Abortive or Minimal-Growth Hemangiomas. A Review of 14 Cases

Hemangiomas abortivos o minimalmente proliferativos. Revisión de 14 casos

To the Editor:

Infantile hemangiomas are frequent, benign endothelial tumors that express the marker GLUT1.1 The diagnosis is generally clinical, based on morphology and a clinical course characterized by a phase of rapid postnatal proliferation followed by a slow spontaneous involution.2,3 In some cases, when growth is minimal, these tumors are referred to as minimal growth hemangiomas, arrested growth hemangiomas, or abortive hemangiomas (AHs).4-7

Our aim was to retrospectively evaluate the clinical and histologic characteristics of AH. We examined the database and photo archives of the dermatology department at our hospital for the period of January 2006 to June 2010. Cases of infantile hemangioma in which the proliferative component of the tumor accounted for less than 25% of the total surface were selected for the review.

Eighteen cases of AH were identified, but 4 were eliminated because of lack of data. The remaining 14 cases affected 13 patients with a female to male ratio of 3:1 (10 girls and 3 boys). All infants were born full term (time of gestation >38 weeks) with a weight greater than 2.760 g (mean weight 3.260 g). During gestation, 2 mothers presented with urinary infection and 1 showed signs of preeclampsia. In 3 cases, a history of classic infantile hemangioma in a sibling was reported. The age of the infants at first consultation ranged between 1 day and 6 months (mean: 2.5 months, median: 3 months). Follow-up was carried out until 7 to 48 months of age. AH was present at birth in 71% of cases and appeared in the first 2 weeks of life in 29% of cases. Sixty-four percent of the tumors were located on the lower half of the body (face: 0; scalp: 1; upper limbs: 4; trunk: 4; lower limbs: 8). Cases were classified as focal AH (42%), partially segmental AH (29%), and segmental AH (29%). The common characteristic in 100% of cases

was telangiectasias on normal or reddish skin (with a reticular distribution in 75% of the segmental tumors). Areas of pallor were seen in 50% of AHs and congenital bruise-like lesions were observed in 14% of cases. Proliferation was minimal and took the form of predominantly peripheral reddish papules in 64% of AHs and a few red spots in 22%; no growth was observed in 14% of cases (Figs. 1–3). Fading of the lesions was evident in 86% of cases, starting between 8 and 12 months of age (Figs. 1 and 2). In 2 cases in which the lesion showed no signs of involution, the final follow-up visit was made at 7 months of age. One segmental AH located in the groin ulcerated (7%). One girl presented with 2 AHs simultaneously. Another infant developed 1 classic infantile hemangioma and 1 AH. The 5 arrested growth tumors that were biopsied were positive for the marker GLUT1 (Fig. 2D). Minor developmental anomalies were detected in 50% of patients (syndactyly, sacral dimple [2 cases], nevus sebaceous on the scalp [Fig. 2C], preauricular tags, conjunctival abnormalities, hyperpigmented nevus, cleft lip, and transient pseudoacoartation of the aorta).

Classic infantile hemangioma is a GLUT1-positive tumor characterized by a rapid postnatal growth phase that is followed by a slow involution phase. Incidence is higher in premature infants and in the female sex, with the ratio of girls to boys ranging from 1:5:1 to 3:5:1. These tumors occur predominantly on the head and neck (60%), with focal hemangiomas appearing more frequently than segmental ones. The risk of ulceration has been estimated at 15%. In our case series the female to male ratio (3:1) was within the range reported in the literature and the lesions were predominantly focal or partially segmental. Most of the hemangiomas showed signs of regression. Histologic examinations, when performed, revealed GLUT1 expression. Postnatal growth of AHs was minimal and there were no premature infants in the group studied. Only 1 tumor was located on the head, and only 1 lesion, located in the groin, ulcerated (7%).

Few studies have described this type of arrested growth infantile hemangioma and proposed a differential diagnosis with capillary malformations, noninvoluting congenital hemangiomas, or other vascular anomalies. Corella et al.3 demonstrated that AH is a true form of hemangioma through histologic findings and GLUT1 expression. It has recently been suggested that dermatoscopy may be useful for diagnosis.8 In a retrospective study involving 47 patients, Suh and Frieden7 indicated that AHs have a particular clinical appearance, occur more frequently on the

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Figure 1  Abortive hemangiomas at the maximum point of growth and after regression. Segmental lesion on the forearm with minimal spread to the wrist at 45 days (A) and 3 years (B) of age. Partially segmental hemangioma on the hand at 45 days (C) and 4 years (D) of age.
Abortive segmental hemangioma and nevus sebaceus on the scalp. Bruislike segmental lesion with areas of pallor around and inside the lesion 48 hours after birth (A), fine telangiectasis on pink patches with a reticular appearance and a small number of dot-like papules at 4 months of age (B), and fading of the hemangioma at 2.5 years of age (C). GLUT1 expression in both the swollen endothelial cells enclosing the small lumina and the flat endothelial cells of dilated capillaries, staining with GLUT1, ×200 (D).

