Rosacea Fulminans Related to Pegylated Interferon Alpha-2b and Ribavirin Therapy

Vincenzo Bettoli, Lucia Mantovani, Sergio Boccia* and Annarosa Virgili
*Dermatology Department and Gastroenterology Unit, University of Ferrara, Arcispedale S. Anna, Corso Giovecca, 203, IT-44100 Ferrara, Italy. *E-mail: bcsi@unife.it*
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Sir,

Rosacea fulminans (RF) is a rare cutaneous eruption, usually involving the face of young women, which is characterized by papules and pustules rapidly coalescing in nodules and plaques discharging puruloid material (1, 2). It is considered a severe form of rosacea rather than a particular type of acne and generally recovers without important scarring sequelae (1–4).

The aetiopathogenesis of RF remains unknown, but it has been reported sometimes to be associated with thyroid and liver disorders or inflammatory bowel disease (5–7). In some cases drug intake, pregnancy, increased androgenic production and emotional trauma have been identified as triggering factors (2–4, 8–10).

We describe here a case of RF that developed during hepatitis C treatment with pegylated interferon alpha-2b and ribavirin; to our knowledge, this is the second case of RF related to pegylated interferon alpha-2b and ribavirin therapy reported in the literature (9) and the first one treated with oral isotretinoin.

CASE REPORT

A 36-year-old woman, with no previous history of rosacea or acne, presented to our department of dermatology with an erythematous facial eruption that had developed during antiviral treatment for hepatitis C. The therapy was based on a 6-month administration of pegylated interferon alpha-2b, in weekly injections, and a daily intake of ribavirin. In April 2004, 3 months after the beginning of that treatment, the patient reported that she had noticed the appearance of transient malar erythema, about 3 days after each pegylated interferon injection. The cutaneous eruption became progressively persistent, spreading to the whole face, so that the diagnosis of erythematous rosacea was made. Despite the employment of specific topical medications, the papulo-pustular phase followed and, within 3 months, at the end of the antiviral treatment, the typical clinical features of rosacea fulminans developed. Based on the recent experience of Jensen & Holmes (9), oral tetracyclines and topical metronidazole were administered with an initial moderate improvement, but systemic therapy was discontinued one month later because of gastric pain. Oral isotretinoin was then started as a monotherapy, at very low dosage (0.2 mg/kg/day), without systemic corticosteroids. Oral isotretinoin induced a marked improvement of the cutaneous eruption after 4 months of treatment; the dermatosis recovered completely after 2 additional months.

DISCUSSION

RF is a rare cutaneous disease characterized by a sudden onset of papulo-pustular lesions rapidly evolving in nodules and plaques draining purulent material. The eruption generally involves the face of young women and may be preceded by an increase in seborrhea or be associated with other rosacea features, such as flushing and blushing. Usually the disease recovers with no or minimal scarring sequelae and recurrences are not frequently observed (1–4). Laboratory investigations generally reveal mild abnormalities of inflammatory parameters; the identification of pathogens by cultures is occasional (11) and biopsy is rarely needed because of the peculiarity of the clinical picture.

The first-line treatment of RF is oral isotretinoin preceded by a short course of systemic corticosteroids and sometimes combined with topical high potency steroids (3, 4). In some cases, healing of the disease has also been induced by administration of tetracycline or dapsone (12, 13).

The current definition of the clinical criteria and treatment guidelines of RF is ascribed to Jansen et al. (3) and Jansen & Plewig (4). These authors renamed the disease, previously known as "pyoderma faciale" (14), and also suggested the present nosographic arrangement, considering the condition a severe form of rosacea, rather than a variety of acne, due to the absence of comedones and systemic involvement.

Since the first case series description, no specific aetiopathogenetic factors have been identified and the onset of the disease remains unexplained in the majority of cases (7). An infective cause must always be investigated, but the presence of micro-organisms has only occasionally been demonstrated (11). To our knowledge, inflammatory bowel disease has shown to be associated with RF in 7 cases reported in the literature (5, 7). Considering the small number of patients affected by RF, this association of RF with inflammatory bowel disease appears to be significant. The development of the disease has sometimes been related to emotional trauma, thyroid and liver disorders, pregnancy and increased androgenic secretion (2–4, 10). Drugs have been considered triggering factors in only a few cases. The onset of RF has been described during the admi-

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nistration of high doses of vitamins B6–B12 (8) and, recently, pegylated interferon alpha-2b and ribavirin for hepatitis C (9). In our experience, out of the 17 cases of RF observed between 1988 and 2004, an iatrogenic cause was suspected in 3 cases; minocycline, anticonvulsant and oral homeopathic drug intakes, respectively (unpublished data).

It is interesting to note that before the use of pegylated interferon alpha-2b and ribavirin for the treatment of hepatitis C, no cases of RF had been related to the hepatic disease. In our patient, unlike the one described by Jensen & Holmes (9), RF occurred at the end of the antiviral therapy, slowly developing from a typical picture of rosacea. Also their patient was much older than the previously described cases (61 years old). The intolerance to tetracycline experienced by our patient induced us to use oral isotretinoin alone, instead of its association with systemic corticosteroids, as she was affected by hepatitis C; infact, ingeneral, in cases of viral infections, the use of systemic Corticosteroids is not recommended. This is the second case of RF triggered by hepatitis C treatment and the first one successfully treated with oral isotretinoin at a low dosage.

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