REVIEW ARTICLES

MANAGEMENT OF INFANTILE HEMANGIOMA

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Introduction

Infantile hemangiomas are the most common cutaneous tumors of childhood. (1) Infantile hemangiomas are vascular tumors which are present at birth as telengectatic macule followed by rapid growth phase and a slow involution, leading to complete regression. (1) They have to be differentiated from congenital hemangiomas and malformations that are usually fully grown at birth and do not involute completely. (2) International society for study of vascular anomalies in 1996 classified vascular birth marks into vascular tumors and vascular malformations. (3) Infantile hemangiomas are more common in females than in males with ratio of 3:1. There is an increased incidence in premature and low birth weight infants and Caucasian ethnicity. (2) They are also more common after chorionic villous sampling. (4,5) Exact aetiology is not known. Since infantile hemangioma cells are positive for markers like GLUT-1, Lewis-Y, merosin, CCR6 similar to that of human placenta it is postulated that they are due to placental embolisation. There is decreased expression of vascular endothelial growth factor receptor (VEGFR 1) resulting in VEGF induced activation of VEGFR2 pathway leading to angiogenesis. Tissue hypoxia induces angiogenesis. (6)

Management of Small Uncomplicated Infantile Hemangioma

Management of infantile hemangioma varies according to site, size, complications, and stage of hemangioma and socioeconomic status of the patient and should be tailored to individual patient. Majority of them are smaller lesions and regress spontaneously. For smaller uncomplicated lesion of cosmetically less prominent area active non intervention is the policy adopted. Serial photographs are taken and consistent reassurance is given to parents and school going children regarding benign nature and spontaneous involution after a period of growth. Gentle massage, compression therapy with pressure dressing, application of ice can be done for proliferative phase. (7) Even smaller uncomplicated lesion if present in visibly prominent area can be emotionally disturbing to parents. They are often not ready to wait for years for regression and are worried about the subsequent scarring. Therapeutic option in such situation would be one which can cause involution without much side effects. Topical and intralesional steroids are often used. Periorbital hemangioma is treated with 10mg/ml of triamcinolone acetonide at monthly intervals. (7) Two to 3 sittings are needed. (7). A study reported 85% of patients responded with 50% reduction in volume. (8) Complications include atrophy, dispigmentation, eyelid necrosis retinal artery embolism. (8). 5% imiquimoid cream has been found useful. (9) The action is mediated through natural killer cells and interferon gamma which has antiangiogenic action. Side effects are minimal erythema and crusting can occur. (9) Topical 0.5% timolol eye drops, a nonselective beta blocker has shown excellent results. (10) It acts by vasoconstriction, decreases the growth factors and aids in apoptosis leading to involution. (10,11) No serious side effects reported except pruritus. (10) One study showed average regression in 3.3 months. (11) Systemic absorption is minimal after topical use of timolol. Prolonged use of timolol eye drops for glaucoma has reported side effects like chyne stokes breathing and exacerbations of asthma. (12,13) So caution is needed for large hemangioma and in children with cardiorespiratory abnormalities. Becaplermin (platelet derived growth factor) has been found useful in ulcerated infantile hemangioma of diaper area. Plermin increases mitogenesis of fibroblasts and helps in re-epithelisation. (14) Local delivery of biphosphonates in treatment of hemangioma is under research. (15)

Management of Large Complicated Infantile Hemangioma

Larger hemangiomas develop complications especially during proliferative phase, most common being ulceration and bleeding. If they are near orifices, it can cause obstruction and impairment with vital functions like vision, feeding, excretion, respiration depending on the site of hemangioma. Such situations need immediate intervention. Besides these, hemangioma of tip of the nose, ear and lip are notorious for disfigurement. They also necessitate early intervention. (7) Systemic steroids can be used to cause faster reduction in size and are the drug of choice especially in life threatening situation. (7) Recommended starting dose is 2 mg per kg body weight as single morning dose and gradually tapered. Steroids have direct inhibitory effect on angiogenesis and they cause enhanced expression of genes coding for markers of apoptosis. They also act by increasing the sensitivity of vessels to vasoconstrictor substances by decreasing 17 beta oestrodiol. (16) High dose of steroids has its own side effect which has to be weighed against benefits. Caution is needed in children regarding growth retardation and in giving live vaccines. (17) Forty percent of hemangioma show rebound after stopping steroid. (1) Thirty percent of hemangioma do not respond to systemic steroids. (7) Recently promising results are reported with systemic propranolol, a non-selective betablocker. (18) started as 2mg per kg bodyweight orally. Mechanism of action is similar to that mentioned with timolol. Results are excellent. Reduction in size of hemangioma is faster and involution occurs completely. (18) But extreme caution is needed in administering propranolol. Vigilant monitoring of blood glucose, cardiac and respiratory system is to be done during treatment. (19) Life threatening hemangiomas that fail to respond to systemic steroids can be treated with interferon alpha given subcutaneously.1-3 million units/m2. It acts by inhibiting angiogenesis. (20) Flu like syndrome, spastic diplegia, neutropenia, renal failure are some of the side effects. (19) Other

immunosuppressive agents like cyclophosphamide, vincristine and intralesional bleomycin are also used for hemangiomas that are refractory to conventional treatments. (21-26) Cidofovir, an antiretroviral drug has antiangiogenic activity, further studies are needed about its use in life threatening hemangioma. (2) Surgical treatment in hemangioma has narrowed its role to pedunculated hemangiomas and redundant scar following involution. (27) Moreover scar following surgery may be worse than that of spontaneous regression. Circular excision followed by purse string suture has shown minimum scar. (27) Cryotherapy can be used to hasten involution but its use is limited due to scarring. (28,29) Sclerotherapy with hypertonic saline and sodium citrate are no longer used. Sclerotherapy with polidoconol has shown convincing results. (30) Superficial hemangiomas can be treated effectively with Flash lamp pulsed dye laser. It is also useful in persistent telengectasia after involution. Pulsed Nd YAG has greater penetration and can be used for deeper lesions but scarring is unavoidable. Carbon dioxide laser can be used in surgical intervention. (6)

Complications need special care. Large segmental facial hemangioma may be associated with PHACES syndrome and needs special care before starting treatment with beta blockers. One study has reported effective clearance with topical timolol. (9) Beard area hemangioma may be associated with subglotic hemangiomas and may require tracheotomy. (6) Multiple hemangiomas may be associated with hepatic hemangiomas and are treated with arterial embolisation. (6) Thalidomide inhibits angiogenesis and is found useful in case of life threatening intracranial haemangiomas. (31)

Conclusion

Majority of hemangiomas are smaller lesions which undergo spontaneous resolution without much sequel .Cosmetically disfiguring and emotionally disturbing lesions even if small has to be treated with modalities which have minimum side effects. Complicated and life threatening lesions needs immediate attention with agents that cause faster regression. Treatment option should be individualized and carefully chosen to give maximum benefit to the patients.

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