Figure 2

lower body, and do not predict the proliferative potential of any other hemangiomas present. Our findings in these 14 cases of AH are consistent with their conclusions; however, 3 of the 4 segmental hemangiomas in our study presented on the upper half of the body. When compared with the cases reviewed in the Suh and Frieden study, our patients were first seen at an earlier age and were monitored more closely for longer periods, factors that may explain the higher rates of growth and regression in our series.

One notable difference is that our case series involved a high frequency of minor developmental anomalies (50%), many of which were located anatomically far from the hemangioma. The present study is limited because of the small number of patients and because it is retrospective.

At present, the etiology and pathogenesis of hemangiomas are not fully understood and more studies are needed before ruling out an etiopathogenic relationship between developmental anomalies and these tumors. Cases of AH associated with urogenital, anorectal, and cardiac anomalies as well as deep recalcitrant ulcers have been described as reticular infantile hemangiomas. One of the patients in the Suh and Frieden study presented with occult spinal dysraphism.

Larger clinical studies are needed to establish the true incidence of AH, confirm the predominance of these lesions on the lower half of the body, determine the risk of other developmental anomalies in these patients, and define the role of dermatoscopy as a diagnostic tool.
Figure 3  Clinical images of abortive hemangiomas. Pink reticular lesion located on the leg with fine telangiectasias and 4 small red papules on the surface (A). Congenital telangiectasias in normal skin with erythematous papules that appeared after birth predominantly in the peripheral areas of the lesion. Note the pallor around the lesion (B). Central and peripheral proliferation in 25% of the surface area of an erythematous lesion (C). Pale halo surrounding a pink telangiectatic lesion on the buttock (D).

References


Vitiligo and Morphea: Autoimmune Cutaneous Side Effects of Interferon Treatment

Fenómenos autoinmunes cutáneos del interferón (vitíligo-morfea)

To the Editor:

The interferons comprise a family of proteins belonging to the cytokines involved in regulation of the immune response. They exert antiviral, antineoplastic, antiangiogenic, and immunomodulating effects.\(^1\) High-dose interferon alfa is the only treatment to date that has been shown to improve disease-free survival in patients with advanced melanoma in randomized prospective trials.\(^2\) Its side effects are generally dose-dependent. The most common manifestations are flu-like symptoms with fever, fatigue, joint and muscle pain, and chills; increased transaminase levels and hypothyroidism are also common. Cutaneous adverse effects are observed in 5%–25% of cases,\(^2,3\) the main ones being hair loss, pruritus, acne, eosinophilic folliculitis, lichenoid eruptions, xerosis, white atrophy, ulcers, vasculitis, cutaneous necrosis, chronic pigmented purpura, panniculitis, dermatitis herpetiformis, linear immunoglobulin A dermatosis, pemphigus, urticaria, fixed drug eruption, taste disorders, exanthema, and—albeit rarely—vitiligo, alopecia areata, and other autoimmune processes.

We present the case of a 20-year-old woman with no personal or family history of interest who, after removal of a melanoma (Breslow depth of 0.5 mm, Clark level II, no ulceration or areas of regression) below the right clavicle, presented local recurrence (in-transit metastasis) in the form of a rapidly growing nodule, which was removed. A sentinel lymph node biopsy of the right axilla was negative. The patient received interferon alfa-2b (Kirkwood regimen) for 1 year. Shortly before finishing therapy, she presented large achromic macules on the upper third of the trunk (consistent with vitiligo) and a hard plaque with hypochromic infiltrate in the center and brownish margins on the lower back (clinically and histopathologically consistent with morphea). The laboratory workup revealed antinuclear antibodies (titer 1/160) associated with a homogeneous nucleolar pattern. Analysis of the thyroid axis was unremarkable (Figs. 1 and 2).

Simultaneous appearance of vitiligo and melanoma, irrespective of whether this occurs after treatment with interferon or not, is unusual yet widely documented. In the absence of treatment with interferon, the incidence of vitiligo and melanoma is lower than 5%, and that of vitiligo in the general population is as low as 3%. Consequently, the association between the two is not considered significant. By contrast, vitiligo affects up to 20% of patients treated with interferon.\(^4\)

Morphea and sclerodermiform conditions are less frequent than vitiligo in patients treated with interferon. There have also been reports of cases in patients receiving pegylated interferon alfa combined with ribavirin for treatment of hepatitis C infection.

The simultaneous presence of vitiligo and morphea in patients with melanoma is very unusual. We only found 2 articles describing this association, and neither states the immunotherapy received or the clinical repercussions.\(^5,6\)

Therefore, the association between vitiligo and interferon remains unclear. Some authors claim that it indicates a favorable prognosis, whereas others reject this theory. What does seem to be true is that patients who present

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**Figure 1** Vitiligo lesions and morphea-like plaque on the back.