CASE REPORT

Isotretinoin for the Treatment of Granulomatous Rosacea: Case Report and Review of the Literature

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Background: Granulomatous rosacea is considered a clinical variant of rosacea and is characterized by hard yellow, brown, red or flesh-colored cutaneous papules or nodules that may be severe and may lead to scarring. The lesions typically appear on the cheeks and periorificial lesions; they are monomorphic in each patient and sit on relatively normal-appearing skin. The diagnosis should be established by excluding other granulomatous disorders and rosacea-like eruptions such as sarcoidosis, tuberculosis, and lupus miliaris disseminatus faciei. The clinical course is chronic and unpredictable, and management can be very difficult.

Case Report: We report the case of a 28-year-old female with granulomatous rosacea who responded successfully to oral isotretinoin. No recurrence was noticed 6 months after the completion of treatment.

GRANULOMATOUS ROSACEA (GR) is considered the only true rosacea variant. It is clinically characterized by hard yellow, brown, red or flesh-colored papules or nodules and histologically by noncaseating epithelioid granulomas. The lesions tend to be discrete, distributed symmetrically across the upper part of the face, particularly around the eyes and the nose. Surrounding erythema is not a marked feature but may be present.

The clinical course of this dermatosis may be chronic and unpredictable and occasionally is associated with scarring. The management can be very difficult and challenging as GR is usually resistant to conventional treatment. We report a patient with chronic GR who was treated successfully with oral isotretinoin.

Case Report

A 28-year-old female was referred to our clinic because of the appearance of a 3-year papular eruption involving the medial and lateral facial areas. The lesions were solid, erythematous papules (Figure 1) distributed almost symmetrically on the face, without any scaling. On diascopy, these papules appeared to have yellowish-brown, apple jelly–like changes in color. A mild facial erythema was noticed at the sites of the eruption, and a few flushes were also reported. No telangiectasias or pustules or any involvement of the ears, neck, and oral mucosa was seen. There was no lymphadenopathy.

According to her history, the patient had been treated unsuccessfully by her physician with oral tetracyclines, macrolides, and topical metronidazole, clindamycin, and pimecrolimus. The persistence of this facial dermatosis and the resistance to treatment made the patient very uncomfortable and distressed.

The patient reported no previous history of tuberculosis or sarcoidosis. A Mantoux test was evaluated as negative, whereas chest radiography was unremarkable. Further clinical examination, complete blood count, and biochemical blood tests were within normal ranges.
Serology for human immunodeficiency virus (HIV), syphilis, and antinuclear antibody was negative. An ophthalmologic examination was performed, and no evidence of keratitis or conjunctivitis was revealed. Skin scraping and culture for fungus or bacteria were negative.

A skin biopsy was performed, and histologic examination revealed the presence of mixed lymphocytic inflammation and epithelioid cell granulomas without caseation (Figure 2). No *Demodex folliculorum* mites were observed. The findings were compatible with GR.

The patient’s body weight was 67 kg. She was treated with oral isotretinoin 0.7 mg/kg/d for 24 weeks as monotherapy, and the response was satisfactory within the first 3 months. Total remission of the lesions was achieved by the end of the fifth month. No recurrence was observed 6 months after the cessation of therapy (Figure 3).

**Discussion**

In 1896, Darier first described the concept of tuberculids.\(^3\) Since then, terms such as “rosacea-like tuberculid of Lewandowsky,” “lupoid rosacea acme agminata,” and “micropapular tuberculid”\(^4-7\) have been introduced to describe a rosacea-like entity. In 1949, Snapp concluded that Lewandowsky tuberculid had no relation to tuberculosis and appeared to be distinct from the usual forms of rosacea.\(^8\) Van Ketel in 1958 showed that clinically typical rosacea could be accompanied by granuloma formation without the coexistence of active tuberculosis.\(^9\)

In 1970, Mullanax and Kierland gave a distinctive form of papular rosacea the term “granulomatous rosacea.”\(^10\) During recent decades, more terms have been used by authors to describe rosacea-like eruptions, such as “lupus miliaris disseminatus faciei” (LMDF), “facial Afro-Caribbean childhood eruption,”\(^11\) and “facial idiopathic granulomas with regressive evolution.”\(^12\)
The numerous denominations and the obscure pathogenesis raised the issue as to whether LMDF and GR should be considered to be the same or different entities. Although both of these conditions share the same histopathologic characteristic (ie, epithelioid granulomas with or without caseation), their clinical features are different. The course of LMDF is often similar to that of cutaneous sarcoidosis. Whether an overlap of rosacea and sarcoidosis exists is controversial.

In our case, the distinction between GR and LMDF was based on the patient’s history of flushes, which is typical for rosacea, and the distribution of the eruption, which extended to the lateral facial areas without involvement of the eyelids, as is commonly seen in LMDF.

The issue of the management of a patient suffering from rosacea has been discussed extensively in the literature. GR represents about 10% of all cases of rosacea and has proved resistant to conventional systemic therapies such as tetracyclines, doxycycline, and macrolides.

The usefulness of isotretinoin in treating therapy-resistant, nongranulomatous rosacea was initially described in 1980. The authors treated three patients with 0.5 mg/kg/body weight per day and two with 1 mg/kg/d isotretinoin for 12 weeks. They concluded that the therapeutic result was superior to the one observed by standard remedies such as oral antibiotics and metronidazole. The efficacy of 0.5 to 1 mg/kg/d isotretinoin in rosacea was also confirmed by other reports. The duration of treatment ranged between 12 and 28 weeks.

The efficacy of lower daily doses of isotretinoin in rosacea was evaluated with satisfactory results, although in some cases, the use of tetracycline was considered to be more effective. Gollnick and colleagues recently reported 573 patients with rosacea who received one of three different dosages of isotretinoin (0.1, 0.3, or 0.5 mg/kg/day), doxycycline (100 mg daily for 14 days and then 50 mg daily), or placebo in a double-blind, randomized study. They concluded that isotretinoin at a dose of 0.3 mg/kg is an effective and well-tolerated therapy option for the treatment of rosacea subtypes II and III and can therefore be used successfully as an alternative to therapy with oral antibiotics.

Isotretinoin at a dose of 1 mg/kg/d has also been used in the treatment of LMDF, and the clinical improvement was attributed to the drug rather than to spontaneous remission.

Oral antibiotics act in rosacea primarily as antiinflammatory rather than antibacterial drugs. The efficacy of isotretinoin in rosacea is probably related to its antiinflammatory mechanisms and antioxidative, angiogenic, and antifibrotic properties. Its antiseborrheic effect might play a role in phymatous type or rosacea fulminans.

The data regarding treatment options for GR are very limited. By searching Medline using the key search terms “granulomatous rosacea” and “isotretinoin,” we found only two relevant reports. Smith in 1990 was the first who reported the effectiveness of isotretinoin in GR, and Krause and colleagues in 1997 reported two patients who responded well to dapsone.

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References
