Paradoxical Worsening of Truncal Acne with Doxycycline

An 18-year-old Chinese male was referred to our hospital for severe chest acne. He had mild truncal acne for the last 2 years and was started by his general practitioner on oral doxycycline and topical 4% sulphur and 2% resorcinol for 1 application twice a day, 3 weeks before his condition worsened acutely. He presented to us with inflammatory papulopustular acne with ulceration over the anterior chest (Fig. 1). He did not have similar acneiform lesions on the scalp, axillae or groin. No polyporous comedones were present. He did not report any fever, musculoskeletal pain or other systemic symptoms.

Laboratory investigations such as full blood count, erythrocyte sedimentation rate and liver function test were normal. Histopathology from the ulcer edge incisional biopsy was performed.

What is the most likely diagnosis?

A. Pseudo-acne fulminans
B. Acne fulminans
C. Acne conglobata
D. Pityrosporum folliculitis
E. Ecthyma

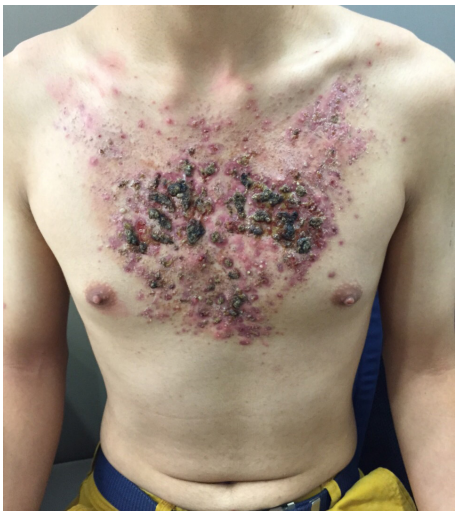

Fig. 1. On the patient's first visit, it was observed that multiple open and closed comedones were present.

Discussion

Lesional biopsy showed mixed inflammatory granulation tissue with foreign body giant cell reaction. No follicles, foreign bodies, fungi or acid-fast bacilli were seen.

Doxycycline was stopped by the patient after the initial 3 weeks due to worsening of his truncal acne. Oral prednisolone was commenced at 30 mg per day and gradually tapered off over 6 weeks. Oral isotretinoin was introduced after 10 days of prednisolone at 10 mg/day, and the patient showed remarkable response to this treatment (Figs. 2 and 3). At the latest clinic follow-up visit 18 weeks after presentation, the patient was on 30 mg of isotretinoin with marked improvement overall.

Acne fulminans (AF) is a severe variant of acne vulgaris associated with systemic symptoms such as fever, weight loss and musculoskeletal pain. Lesions consist of acneiform papules or nodules, some of which break down to form haemorrhagic ulcers with overhanging borders. The absence of systemic symptoms in a patient with characteristic lesions of AF represents a subtype called "AF sine fulminans" or "pseudo-AF". Acne conglobata (AC) can present similar to AF but polyporous comedones and non-inflammatory cysts,

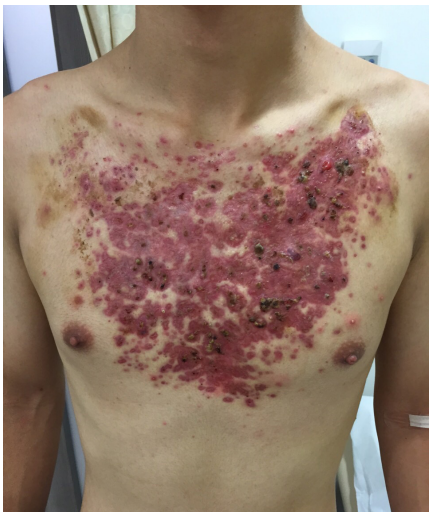

Fig. 2. The patient, 10 days after starting oral prednisolone.

Answer: A

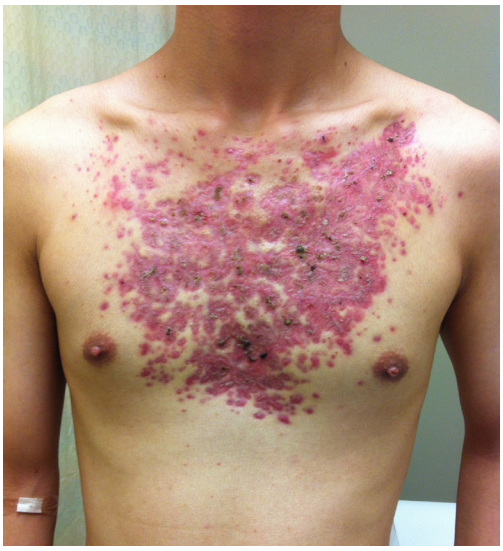

Fig. 3. The patient, 7 days after starting oral isotretinoin while still on oral prednisolone.

not seen in AF,[1] are present. In addition, patients with AC do not have systemic involvement unlike AF.

This patient had the typical cutaneous findings of AF without the associated systemic involvement, making this a case of pseudo-AF triggered by doxycycline. Pityrosporum folliculitis typically presents with erythematous monomorphic pustules on the chest and back, while ecthyma is a deep bacterial infection of the skin that presents with discrete lesions consisting of erythematous purulent ulcers with an overlying thick crust. The features of these 2 conditions were not seen in our patient.

AF has been associated with the commencement of isotretinoin and rarely, with doxycycline.[2] There are 3 kinds of acne flare-up with isotretinoin that may occur: inflammatory attacks in the first month which should resolve; recurring inflammatory attacks in the following months which are associated with the presence of open or closed comedones; and inflammatory attacks in the second and third month in which the clinical picture is of AF.[3]

Promoting factors for patients developing a flare of acne during initiation of isotretinoin therapy include young age, male gender, presence of large closed comedones[4] and truncal nodules, and isotretinoin administered at a starting dose of 0.5 mg/kg. We hypothesise that macrocomedones are also a risk factor for acne flare-up with doxycycline. Recognising predictive factors for severe flare may help in anticipating and ameliorating severe flares which may result in permanent scars.

A commonly proposed pathophysiological mechanism for AF would be a hypersensitivity reaction to bacterial antigens of *P. acnes* released during treatment with oral isotretinoin.[2] Similarly, we postulate that treatment with doxycycline could possibly result in a release of *P. acnes* bacterial antigens with subsequent hypersensitivity reaction in those predisposed.

The treatment of patients with pseudo-AF consists of a combination of oral isotretinoin and corticosteroids. Patients who previously received isotretinoin should have this stopped or reduced to 0.2 mg/kg/day while concurrent prednisolone at a dose of 0.5 to 1.0 mg/kg/day is implemented and gradually tapered according to the patient's response. Patients who did not receive prior isotretinoin can be started on a low dose of this after 2 weeks' treatment with prednisolone. Long-term low dose isotretinoin is frequently required thereafter.[5] Macrocomedonal extraction prior to starting isotretinoin may prevent severe flares during the initiation phase of isotretinoin.

This case brings to attention that an entity of pseudo-AF exists, and that conventional acne treatment with doxycycline can possibly trigger an attack.

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