Craniofacial cavernous hemangioma: succesful treatment with methylprednisolone

L. A. Dourmishev and A. L. Dourmishev

SUMMARY

Systemic corticosteroid treatment is reported as effective for problematic cutaneous hemangiomas occuring in infancy, and depend on the dose, the duration of treatment, and the age at which the course of drugs is initiated.

A 7-month-old female infant with extended cavernous hemangioma on the left part of forehead, face, and neck which appeared 15 days after birth is presented. She was successfully treated with oral methylprednisolone (initial doses of 3 mg/kg/daily and reduced in steps over 6 months) with significant involution of the lesions and with good aesthetic results.

The oral corticosteroid treatment is an efficient medical therapy for common extended cavernous infantile hemangiomas with accelerated growth if initiated early in the proliferative phase.

Introduction

Hemangiomas of the skin are the most common benign tumors of childhood, characterized by a unique natural history of growth in early infancy, followed by slow involution in the following years (1–3). The large forms of infantile cavernous hemangiomas are visually displeasing, frequently have accelerated growth, and may cause significant functional disturbances and existential complications. Several noncontroversial indications that demand treatment include hemangiomas affecting vision or producing serious permanent disfigurement (that is unlikely to resolve on its own and cause long-term adverse psychological consequences), or other problematic symptoms that depend on the anatomic location (3, 4). Different methods of treatment including cryotherapy, sclerosing solutions, surgical removal and laser therapy have been used with differing results (5–7). The conservative approach that leaves the lesions untreated is widely accepted, because the results of the destructive treatment are usually worse than those that result from spontaneous involution (3, 8). The mainstay of medical therapy are corticosteroids (9) but the recommended dosage, duration of treatment, recommended monitoring during and after treatment, and methods of tapering vary widely (4). Corticosteroids have been used for decades (10–23) in the treatment of infantile hemangiomas that cause functional impairment of vital organs, due to the location and dimension of the hemangioma.

The conservative approach of leaving such lesions untreated is still widely accepted, because the results of destructive treatment may in some cases be worse than those from spontaneous involution (3, 8).

We present a 7-month-old girl with a craniofacial cavernous hemangioma that was successfully treated

KEY WORDS

hemangioma, corticosteroids

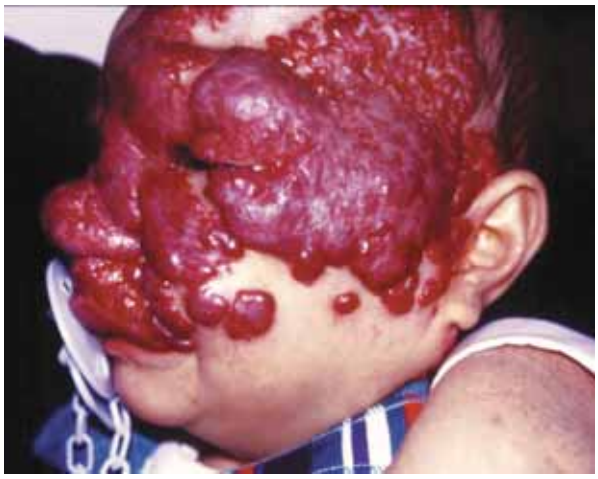

Figure 1. Extended craniofacial cavernous hemangioma before treatment.

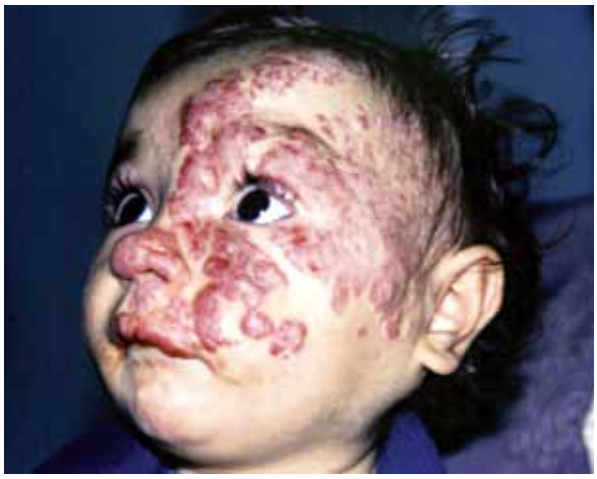

Figure 2. Results after three months of methylprednisolone therapy of a left-side segmental hemangioma resulting in normalized left eye vision and a cosmetically acceptable appearance.

with oral methylprednisolone, and that resulted in significant involution of the lesions and good aesthetic results.

Case report

A 7-month-old female infant with an extended cavernous segmental hemangioma on the left part of the forehead, face, occipital area and neck was presented to the dermatological outpatient service. The cavernous tumor on her face had appeared 15 days after birth and rapidly progressed. During the fourth month of age oral treatment with prednisone (1 mg/kg/24 h) had been initiated for one month without effect.

Physical examination revealed a large deep hemangioma on the left forehead, face, eyelids, nose, and upper lip that measured 14 x 12 cm (Figure 1) affecting vision in the left eye as well as several aberrant vascular tumors of the skin in the occipital area and over the left sternocleidomastoideus muscle.

Laboratory investigation, the complete blood count and routine blood chemistry were within normal ranges and no lesions in the brain and leptomeninges were found by CT.

Treatment with 3 mg/kg/daily methylprednisolone for 1 month was initiated, the dose was reduced gradually over the the next 5 months. At the end of the first month, during steroid therapy the child developed acute stomatitis (with fever and regional lymphadenopathy) which disappeared 2 weeks after therapy with nonsteroid anti-inflammatory drugs (NSAID). At this time the steroid treatment was not interrupted. At the end of the third month of therapy the aesthetic results were estimated as good with significant involution of the hemangiomas (Figure 2).

