

Although diagnosis is essentially clinical, histology, if performed, shows dilation of the vessels in the papillary dermis and occlusion of the vessels in the reticular dermis, with a normal number of vessels. Results of vasomotor tests are normal in both the uninvolved and involved skin<sup>1-3,5</sup> and the finding supports the hypothesis that this is a functional anomaly. The only recognized trigger is prolonged bathing in cold water, which has led to the appearance of nevus oligemicus on the hands.<sup>2</sup> Contributing factors such as obesity, a sedentary lifestyle, and proximal pressure (such as that caused by a tight belt) have been suggested for lesions located on the abdomen, but weight loss and removing the pressure failed to resolve the lesions.<sup>5</sup> Our patients were overweight, predominantly around the abdomen, and had large, sagging breasts.

The differential diagnosis should include inflammatory erythema (mastitis, cellulitis, erysipelas), which involves warm lesions that tend to resolve, capillary malformations with no changes in local temperature and with characteristic histologic signs, and livedo reticularis, which is characterized by an erythematous-violaceous reticular pattern.<sup>5,6,8</sup>

In our patients, the lesions remained stable over time, with no changes in size or appearance, and no new lesions developed. Treatment with systemic corticosteroids was ineffective.<sup>5</sup>

In conclusion, we report 2 cases of nevus oligemicus on the breasts, which is a rare site; the only previously reported case on this site involved a single breast.<sup>7</sup> The key to diagnosis is the finding of permanent local hypothermia; it is therefore important to palpate the lesion to detect a reduction of between 2 and 2.5°C in local temperature. We consider that the frequency of this entity is probably greater than indicated by a review of the literature, but that it may go unnoticed or unreported by patients.

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## Infantile Hemangioma of the Eyelid Treated with Timolol Gel<sup>☆</sup>

### Hemangioma infantil palpebral tratado con timolol gel

*To the Editor:*

Hemangioma is the most common benign tumor in childhood, with a prevalence of 10% to 12% in the first year of life.<sup>1</sup> This vascular tumor appears in the early months of life and has 2 phases: a proliferative phase of rapid growth in the first few months, followed by a slow, involuting phase that can last years.<sup>2</sup> Tumors in certain sites require early treatment to prevent sequelae; for instance, periocular tumors have been associated with complications such as amblyopia,

asymmetric astigmatism, proptosis, strabismus, and exposure keratitis.<sup>3-5</sup>

The classic treatment of hemangiomas has essentially been systemic corticosteroids.<sup>6</sup> Other treatments used are topical and intralesional corticosteroids, laser therapy, surgery, and interferon- $\alpha$ <sup>1</sup>. In 2008 Léaute-Labréze<sup>7</sup> described the treatment of hemangiomas with propanolol, which is currently one of the most effective alternatives. In recent years timolol has been successfully used for certain hemangiomas.<sup>3,8-10</sup>

We describe the case of a 2-month-old preterm infant who, at 2 weeks of life, developed a focal hemangioma of infancy on the upper left eyelid; the hemangioma blocked the child's vision and exerted moderate pressure on the eyeball (Fig. 1). The patient was assessed by the ophthalmology department and other eye conditions were ruled out. Because treatment was needed to prevent complications but the parents declined systemic treatment, timolol 0.1% ophthalmic gel was applied twice daily. The gel was instilled into the palpebral conjunctiva by everting the eyelid slightly

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**Figure 1** Infantile hemangioma of the eyelid before treatment.

and applied to the outer surface of the hemangioma. The nasolacrimal duct was then occluded at the punctum to achieve stronger local activity and lower systemic absorption.

The tumor shrunk noticeably in the first week of treatment, leaving the pupillary area free; the proliferative component was also greatly reduced (Fig. 2). After 4 months of treatment, the hemangioma had disappeared almost entirely (Fig. 3), with no local or systemic adverse events during treatment. By 5 months post-treatment, the hemangioma had not recurred.

Oral propranolol is currently one of the most commonly used drugs used to treat hemangiomas.<sup>2</sup> Its therapeutic effects are achieved through several mechanisms: vasoconstriction and decreased expression of vascular endothelial growth factor (VEGF) and fibroblast growth factor (bFGF).<sup>8</sup> Although propranolol is considered safe, its use has been associated with adverse reactions, such as bronchospasm, arrhythmias, bradycardia, hypotension, and hypoglycemia.<sup>3,4,9</sup> Traditionally, systemic corticosteroids have been the first-line treatment for hemangiomas; however, their prolonged use has been associated with adverse effects, including hypertension, glaucoma, myopathy, and decreased weight and height gain.<sup>6</sup> Other therapeutic alternatives, for instance, intralesional corticosteroids, can cause complications, including deformation of the eyelid, elevated intraocular pressure, and occlusion of the central retinal artery.<sup>3</sup>

Timolol is a noncardioselective beta blocker similar to propranolol. The drug is available in several forms: 0.5% eye drops,<sup>3</sup> 0.5% gel<sup>8</sup> (not sold in Spain), and 0.1% gel (used in this case). In this form, the pharmacokinetic data suggest almost no systemic exposure, with plasma concentrations below the quantitation limit (QL=0.8 ng/mL). However, the contraindications and adverse effects of systemic beta blockers should be taken into account, although side effects are rarely observed after ocular instillation.



