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Original Research Article

Pulse steroid therapy in infantile facial hemangiomas: the early experience

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ABSTRACT

Background: To investigate the efficacy and safety of Pulse steroid therapy in the management of Infantile facial hemangioma in five subjects.
Methods: Consecutive patients who presented with facial hemangioma were prospectively enrolled in this study between January 2014 till August 2017. All subjects underwent treatment with 30mg/kg/day I/V methyl prednisolone for 6days and then weekly for 6weeks and then followed by oral daily dosing. All subjects underwent systemic, and radiologic evaluations before treatment and at periodic intervals after starting therapy. Side effects from therapy were also evaluated.
Results: Five subjects under 6 months of age, with facial hemangioma were enrolled in this study. After hospital admission, I/V steroid therapy was initiated in all subjects under monitoring by a pediatric cardiologist. Subsequent oral therapy after 6 weeks was performed with periodic out-patient monitoring. All subjects had excellent response to treatment, with regression of facial hemangioma. There were no side effects from therapy.
Conclusions: I/V methyl prednisolone pulse steroid therapy for facial hemangioma was effective in all the five subjects.

Keywords: Infantile facial hemangioma, Pulse steroid therapy

INTRODUCTION

An infantile hemangioma (hem-an-gee-o-ma), or strawberry mark, is a very common type of birthmark made of blood vessels. Most hemangiomas are not visible at birth.

Most hemangiomas are not visible at birth, but they often begin to appear during the first four to six weeks of a child's life. All skin hemangiomas will be visible by six months of age.

They may occur anywhere on the skin surface, but they are most common on the scalp, face and neck. Infantile hemangiomas usually appear within the first weeks of life and grow most rapidly during the first three to six months of life.[1-4] For most hemangiomas, 80% of infantile hemangioma size is generally reached by 3 months of age.[5]

Hemangiomas can occur anywhere on the skin, including, rarely, in the organs of the body. Most often, hemangiomas grow on the skin of the head or neck.

There are three general types of infantile hemangiomas

- Superficial hemangiomas, which occur on the outer layers of the skin, are typically bright red to purple in color.

- Deep hemangiomas, which grow under the skin in the fat, may be blue, purple or even skin color (if they are deep enough under the skin surface).
- Mixed hemangiomas are the most common type of hemangioma. These hemangiomas have both superficial and deep components.

Hemangiomas' shape, size and growth rate

- Most hemangiomas are round or oval in shape, but larger lesions may follow the shape of the affected body part.
- The size of hemangiomas varies. Some are very small (1mm), while others are very large (≥20cm).
- Every hemangioma differs in how fast it grows and how long it grows before it stops.

Infantile hemangiomas grow rapidly for the first few weeks or months. They then enter a rest phase by about 8 months of age. And they usually begin to shrink (involution phase) around 1 year of age. As the lesion shrinks, the color may change from red to purple and gray. It may take several years for the hemangioma to go away completely. Larger lesions take a longer time to go away and have a greater chance of scarring.

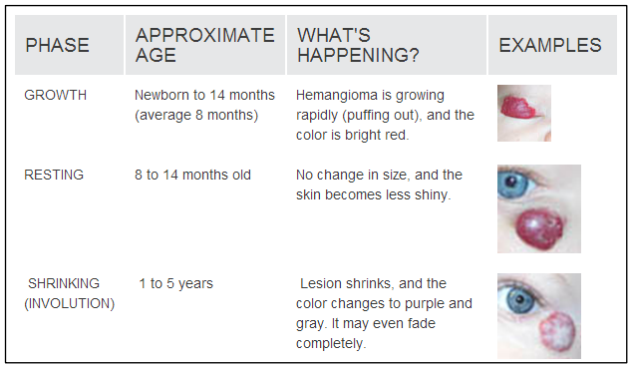

Figure 1: Different phases of hemangioma.

METHODS

Consecutive patients with facial including periorbital capillary hemangioma, with vision threatening lesions, who presented to our institution between January 2014 to August 2017 were treated with I/V Steroid therapy and followed up prospectively. Prior to commencing, thorough examination of the patient was done using radiologic investigations. Magnetic resonance imaging (MRI) of the face and orbits was performed to establish the diagnosis and determine the extent of involvement. All subjects underwent a pediatric evaluation to exclude systemic anomalies, neuroimaging to rule out intracranial abnormalities, and abdominal ultrasonography to assess visceral involvement. All subjects underwent a complete systemic examination to establish cardiovascular and respiratory fitness, chest x-ray, electrocardiography (EKG), and echocardiography (echo). Segmental hemangiomas may be associated with visceral hemangiomatosis, with the location of visceral lesions often correlating with the site of cutaneous involvement. Infants with large segmental hemangiomas on the face are at risk for PHACES syndrome (Posterior fossa anomalies, haemangiomas, arterial anomalies, coarctation of aorta and cardiac defects, eye abnormalities, sternal clefting and supra-umbilical raphe) and should undergo a thorough ophthalmological, cardiac and neurological evaluation. Magnetic resonance imaging (MRI) with angiography of the head and neck region is usually indicated in such infants.[6-8]

