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A. Agusti-Mejias,<sup>a,\*</sup> F. Messeguer,<sup>b</sup> R. García-Ruiz,<sup>a</sup>  
J. de la Cuadra,<sup>a</sup> A. Pérez Ferriols,<sup>a</sup>  
and V. Alegre-de Miquel<sup>a</sup>

<sup>a</sup>*Servicio de Dermatología, Consorcio Hospital General de Valencia, Valencia, Spain*  
<sup>b</sup>*Servicio de Dermatología, Instituto Valenciano de Oncología, Valencia, Spain*

\*Corresponding author.

E-mail address: annaagusti@comv.es (A. Agusti-Mejias).

## Pityriasis Rubra Pilaris With Focal Acantholytic Dyskeratosis During Treatment With Imiquimod 5% Cream

### Pitiriasis rubra pilaris acantolítica durante tratamiento con imiquimod 5% crema

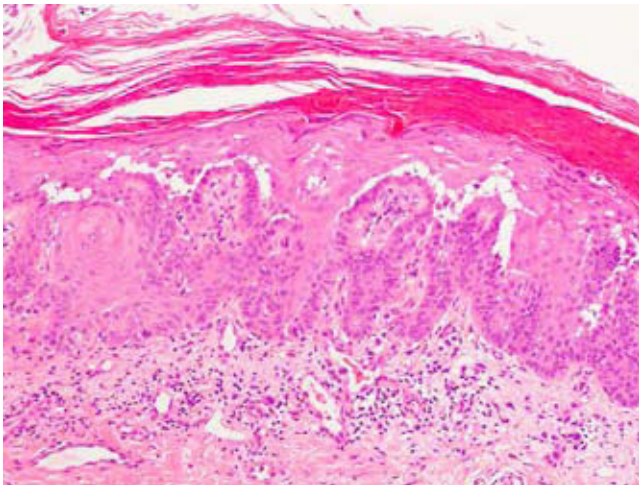
*To the Editor:*

A 56-year-old man was in his second week of treatment with imiquimod 5% cream for superficial basal cell carcinoma on his back when he developed influenza-like symptoms accompanied by a desquamative erythematous eruption that started on his head and quickly extended

caudally. Examination revealed erythroderma with small islets of healthy skin, incipient peau d'orange on the palms and soles, orange-colored erythema of the face, mild ectropion, and small keratotic follicular papules on the chest (Figure 1). The mucosas were not affected. Two skin biopsies—one from the abdomen and the other from a keratotic papule on the chest—revealed identical findings, namely, alternating areas of parakeratosis and focal dyskeratosis with acantholysis, discreet spongiosis, and a band-like lymphocytic infiltrate in the superficial dermis (Figure 2). Laboratory results were normal and HIV serology was negative. Treatment with imiquimod was stopped and acitretin (35 mg/d) started, leading to complete resolution of the lesions after 2 months. The patient refused to undergo an allergy workup to rule out a possible role for



**Figure 1** A, Shiny erythematous skin on the legs. B, Erythroderma with sparing of skin islets (arrows). C, Orange keratoderma with a waxy appearance on the palms and soles. D, Keratotic follicular papules on the anterior thorax.



**Figure 2** Suprabasal acantholysis, dyskeratosis, and focal parakeratosis (hematoxylin-eosin,  $\times 200$ ).

imiquimod in the development of the symptoms. No new lesions have been observed after 14 months of follow-up.

Pityriasis rubra pilaris encompasses a group of chronic disorders characterized by desquamative red-orange plaques, with follicular hyperkeratosis, palmar-plantar keratoderma, and, occasionally, erythroderma. It is a keratinization disorder caused by accelerated epidermal turnover in which underlying defects of vitamin A metabolism are believed to be involved. Some patients have a history of tumors, infection, fever, autoimmune disease, or trauma.<sup>1</sup>

Histopathology findings vary with the stage and development of the lesions, and the histopathological diagnosis can prove complicated in cases of erythroderma. Alternating vertical and horizontal parakeratosis and orthokeratosis are usually present, as are hypergranulosis, irregular acanthosis, and a perivascular lymphocytic infiltrate in the dermis. The follicles are dilated and filled with keratotic material. To date, acanthosis and focal acantholytic dyskeratosis have been observed in 11 cases of adult pityriasis rubra pilaris.<sup>2-9</sup> These histological findings can help in the differential diagnosis with psoriasis,<sup>9</sup> although they can lead to diagnostic errors through confusion with Darier disease, Grover disease, or pemphigus.

In most cases, acantholysis is interpreted as an incidental finding; however, in some cases it has been associated with the appearance of visceral tumors<sup>2</sup> or skin tumors,<sup>3</sup> as in our patient.

Furthermore, the manifestations of postinfectious pityriasis rubra pilaris are believed to result from a massive release of cytokines in the skin and an inflammatory response that, either through an idiosyncratic reaction or as a result of cross-reactivity, alters differentiation of cutaneous and follicular epithelial cells.<sup>1</sup> This may also have been the underlying pathogenic mechanism in our case, as therapy with imiquimod can induce multiple proinflammatory cytokines, chemokines, and other mediators that finally lead to apoptosis.<sup>10</sup> The release of these inflammatory mediators accounts for the onset of influenza-like symptoms, which are an adverse reaction

included in the Summary of Product Characteristics and were observed in our patient.

