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LETTERS TO THE EDITOR

Acute Acneiform Eruption Secondary to Cetuximab With Good Response to Metronidazole

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To the Editor:

We report a typical case of the sudden appearance of an acneiform reaction in a patient who began treatment with cetuximab due to metastatic disease arising from a colonic adenocarcinoma. In addition to calling attention to this common side effect, we also report that the use of metronidazole can be effective as a first-choice alternative. Cetuximab (C225) is a monoclonal antibody that targets the epidermal growth factor receptor (EGFR) and is currently used to treat advanced malignant solid tumors. The use of the drug is associated with a characteristic cutaneous toxicity and its most common side effect is the development of a follicular acneiform eruption that is more pronounced in seborrheic areas (face, chest, and upper region of the back) and generally appears between the first and fourth weeks after the initiation of treatment.

The patient was a 51-year-old woman who was referred urgently to our hospital's dermatology department from the gastroenterology department due to the rapid onset of an acneiform eruption after the initiation of immunosuppressant treatment. Notable in the patient's history were surgery for colon cancer 3 years before, with subsequent metastases to the lung, and continuous headache which raised suspicion of intracranial hypertension (currently under study). The patient noticed the sudden appearance of multiple lesions reminiscent of juvenile acne after starting cytotoxic chemotherapy with C225 and irinotecan (CPT-11). The lesions first appeared 2 weeks after the first chemotherapy session, initially in the central region of the face with subsequent extension to the cheeks and scalp.

Clinical examination revealed numerous acneiform lesions appearing on the face and, to a lesser extent, the scalp as papules and pustules with intense erythema (Figure 1).

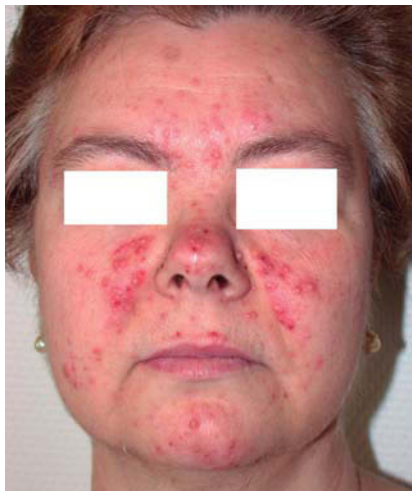

Figure 1. Figure 1. Acneiform lesions on the face appearing as papules and pustules with intense erythema.

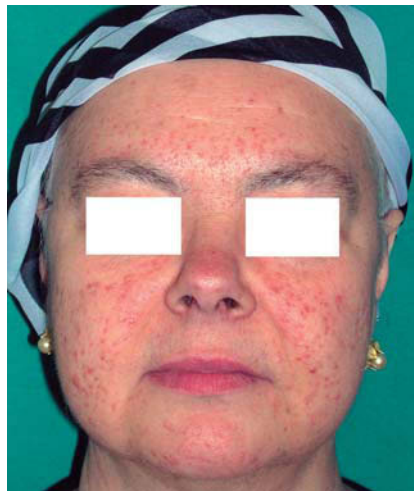

Figure 2. Resolution of the lesions after a month of treatment. Postinflammatory scars.

In view of the initial clinical suspicion and the normal course of the disease we cultured bacteria and fungi (with negative results), and initiated treatment with metronidazole at a dose of 1 g/d for 1 month. The response was favorable and most of the lesions disappeared (Figure 2). We initially ruled out treatment with tetracycline or doxycycline as the patient was undergoing evaluation for intracranial involvement and we wanted to avoid the possibility of secondary intracranial hypertension.

As mentioned in our brief introduction, C225 is a monoclonal antibody that targets EGFR and inhibits the cell proliferation in various tumors. It is currently being used to treat advanced solid malignant tumors.[1] Studies of small series of patients have shown that the most common side effect (in up to 80% of patients) is the development of a follicular acneiform eruption[2-4] that is most pronounced on the face, chest, and upper region of the back[3,5] and that typically manifests between the first and fourth weeks after the initiation of therapy.[6-8] Pruritus is generally either mild or absent, and no comedones are formed.[3,9] Other side effects described that are frequently associated with EGFR inhibitors are the development of asteatotic eczema,[10] paronychia,[11] or aphthous ulcers of the oral mucosa.[6,11] The mechanism underlying such side effects, especially on the follicle, is becoming increasingly clear. Several immunohistochemical and in situ hybridization studies have shown that there is an increase in the expression of the protein p27Kip1 (a cyclin-dependent kinase inhibitor that regulates the G1 to S phase transition in the cell cycle as well as controlling

cellular migration) in epidermal keratinocytes following treatment with C225. This is related to a change in the in vivo regulation of follicular and epidermal homeostasis mediated by EGFR, leading to the appearance of the acneiform eruption.[5,12,13]

Cultures fail to show an infectious agent as the cause of the eruption, a factor which supports the diagnosis.[3-5,8,9] The histopathologic study of the lesions shows a follicular reaction consisting of an intense neutrophilic inflammatory infiltrate surrounding the infundibuli,[5,12] which sometimes appear hyperkeratotic.[6] A differential diagnosis should be established with rapid-onset follicular eruptions, whether they are established entities or drug reactions; among the most common drug reactions are those produced by vitamin B_{12}, corticosteroids, androgens, lithium, tuberculostatic drugs, halogens, some tricyclic antidepressants, anticonvulsive drugs, and immunosuppressors. The eruption usually responds to tetracyclines such as minocycline at 100 mg/d, or doxycycline at the same dose. Currently no consensus exists as to the duration of treatment.[3,9,10,14] Recurrence is relatively frequent, although less intense than the initial episode. In view of the increased use of biological therapy in a variety of specialties, we can expect to see this entity with increased frequency in everyday dermatological practice. Dermatologists should therefore consider it as soon as the patient's history is taken, thus avoiding invasive tests such as biopsy in many cases. Tetracyclines are currently the treatment of choice and there have been few reports of therapeutic success with alternatives such as metronidazole, used in the present case, or other systemic antibiotics.

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Solitary Congenital Plaque-Like Telangiectatic Glomangioma

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To the Editor:

Glomus tumors comprise a group of relatively rare neoplasms. They may be either solitary or multiple. The latter constitute less than 10% of all cases, and in the traditional classification they were divided into disseminated and localized forms.[1,2] In 1990, another form, called congenital multiple plaque-like glomus tumors, was described by Landthaler et al.[3] Subsequently, in 1998, Requena et al[4] described a rare variety