Laryngeal involvement can occur if haemangiomas are present on the cervicofacial, mandibular or the 'beard' distribution. Affected infants should be watched for signs and symptoms of airway obstruction (stridor, hoarseness) and referred for a laryngeal examination.[9] Infants with multiple cutaneous haemangiomas (diffuse neonatal haemangiomatosis) constitute another group which is at risk for visceral involvement, and it is generally recommended to screen the patient for hepatic involvement by abdominal ultrasound.[10,11]

Pulse steroid therapy was started at the dose of 30mg/kg/day of methyl prednisolone for 6 consecutive days and then weekly dose of 30mg/kg/day for 6 weeks which is followed by oral prednisolone 2mg/kg/day in 3 divided doses for 15 days and then taper down every 15 days to finally stopping the drug after 45 days. While initiating therapy, all children were admitted in order to monitor pulse rate and blood pressure every half an hour for the first 4 hours. If the child tolerated the treatment well, therapy was continued on an out-patient basis and the subjects (subject's caregivers/parents) were requested to return 1 week after discharge. Additionally, screening for cardiovascular and metabolic side effects of steroid was performed at each visit by a cardiologist.

RESULTS

Five subjects (three females; two male) under 5 years of age met the inclusion criteria.

Two subjects had passed the proliferative phase and were older than 1 year of age when therapy was initiated. These subjects had undergone treatment with high-dose prednisone for several months with a poor response and had rebound growth of the hemangioma after steroid withdrawal. Rest three under 1 year of age showed excellent response and complete remission of infantile facial hemangioma by following the pulse steroid therapy regimen during their follow up.

All subjects remained systemically stable at the initiation of treatment and during follow-up. Although all subjects showed visible signs of tumor regression, an accelerated involution of the hemangioma was observed in the subjects who were below 6 months of age at the time of initiation of therapy.

DISCUSSION

Infantile hemangiomas are benign vascular tumors of childhood, characterized by endothelial cell proliferation. They are the most common soft-tissue tumors of childhood, occurring in 3% to 10% of the population.

Known risk factors for the development of infantile hemangiomas are: females (female to male ratio of 2.4:1), Caucasians, low birth weight, and children of multiple gestations.

Table 1: Clinical presentation of the five subjects.

Subject	Age at initiation of treatment with prednisolone	Sex	Hemangioma site	Side	Previous treatment
1	19 months	F	Extensive facial hemangioma	Right	Intralesional steroid
2	12 months	F	Extensive hemangioma of face, airways, upper limb and chest	Both sides	Nil
3	4 months	M	Upper eyelid and small lesions on chest	Left	Nil
4	3 months	F	Upper eyelid and left cheek	Right	Nil
5	4 months	M	Cheek	Left	Nil

The causes of infantile hemangiomas are not well understood. The tumor is formed from the proliferation of the endothelial cells. Studies suggest the role of fetal hypoxic stress as the triggering signal that initiates the proliferation and abnormal blood vessel formation through activation of certain genes. Incomplete vasculature maturation and maternal chorionic-villus sampling has also been suggested as a potential cause of hemangiomas. Placental and infantile hemangioma cells have similar cell markers which supports the theory of IH representing "benign metastases" originating from placenta. Endothelial progenitor cells (EPCs) are vascular stem cells that are now believed to play a role in the etiology of IH; they are increased 15-fold as compared to controls.

Approximately 10% to 20% of infants with hemangiomas require intervention to prevent or decrease complications related to their proliferation.[12]

Systemic corticosteroids are the most common treatment modality used in the management of problematic hemangiomas. Systemic corticosteroids (prednisolone) have been the mainstay of treatment for IH, for several decades. The mechanism of action of steroids is not entirely clear, though it is postulated to have an inhibitory effect on the production of vascular endothelial growth factor A (VEGF-A) by stem cells in haemangioma.[13,14] This is the study to demonstrate the efficacy of corticosteroids in halting the proliferation of IHs clinically (decrease in hemangioma size and improved visual function) and biologically (decrease in the circulating proangiogenic proteins). The effect, measured over the first year of life, was more pronounced with high-dose, intermittent pulses with methylprednisolone. One of the biggest limitations in designing studies of infantile hemangiomas is quantifying the response to treatment. To date, there are no good clinical, laboratory, or imaging tools that can accurately size these lesions. present efficacy data are comparable to previous reports.

In a study using high-dose oral methyl-prednisolone (30mg/kg per day for 5 days with tapering every 5 days for a total of 6 weeks), a high initial response rate with high doses was noted. Given the lower rate of adverse effects and shorter duration of treatment, this regimen was preferable to longer, lower-dose courses.[15]

The frequency of complications (hypertension, adrenal suppression, growth retardation) was not seen in our study which was usually seen in oral prednisolone taking groups.

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