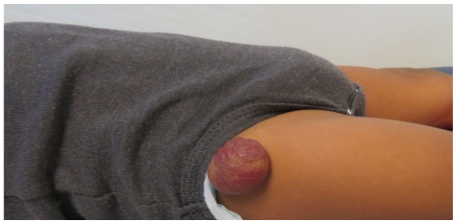

Figure 1: Untreated infantile hemangioma on right thigh in plateau phase.

Clinical Appearance	Condition or Syndrome	Characteristics	Work Up
5 or more hemangiomas	Diffuse neonatal hemangiomatosis [7]	Hepatic hemangiomas most common gastrointestinal tract, central nervous system and lungs less commonly involved hypothyroidism with diffuse hepatic hemangiomas	Ultrasound liver other imaging based on symptoms thyroid function tests
Segmental hemangiomas of the lower face and neck (beard distribution)	Upper airways or sub-glottic hemangioma [8,9]	Progressive airway obstruction manifesting clinically as stridor	Endoscopic airway examination
Large facial hemangiomas	PHACE(S) syndrome [10]	Segmental facial hemangioma in trigeminal distribution, plus one other finding: Posterior fossa brain malformations Hemangioma Arterial cerebrovascular anomalies Coarctation of aorta, Cardiac defects Eye and endocrine abnormalities Sternal clefting, Supraumbilical raphe	MRI & MRA of head and neck ophthalmologic, cardiac and endocrine consults
Segmental lumbosacral or perineal hemangiomas	PELVIS syndrome [11] SACRAL syndrome [12] LUMBAR syndrome [13]	Perineal hemangioma External genitalia malformations Lipomyelomeningocele Vesicorenal abnormalities Imperforate anus Skin tag Spinal dysraphism Anogenital anomalies Cutaneous anomalies Renal & urologic anomalies Angioma of lumbosacral localization Lower body hemangioma & other cutaneous deformities Urogenital anomalies Ulceration Myelopathy Bone deformities Anorectal malformations Arterial anomalies Renal anomalies	Ultrasound of genitourinary system Ultrasound of spine

Table 1: Conditions associated with hemangiomas.

Management

The management of IH depends on their stage. Expectant management is usually undertaken during the proliferative phase as the majority of hemangiomas run a benign course. Pharmacologic management is very effective in the proliferative phase. Steroids have historically been the drugs of choice. They halt growth and hasten involution. Oral prednisolone is typically started at a dose of 3 mg/kg administered once a day in the morning. After 1-2 months, the dosage is slowly tapered and then eventually discontinued at 10 to 12 months of age. H2 receptors blockers are also administered concurrently to counteract the gastric side effects of steroids. Other adverse effects from steroid treatment include mood changes, cushingoid features and growth restriction. The growth catches up after discontinuation of steroids. Steroids can also be injected intralesionally for small hemangiomas in critical or cosmetically sensitive areas [14]. Injections are performed 4 to 6 weeks apart for a total of 3 to 5 injections. Topical ultra-potent steroids have efficacy for thin superficial hemangiomas [15].

Propranolol was introduced in 2008 for treatment of hemangiomas and is now considered the first line therapy in the proliferative phase [16]. It has a 98% response rate [17]. Propranolol is a non-selective beta-antagonist and thus affects beta-receptors in the cardiovascular system, lungs and pancreas. Patients with certain congenital cardiac conditions are not candidates for the drug. Patients require baseline EKG and monitoring of vitals when therapy is initiated. The most common adverse effect is sleep disturbances. Other rare but life-threatening side effects are bradycardia, bronchospasm, and hypoglycemia. Propranolol can cross the blood-brain barrier and therefore there are concerns about possible long-term effects. Nadolol (a non-selective beta-antagonist) and acebutolol (a selective beta-1 antagonist) do not cross the blood-brain barrier and have been shown to be effective in small non-controlled studies [18,19]. Atenolol, a selective beta-1 antagonist that does not cross the blood-brain barrier, has been shown to be as effective as propranolol but with less reactive airway adverse effects [20].Topical beta-blockers like timolol have been found to be effective in small superficial hemangiomas [21]. They may be more effective than topical steroids [22]. Topical imiquimod 5% has been found to be efficacious for superficial hemangiomas; however, timolol is more effective with less adverse effects [23].

Lasers are typically not used during the proliferative phase, as they can cause ulceration and pain. The 595 nm Pulsed Dye Laser (PDL) can improve the appearance and clearance of hemangiomas [24,25]. PDL can also be used in conjunction with topical or systemic beta-blockers, and the combination has been shown to improve the clearance of hemangiomas [26,27]. PDL has also been used with topical 5-aminolevulinic acid as a photosensitizer. This combination has been shown to be superior to PDL alone [28]. Surgical excision of

IH during the proliferative phase can be performed for obstructive lesions of the visual or auditory axis, for ulcerated lesions causing pain or recurrent bleeding, or for large hemangiomas in cosmetically sensitive areas where the final deformity after involution will result in the same extent of surgery.

