



Figure 3 The lesion resolved spontaneously leaving a residual pink macule.

The exact etiology of IFAG is unknown, although Boralevi et al.² have postulated that these lesions may be related to a granulomatous process around an embryological remnant or may belong to the spectrum of granulomatous rosacea in infants. A prospective multicenter study of 30 cases by the same authors reported the mean duration of the lesions to be 11 months and found antibiotic treatment ineffective.

The principal differential diagnosis for this type of lesion includes benign tumors (especially pilomatricomas of the eyelids or eyebrows,^{4,5} dermoid or epidermoid cysts, and chalazia), pyogenic granulomas, Spitz nevi, and xanthogranulomas. It is also important to rule out the possibility of a bacterial or fungal infection, or infection with mycobacteria or parasites (leishmaniasis), all of which are more common in immunocompromised patients.² These lesions can sometimes resemble vascular malformations or hemangiomas, although the clinical course is very different.³ Other differential diagnoses include nodulocystic acne presenting few symptoms.^{2,6}

Our aim in presenting this case is to emphasize the importance of considering IFAG in the differential diagnosis of

acquired facial nodules in children. It is important to inform parents of the benign course of these lesions. Follow-up until the lesion resolves is recommended.¹

The characteristic clinical appearance and location of IFAG and the lack of lymphadenopathy or constitutional symptoms may make a direct clinical diagnosis possible and thereby avoid unnecessary interventions.

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Periorbital Necrobiosis Lipoidica[☆]

Necrobiosis lipoidica periorbitaria

To the Editor:

Necrobiosis lipoidica (NL) is a granulomatous disease of unknown etiology that typically occurs in diabetic patients. It is characterized by sclerotic plaques that most often appear on the legs.

A 15-year-old girl was admitted to our hospital with facial lesions that had appeared 5 months earlier. She had previously consulted with a surgeon who had suggested surgical excision of the lesions. Physical examination revealed yellowish nodules and plaques with superficial telangiectasias

on the upper and lower eyelids of the left eye (Fig. 1). The patient had been diagnosed with type 1 diabetes mellitus at age 6 years and had a history of marked insulin resistance and chronic poor blood glucose control (hemoglobin A_{1c}, 13%). Skin biopsy revealed an inflammatory infiltrate in the reticular dermis and hypodermis, predominantly composed of histiocytes that had aggregated to form granulomas surrounded by degenerated collagen fibers. Other findings included extracellular lipid deposits and no increase in stromal mucin. Plasma cells and multinucleated giant cells were also observed (Fig. 2). A diagnosis of NL was established on the basis of clinical and histologic findings and the patient's past history. Because the site of the skin lesions made the use of topical or intralesional corticosteroids inadvisable, treatment was started with twice daily applications of 0.1% tacrolimus ointment. After 2 months of treatment with no improvement, oral pentoxifylline (600 mg/12 h) was added but was subsequently discontinued owing to gastrointestinal intolerance. When the lesions had resolved only

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Figure 1 Yellowish-red plaques in the periocular region.

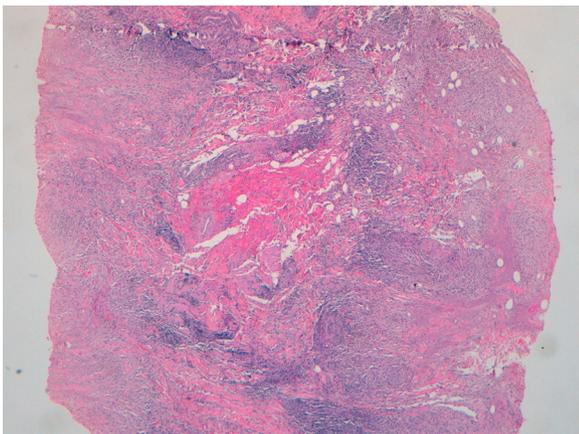


Figure 2 Inflammatory infiltrate composed of histiocytes with degenerated collagen and lipid deposits (hematoxylin-eosin, original magnification $\times 40$).

partially after 4 months of treatment, topical tacrolimus was replaced with acetylsalicylic acid (300 mg/d). After a further 10 weeks of treatment, the periocular plaques had clearly improved, but other plaques of NL, including 1 with ulceration, appeared in the pretibial region. The pretibial plaques were treated with intralesional corticosteroids and hyperbaric oxygen therapy and resolved almost completely. After 2 years of treatment with acetylsalicylic acid, the periocular lesions had decreased in size until only a few small, infiltrated, slightly erythematous plaques remained. Ten months after withdrawal of the treatment, the plaques had not increased in size.

NL is 3 times more common in women than in men, with the age of onset usually between 30 and 40 years. It is often associated with type 1 diabetes mellitus; between 75% and 90% of patients with NL have or will develop diabetes, although NL is present in only 0.3% to 3% of diabetic patients. NL has also been associated with autoimmune thyroid disease, rheumatoid arthritis, inflammatory bowel disease, and sarcoidosis.