**Figure 2** Infantile hemangioma of the eyelid after 1 week of treatment.



**Figure 3** Infantile hemangioma of the eyelid after 4 months of treatment.

Nine cases of palpebral hemangioma treated with timolol have been described to date. The condition was first reported in 2010 by Guo and Ni<sup>3</sup> and more recently by Khunger and Pahwa,<sup>9</sup> who described a hemifacial hemangioma associated with PHACE (posterior fossa malformations, hemangiomas, arterial anomalies, coarctation of the aorta and cardiac defects, and eye abnormalities) syndrome, and by Ni et al,<sup>10</sup> who published a series of 7 cases. All of these authors reported satisfactory outcomes. However, in the 2010 study by Guo and Ni<sup>3</sup> and the 7 cases reported subsequently by Ni et al,<sup>10</sup> response to treatment was slower than in our patient, occurring 4 to 5 weeks after start of treatment. This difference may be attributable to the fact that we used a gel formulation and also applied the drug to the conjunctival surface.

In our case, timolol gel 0.1% was shown to be a safe and effective treatment and we believe that its use at certain sites, such as the periocular region, could be an effective option that should be considered when systemic treatment is contraindicated.

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## Dermoscopic Features of Cutaneous Rosai-Dorfman Disease<sup>☆</sup>

### Características dermatoscópicas de la enfermedad de Rosai-Dorfman cutánea

To the Editor:

Rosai-Dorfman disease is a benign histiocytic proliferative disorder of unknown etiology. The presenting sign is usually asymptomatic massive lymphadenopathy. Exclusively cutaneous cases of Rosai-Dorfman disease are rare. We present a case report of the disease and describe its dermoscopic features.

A 29-year old man with no relevant medical or surgical history was seen for a lesion that had been growing progressively for several years in the left pectoral region. A biopsy report from another hospital indicated diagnosis of atypical xanthogranuloma.

The physical examination showed an infiltrated plaque with a heterogeneous surface and well-defined borders. Its longest diameter was 4.5 × 4 cm and it had an erythematous-orange appearance, a central whitish area, and multiple yellowish structures at the edges (Fig. 1).

The dermoscopic image showed a milky-red area in the center of the lesion, whereas the outer part had multiple yellowish homogeneous areas of different sizes with irregular borders, surrounded by large telangiectatic vessels on a red-orange background (Fig. 2). Given the progressive growth of the lesion and the discomfort it caused the patient, radical excision was performed.

Histologic examination revealed a poorly-defined dermal proliferation of large histiocytes, extending downwards into the subcutaneous adipose tissue. The histiocytes had large eosinophilic vacuolated cytoplasm and round homogeneous nuclei and some contained intact lymphocytes (Fig. 3). In addition to the histiocytes, there was abundant inflammatory infiltrate composed mainly of plasma cells, with lymphocytes, giant multinucleated cells, and xanthomatous histiocytes with small nuclei. A prominent fibrous stroma was seen with a highly vascularized storiform pattern. Immunohistochemical staining was positive for S-100 and CD68 and negative for CD1a. The presence of emperipolesis and the immunohistochemical profile pointed to diagnosis of a cutaneous variant of Rosai-Dorfman disease. No hematologic abnormalities, lymph node involvement, or

abnormalities in other organs were observed in the staging study.

Rosai-Dorfman disease, or massively enlarged lymph nodes with sinus histiocytosis, is a histiocytic proliferation in which approximately 40% of the patients have extranodal involvement.<sup>1,2</sup> The skin is the most frequently affected organ. Purely cutaneous forms of Rosai-Dorfman disease are rare. Skin lesions are nonspecific and may take the form of solitary or multiple lesions of different sizes and morphologies. They can present on any part of the body and the clinical differential diagnosis includes a broad range of conditions including panniculitis, vasculitis, acne vulgaris, suppurative hidradenitis, granuloma annulare, and sarcoidosis, as well as other histiocytoses.<sup>3</sup> Kong et al.<sup>4</sup> proposed a classification based on the morphologic features of 39 lesions. Papulonodular lesions were the most common form (accounting for almost 80%) followed by the infiltrated plaque type (12.5%) and the tumor type (7.7%). The histologic findings in cutaneous lesions are similar to those found in lymph tissue. The main finding is a dense infiltrate of large histiocytes and a large pale cytoplasm with rounded nuclei. The cytoplasm contains intact leukocytes, usually lymphocytes, a phenomenon known as lymphophagocytosis or emperipolesis. Typically, these histiocytes are positive for S-100 and negative for CD1a, and can be either positive or negative for CD68. The immunohistochemical profile is essential for histologic diagnosis, as fibrosis, vascular proliferation, lymphoid clusters, foam cells, and multinucleated Touton giant cells may or may not be present, and so confusion with other histiocytic processes, and with juvenile xanthogranuloma in particular, is possible. The dermoscopic features of Rosai-Dorfman disease have not been widely reported in the literature.<sup>5,6</sup> Rodríguez Blanco et al.<sup>6</sup> reported a case of Rosai-Dorfman disease on the sole, characterized by cotton-like ovoid structures on an erythematous background in the dermoscopic image. In contrast, the dermoscopic features in our case were similar to those described for juvenile xanthogranuloma, that is, a yellow-orange homogeneous central area and a somewhat more erythematous peripheral area. This is known as the setting sun feature.<sup>7</sup> The presence of clouds of pale yellow globules is considered indicative of xanthomatous histiocytes in the superficial dermis.<sup>8</sup> The presence of comma vessels,<sup>9</sup> arborizing telangiectasia,<sup>10</sup> and whitish linear projections has also been reported, particularly in advanced cases of juvenile xanthogranuloma. The differential dermoscopic diagnosis should be performed with solitary yellow lesions, such as juvenile xanthogranuloma, organoid nevus or sebaceous nevus, xanthomatous dermatofibroma, and solitary reticulohistiocytoma.<sup>9-11</sup>

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