The most common complication during hemangioma proliferation is ulceration. This occurs most commonly in the anogenital and perianal regions. It can result in pain and bleeding, which is very distressing to the patients and the parents. The primary management of an ulcerated hemangioma is local wound care with an occlusive dressing to protect the wound from desiccation and friction. Topical lidocaine jelly can be used for pain control. Pulsed Dye Laser (PDL) therapy can promote healing of ulceration [29]. Typically, a few treatments are needed, spaced 3-4 weeks apart. Propranolol helps accelerate involution and thus promotes healing of ulceration. Therapy with both oral propranolol and prednisone can be effective for ulceration that does not respond to propranolol monotherapy [30]. Surgical excision can be performed for recalcitrant pain, recurrent bleeding or if parents are extremely anxious and want the problem to be resolved quickly.

Hemangiomas, especially of the head and neck, can result in functional impairment. Periorbital hemangiomas can cause deprivation amblyopia, astigmatism and strabismus. Preauricular hemangiomas can obstruct hearing. Large nasal hemangiomas can result in nasal obstruction. Hemangiomas of the lip can impair feeding. Large neck hemangiomas can cause torticollis. Urgent treatment is thus needed to prevent permanent dysfunction. Hemangiomas in a beard distribution can be concerning for airway involvement, and warrant airway evaluation by an otolaryngologist.

Hemangiomas can involve any organ system. Visceral hemangiomas are most commonly located in the liver. Hepatic hemangiomas are solitary, diffuse or multifocal. Solitary and diffuse hemangiomas can develop Arteriovenous (AV) shunts and cause high output cardiac failure. Pharmacotherapy with oral propranolol or prednisone is initiated. Vincristine is second line therapy and is used when steroids or beta-blockers are ineffective or contraindicated [31]. If there is worsening of heart failure, percutaneous embolization of the AV shunts can be performed [32]. Pharmacotherapy is continued till one year of age when natural involution of the hemangioma starts to occur. Multifocal and diffuse hepatic hemangiomas can cause severe hypothyroidism due to expression of type 3 deiodinase.

During the involutional phase, expectant management is usually undertaken to allow the hemangioma to naturally regress. However, surgery can be performed for an area of significant cosmetic deformity prior to school age i.e., around 4 to 5 years of age to normalize appearance and prevent teasing by peers (Figure 2) after involution, the residual superficial capillaries and telangiectasias can be treated with PDL therapy. PDL with a wavelength of 585 nm most closely matches the absorption spectrum of oxyhemoglobin, which is 577 nm. However, its depth of penetration is only 1 mm and thus it does not affect the deeper components. Redundant and damaged tissue can be surgically excised to improve appearance and contour.

Future therapies

Newer therapies for hemangioma are being developed. Molecular targets are being investigated in the lab that can be exploited for drug development [33]. Rapamycin (Sirolimus) is an immunosuppressive drug that also has anti-angiogenic properties. Rapamycin-loaded polymer-lipid hybrid nanoparticles delivered directly to hemangioma cells as a local controlled release system have been shown to decrease hemangioma volume *in vitro* and in rat studies [34].

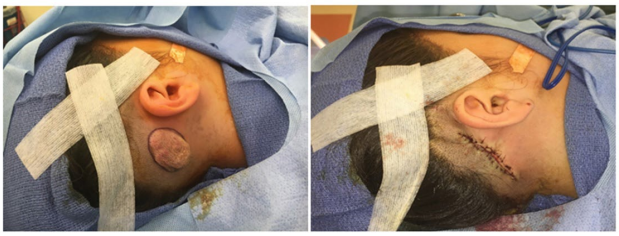

Figure 2: Intraoperative views of involuted postauricular hemangioma.

Congenital Hemangiomas

Congenital hemangiomas are fully developed at birth. They are typically raised, red to purple, with superficial telangiectasias and a pale halo around them. They are GLUT-1 negative. There are 3 types of congenital hemangiomas: 1) Rapidly Involuting Congenital Hemangioma (RICH), 2) Non-Involuting Congenital Hemangioma (NICH), and 3) Partially Involuting Congenital Hemangioma (PICH). RICH undergo rapid involution after birth, which is usually completed by 14 months of age [35]. NICH (Figure 3) on the other hand do not undergo involution. PICH start as a RICH but fails to completely involute [36]. RICH typically leave behind hypoplastic tissue that can be surgically excised. NICH and PICH can also be treated surgically, once the clinical course and diagnosis are clear.

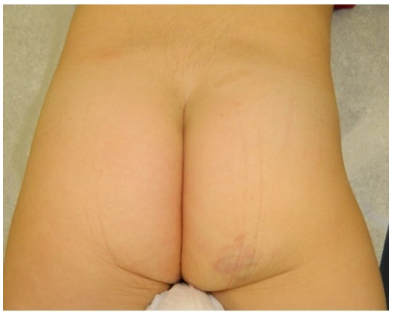

Figure 3: Untreated NICH on right buttock.

Conclusion

Hemangiomas are the most common pediatric vascular anomalies. They can be distinguished from other vascular anomalies by their characteristic life cycle, features on physical exam, and imaging characteristics. Biopsy is rarely performed and is usually to rule out a malignant process. Most infantile hemangiomas can be treated expectantly. Propranolol is considered the first line management in most centers for symptomatic infantile hemangiomas. Management of vascular anomalies should ideally be done in the setting of a multidisciplinary vascular anomalies team.

Conflict of Interest

The authors have no conflicts of interest to disclose.

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