

# Management of hemangiomas in children

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Hemangiomas are the most common tumors of infancy.<sup>[1]</sup> Traditionally, this term has been applied to benign tumors of vascular tissues and vascular malformations. Hemangiomas are classified as capillary, cavernous, and mixed lesions. The incidence in newborns is 1–3%, and this increases to 10% by the age of 1 year.<sup>[2]</sup> In the biologic classification proposed by Mulliken and Glowacki<sup>[3]</sup> in 1982, hemangiomas are defined as vascular tumors that enlarge by rapid cellular proliferation. Angiogenic factors such as heparin play an important role in the growth and involution of hemangiomas. These factors bring forth rapid endothelial growth by direct action on the endothelium and indirectly through cells such as macrophages and mast cells.<sup>[4,5]</sup> In contrast to hemangiomas, vascular malformations are hamartomatous lesions composed of dysplastic vessels lined by non-proliferating endothelium. They almost never regress and may expand in size.<sup>[3]</sup>

Hemangiomas are absent at birth or present as cutaneous marks. They grow rapidly beyond the child's growth rate for 6–8 months followed by slow regression, often resulting in complete regression. In one study, the lesion was present at birth in 36% of patients and 75% had developed it by the age of one month.<sup>[6]</sup> Rarely, it can be present as a fully grown lesion at birth, and has also been reported to be diagnosed by antenatal ultrasound.<sup>[7]</sup> The head and the neck are the common

sites of appearance of infantile hemangiomas.<sup>[6]</sup> Finn et al,<sup>[2]</sup> in a large series, found that 60% of hemangiomas occurred on the head and the neck, 25% on the trunk, and 15% on the extremities. Whereas 80% of patients have a single hemangioma, others have multifocal ones. Infants with multifocal lesions are at a higher risk of having visceral hemangiomas, especially intrahepatic ones.<sup>[8]</sup>

Complications of hemangiomas are cosmetic and functional, and depend on their location, size, or rapid proliferating phase. Some type of complication is found in 40% of lesions, the commonest being ulceration (21%) and bleeding (7.5%).<sup>[6]</sup> Cervicofacial hemangiomas can result in airway obstruction and difficulty in swallowing.<sup>[9]</sup> Large hemangiomas can result in cardiac failure and platelet trapping with coagulopathy (Kasabach-Merritt syndrome). Periorbital hemangiomas can cause astigmatism, ptosis, strabismus, amblyopia, and blindness.<sup>[10]</sup>

After a thorough physical examination, investigations may be indicated if complications are present or if surgical intervention is contemplated. Coagulation studies should be done if platelet trapping is suspected. Computed tomography and magnetic resonance imaging can delineate the extent and involvement of the hemangioma and can help to differentiate deep hemangiomas from lymphatic anomalies in the

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neck.<sup>[11,12]</sup>

The treatment of congenital vascular anomalies is based on an understanding of the clinical behavior and natural history of individual lesions. Most hemangiomas do not require immediate intervention and 90% can be expected to undergo gradual involution before the age of 9 years.<sup>[13]</sup> In 50% of these cases, normal skin is restored, whereas in the remaining, the cosmetic result is much better than that offered by surgical intervention.<sup>[2]</sup> Hence, explanation about the natural course of the disease is vital to alleviate parental anxiety. An ulcerated hemangioma can also be managed conservatively with cleansing and topical antibiotics and epithelializes within 2 weeks. Pulsed dye laser has been reported to accelerate healing in such cases.<sup>[14]</sup>

Active intervention is required in those cases that do not show signs of involution and in those with local or systemic complications. Sclerotherapy is effective in more than 90% of hemangiomas, but not in involuting lesions. Superficial lesions of the lip and eyelid and bulky hemangiomas of subcutaneous tissue have been treated with sclerotherapy without complications other than very minimal epithelial desquamation.<sup>[15]</sup> Sclerosing solutions are both tissue irritants and thrombogenic agents that provoke an inflammatory reaction, which causes fibrosis and obliteration of vascular channels; 1% and 3% sodium tetradecyl sulfate (Setrol®) is the currently favored sclerosant. With each thrust into the lesion, 0.1 ml of the solution is instilled in various directions, avoiding the skin surface to prevent necrosis. Repeated injections may be required at an interval of 21 days. Postinjection swelling and pain are treated with nonsteroidal anti-inflammatory drugs.

Laser therapy is indicated in infants with proliferative hemangiomas in whom active intervention is indicated owing to associated functional impairment or surface ulceration.<sup>[16]</sup> The flash lamp pulsed dye laser (585 nm) has been used successfully in ulcerated lesions in infants.<sup>[14]</sup> The CO<sub>2</sub> laser (10600 nm) with nonselective action and neodymium-yttrium aluminum garnet (Nd : YAG) laser (1060 nm),<sup>[17]</sup> which penetrates deeper in the tissues, produce considerable scarring. Scarring appears to be less with a tunable dye laser (577 nm).