Discussion

Seventy percent of hemangiomas initially appear in the first several weeks of life. Rapid growth during the neonatal period is the historical hallmark of hemangiomas (2). It is known that hemangiomas of infancy occur more frequently among female infants (male / female ratio is 1:3) (3) and are most commonly located on the head and neck (< 60% of cases) (1, 2). The enlargement of these lesions during the first phase of the neonatal period is a result of rapidly dividing endothelial cell proliferation. The proliferation phase occurs during the first six months of life. Takahashi et al. hypothesized that during the third trimester of foetal development, immature endothelial cells coexist with immature pericytes which maintain their proliferative capacity for a limited period during postnatal life (24). Angiogenic peptides, such as α fibroblast growth factor (α-FGF), vascular endothelial growth factor (VEGF) and prolifarating cell nuclear antigen (PCNA), induce proliferation of these immature cells, resulting in the development of the hemangioma[2]. As the endothelial cells differentiate, an influx of mast cells and tissue inhibitors of metaloproteinases (TIMPs) occurs. TIMPs, along with interferons and TGF produced by the mast cells terminate the endothelial cell proliferation and passively induce involution by senescence of the endothelial cells (2).

The PHACE syndrome (25), including posterior fossa brain malformations, segmental cervicofacial hemangiomas, arterial anomalies, cardiac defects, coarctation of the aorta and eye anomalies was suspected, but clinical examination, laboratory findings and CT failed to confirm the presence of any such abnormalities except cervicofacial hemangioma.

The choice of therapy in hemangiomas depends on a

careful assessment of the factors (anatomic location, accelerating growth, significant functional disturbances, unaesthetic markings) along with a comparison of the risks and benefits of the treatment (3). Different methods of treatment as well as systemic corticosteroids, intralesional corticosteroids, interferons, sclerosing solutions, cryotherapy, surgical removal and laser therapy have been used with uncertain results (2, 3, 5-7, 23).

Systemic corticosteroid treatment has been established as the most efficient medical therapy for common cutaneous infantile hemangiomas (4, 8). It is appropriate to administer the steroid therapy during the proliferative phase, and it will have only a negligible effect on involuting hemangiomas (2). There is a wide variation in response rates, from less than 40% to greater than 90%, depending on dose, duration of treatment, and age at which corticosteroids are initiated (2). According to various clinical studies, the efficacy of steroid therapy in patients with cutaneous hemangiomas in infancy has been evaluated at 30% (14,18) , 53% (17), 83% (11), 86% (15), 93% (20), and 100% (10, 12). The meta-analysis of literature shows that the average cumulative response rate is 84% after 2-months therapy with standard doses of oral corticosteroids (4). Usually, higher doses of corticosteroids in the treatment of hemangiomas has been associated with a better response rate (4,20), although others attribute better response to early therapy and to the size of the tumour, regardless of the dosage of steroids (22). The oral route is generally preferred over intralesional therapy (4). High-risk lesions (i.e. large lesions in prognostically unfavourably locations, likely to leave permanent disfigurement or causing functional impairment) are generally given high doses (3-5 mg/ kg/d prednisolone) of systemic corticosteroids (2, 16). It has been demonstrated that higher doses (5 mg/kg/d) have a greater response rate than moderate doses (3 mg/ kg/d) (4, 20). Our result confirmed that oral corticosteroids give good aesthetic results and initiate a significant involution of extended cavernous hemangiomas with accelerated growth. Steroid therapy of hemangiomas is not recommended in patients over 2 years-old (16).

The precise mechanism by which steroids act upon hemangiomas has not been elucidated completely; however, corticosteroids appear to act by: (i) inhibiting the proliferative capacity of immature pericytes; (ii) intensifying the vasoconstrictive effects of epinephrine and norepinephrine on vascular smooth muscle; (iii) blocking of the estradiol receptors in hemangiomas; and (iv) inhibiting angiogenesis (8, 24, 26).

If the lesion involves the eyelids and periorbital tissues as in our case, a visual obstruction should be considered. Hemangiomas on the eyelids and periorbital area can lead to visual deprivation amblyopia by one of the following three separate mechanisms: (a) physical obstruction of the visual axis, (b) astigmatism from direct pressure on the anterior segment from eyelid involvement, and (c) unilateral myopia (2). Systemic corticosteroids in combination with other medical, surgical or laser modalities have also been used in periorbital or periocular infantile hemangiomas to prevent deprivation amblyopia with variable effectiveness (27, 28).

The adverse effects of corticosteroid treatment of infantile hemangiomas in the vast majority of reported cases were transient and did not necessitate cessation of the therapy (4, 8). In our patient gingivostomatitis (herpes simplex infection) appeared as a side effect of steroid therapy and this did not enforce the discontinuation of the steroid treatment. Potential adverse reactions as hypothalamic-pituitary-adrenal axis suppression and hypertension are are to be mentioned but were neither observed nor reported during treatment (29).

An involutional phase of most hemangiomas occurs often between the fifth and the ninth year: 50 % by the age of five, 70 % at seven years, and by the age of nine years the recovery can be 90 %. The process may be rapid or prolonged.

Conclusion

Our result shows that oral corticosteroids are the method of choice in the treatment of extended cavernous hemangiomas occurring in infancy. Oral steroid treatment is an efficient medical therapy for common cavernous infantile hemangiomas with accelerated growth if is initiated early in proliferative phase.

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AUTHORS' ADDRESSES *Lyubomir A. Dourmishev MD, PhD, Department of Dermatology and Venereology, Medical University of Sofia, 1 St. George Sofiiskyi Str., 1431 Sofia, Bulgaria, e-mail: L_Dourmishev@yahoo.com*
Assen L. Dourmishev MD, same address