Although NL lesions are typically located on the anterior and lateral aspects of the legs, cases affecting the trunk, upper limbs, face, and penis have also been described. NL

lesions in the periocular region are extremely rare, but they have been found both in isolation¹ and in association with NL lesions in other areas.²

The lesion begins as an erythematous papule or plaque, which extends peripherally, developing a yellowish atrophic center and a raised erythematous border. The main complication of NL is ulceration, which occurs in 25% to 33% of patients. Atypical lesions on the face and the edge of the scalp have been described³⁻⁵ in association with Miescher granuloma, actinic granuloma, granuloma multiforme, and necrobiotic xanthogranuloma.⁶

NL is histologically characterized by a normal or atrophic—and frequently ulcerated—epidermis and necrobiotic collagen with sclerosis. In the dermis, palisading granulomas arranged in layers parallel to the epidermis can be observed. The dermal inflammatory infiltrate is composed of histiocytes, multinucleated giant cells, lymphocytes, and plasma cells. The histopathological differential diagnosis must primarily rule out granuloma annulare, rheumatoid nodules, and necrobiotic xanthogranuloma.

In cases with periocular involvement it is essential to rule out the possibility of necrobiotic xanthogranuloma, a form of histiocytosis associated with paraproteinemia that usually occurs in periocular sites. This disorder manifests as yellowish-red indurated nodules or plaques, frequently with atrophy, ulceration, and telangiectasias. Histologically, necrobiotic xanthogranuloma is differentiated from NL by its denser infiltrate of histiocytes, more pronounced inflammation and more severe degeneration of the subcutaneous cell tissue, and the presence of foamy histiocytes, Touton giant cells, bizarre foreign-body giant cells, and cholesterol clefts.⁷

NL is treated for cosmetic reasons or to avoid ulceration and the risk of secondary infection and deep tissue destruction. Topical and intralesional corticosteroids are the drugs most widely used to treat NL. Other drugs that have been used include acetylsalicylic acid, ticlopidine, pentoxifylline, tretinoin, clofazimine, mycophenolate mofetil, tumor necrosis factor (TNF) inhibitors, ciclosporin, thalidomide, fumaric acid esters, hydroxychloroquine, niacinamide, photodynamic therapy,⁸ psoralen-UV-A,⁹ and topical tacrolimus.¹⁰ Blood glucose control and treatment for diabetes do not appear to have any beneficial effect on NL lesions. Surgical excision of the affected area can ensure resolution of the lesions but may also lead to considerable cosmetic and functional sequelae in the case of periocular lesions.

In conclusion, when NL lesions occur in atypical sites, a high index of suspicion is required if we are to avoid misdiagnoses and inappropriate treatment decisions. Although it was only partially effective in the case of our patient, topical tacrolimus appears to be effective and particularly safe for the treatment of periocular NL lesions.

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Milia en Plaque[☆]

Quistes miliares múltiples agrupados

To the Editor:

Multiple grouped milia or milia en plaque, as it is normally called in the literature, is a rare skin condition of unknown etiology and pathogenesis that is clinically characterized by multiple grouped cysts at a specific site.

We report the case of a 53-year-old Brazilian woman who presented with multiple lesions and mild pruritus that had appeared 6 weeks earlier on both ear lobes. She had been living in Spain for 8 years, had no relevant past medical history, and was receiving no regular treatment. She reported no history of injury, burns, dermabrasion, or use of cosmetics or topical drugs at the site of the lesions.

Physical examination revealed multiple grouped, smooth, yellowish-white cystic lesions, measuring 0.1 to 0.2 cm in diameter, with a faintly erythematous surface, on the right helix and ear lobe (Fig. 1). Lesions of similar characteristics were observed on the left ear lobe, but in smaller numbers.

Biopsy of the lesions on the right ear lobe showed multiple follicular infundibular cysts with a perifollicular foreign body–type granulomatous infiltrate response. The cysts were lined with squamous epithelium with a granular layer and slightly basophilic lamellated keratin (Fig. 2).

Based on these clinical and pathologic findings, we diagnosed milia en plaque.

The patient received 4 sessions of photodynamic therapy (PDT) with methyl aminolevulinate hydrochloride cream at 2-weekly intervals. There was a marked reduction in the number of cysts and response was maintained at 5 months (Fig. 3).

Milia are small epidermoid cysts located in the superficial dermis that present clinically as smooth, round white

to yellowish lesions. They are classified as primary if they arise spontaneously and are of unknown etiology, and as secondary if they appear in response to repeated trauma, burns, radiation therapy, topical corticosteroids or topical 5-fluorouracil, oral ciclosporin, or other types of aggression.¹



Figure 1 Multiple grouped smooth cystic lesions on the right helix and ear lobe.

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