Strawberry hemangiomas have been successfully treated with argon and Nd:YAG lasers.

Intralesional injection of steroids has been used for lesions that are not suitable for excision, such as those situated around the eye and on the upper part of the face, with a response rate of 77%.<sup>[18]</sup> Strawberry lesions respond well to intralesional steroids, whereas deeper and cavernous lesions have been reported to respond to 50% dextrose injections.<sup>[19]</sup> A mixture of triamcinolone acetonide (2–100 mg per injection) and betamethasone acetate (0.3–15 mg per injection) is preferred to injection of a single agent.<sup>[20]</sup> It is injected directly into the hemangioma in different directions through the same needle hole. Direct pressure is applied for 2–10 minutes to prevent bleeding. The complications include sclerodermiform atrophy, eyelid necrosis, and central retinal artery occlusion.<sup>[21]</sup>

Intralesional bleomycin injection is an effective treatment in hemangiomas, obviating the need for invasive primary surgery or systemic treatment regimens in 80% of cases. A complete response is seen in 49% of lesions. The side effects are superficial ulceration and cellulitis.<sup>[22,23]</sup>

In case of large hemangiomas in small children, where urgent treatment may be required for life-threatening complications, multimodality treatment may be more effective. Embolization is effective for large lesions that are not amenable to other treatment options or in preparation for surgical excision.<sup>[24]</sup> Occlusion of the blood vessel can be temporary or permanent depending on the material used (absorbable gelatin sponge, polyvinyl alcohol sponge, metallic coils, autologous blood clot, methacrylate spheres, and cyanoacrylate tissue adhesives) and is particularly useful in the presence of complications such as bleeding, cardiac failure, or Kasabach-Merritt syndrome.

A hemangioma is surgically excised when it has not responded to more conservative measures or when complications occur. The surgical approach depends on the size and location of the hemangioma.<sup>[25]</sup> Magnetic resonance imaging (MRI) is the preferred investigation before surgical management is considered. Preoperative

embolization is helpful in reducing the size of the hemangioma and also blood loss during surgery. In contrast to hemangiomas, majority of vascular malformations will ultimately require surgical excision because the potential for involution is minimal.<sup>[3]</sup>

Compression treatment has been used successfully to treat giant hemangiomas of the extremities.<sup>[26]</sup> Compression can be applied continuously (with bandages, garments, or splints) or intermittently (with pneumatic compression devices). It promotes emptying of vascular channels with thrombosis and endothelial damage.

Systemic therapy with steroids or interferon- $\alpha$  (INF- $\alpha$ ) has been successfully used in infants with cutaneovisceral hemangiomatosis presenting with life-threatening complications. The other agents used systemically are chemotherapeutic drugs such as bleomycin and cyclophosphamide.

Immature and proliferating hemangiomas respond better to steroids.<sup>[27]</sup> Oral prednisolone is given in the dosage of 5 mg/kg/day for 6–9 weeks, then 2–3 mg/kg/day for 4 weeks, and followed by alternate day therapy for up to 6 weeks. Methylprednisolone has also been used successfully in children with hemangiomas and Kasabach-Merritt syndrome.<sup>[28]</sup> Steroid treatment should always be tapered gradually and never stopped abruptly because of the possibility of regrowth of hemangioma and to avoid adrenal crisis.<sup>[29]</sup>

INF- $\alpha$ -2a induces early involution of large hemangiomas. It blocks migration and proliferation of endothelial cells, smooth-muscle cells, and fibroblasts by decreasing the production of collagen and basic fibroblast growth factor. The dosage used is  $3 \times 10^6$  U/m<sup>2</sup>/day subcutaneously for 6–18 months. Complete involution may take a long time. Its potential side effects include fever, malaise, leucopenia, interstitial nephritis, and hemolytic anemia.<sup>[30]</sup> The use of radiation in the management of hemangiomas is controversial owing to the high complication rate.<sup>[31]</sup>

To conclude, small and uncomplicated hemangiomas in children can be managed conservatively with

observation and follow-up alone. Parents need to be reassured regarding these rapidly progressing tumors in an otherwise normal child. Most of them involute completely with minimal scarring. Complicated lesions and those involving eyelids, ears, tongue, or lip require active management. Superficial ulcerated lesions can be managed with laser treatment. If the lesion is less than 2.5 cm diameter, sclerotherapy, intralesional steroid, or bleomycin injections are recommended. Systemic treatment is needed for a lesion larger than 2.5 cm<sup>[32]</sup> and also for complications such as cardiac failure and coagulopathy. Corticosteroids and interferon form the first line of treatment. Vincristine and bleomycin are considered for problematic hemangiomas in infants, which fail to respond to steroids. Surgery is indicated in small, well-localized lesions of the eyelid, lip, and neck or other parts of the body and when it is likely to lead to an aesthetically more acceptable scar.

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