Imiquimod can induce or exacerbate inflammatory diseases of the skin. Yang et al<sup>11</sup> recently reported a case of pityriasis rubra pilaris in a 67-year-old man whose lesions worsened during treatment of actinic keratosis of the scalp with topical imiquimod 5%.

Bauza et al<sup>12</sup> also reported 3 patients who developed pemphigus-type lesions during treatment with imiquimod; all 3 improved after stopping this treatment. These cases, which are compatible with the one described here, lead us to ask whether acantholytic dermatitis could result from treatment with imiquimod, although a causal association with pityriasis cannot be ruled out.

In most cases of inflammatory dermatosis exacerbated or induced by imiquimod reported to date, the patients presented influenza-like symptoms, thus pointing to systemic absorption of the drug or to a greater release of inflammatory cytokines that might explain the systemic symptoms and the skin lesions at a distance from the site of application.

To conclude, the association between focal acantholytic dyskeratosis and pityriasis rubra pilaris should be taken into account, especially in biopsy specimens taken during the early stages of the disease. The role of imiquimod in our case is unknown; however, the time between application and onset leads us to question whether this drug triggered the disorder.

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E. Gómez-Moyano,<sup>a,\*</sup> A. Crespo-Erchiga,<sup>a</sup> A. Vera Casaño,<sup>a</sup>  
A. Sanz Trelles<sup>b</sup>

<sup>a</sup>Servicios de Dermatología, Complejo Hospitalario Carlos Haya, Málaga, Spain

<sup>b</sup>Anatomía Patológica, Complejo Hospitalario Carlos Haya, Málaga, Spain

\*Corresponding author.

E-mail address: eligm80@hotmail.com

(E. Gómez-Moyano).

## Vitamin A Deficiency and Bowel-Associated Dermatitis-Arthritis Syndrome Secondary to Biliopancreatic Diversion for Obesity

### Deficiencia de vitamina A y síndrome de dermatosis-artritis asociado a intestino secundario a derivación biliopancreática por obesidad

To the Editor:

Morbid obesity is a public health problem in the developed world and is considered the second most important preventable cause of death after smoking. Biliopancreatic diversion (BPD), consisting of a distal gastrectomy with Roux-en-Y reconstruction, is a surgical technique used to treat obesity.<sup>1,2</sup> The reduction in fat and carbohydrate absorption associated with this procedure can achieve a maintained loss of 75% of the excess weight.<sup>2</sup> We describe the case of a patient with BPD who presented 2 different types of skin lesions. The patient consulted 2 years after surgery with phrynoderma and night blindness due to vitamin A deficiency and later, 8 years after surgery, she presented skin lesions consistent with intestinal bypass arthritis-dermatitis syndrome.

## Case Report

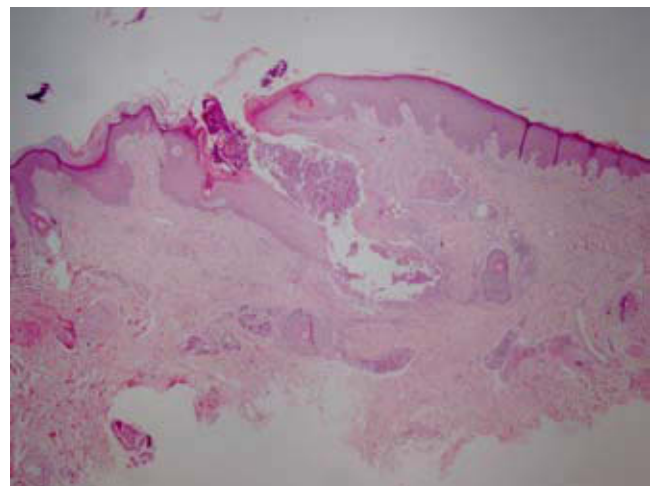
The patient was a 40-year-old woman with a history of morbid obesity treated by BPD in May 2000. She had taken vitamin supplements sporadically in the years following the surgery. In September 2002, the patient who was at full-term pregnancy, consulted for a 1-month history of night blindness and skin lesions. Examination revealed erythematous follicular papules, many of which showed central hyperkeratosis; the lesions were distributed all over the body but were found in a higher concentration on the upper back and along the extensor surfaces of the arms and legs (Figure 1).

Histology showed dilation of the follicular infundibula and a central keratotic plug with cell remnants, rupture of the follicular epithelium, and associated perifollicular inflammation (Figure 2). Blood tests revealed moderate anemia, hypoproteinemia, and deficiencies of iron, folic acid, zinc, and vitamins A, B6, B12, and D. Vitamin A levels were almost undetectable at less than 0.02 mg/L (normal values, 0.3-1 mg/L). The patient had a healthy baby girl by normal delivery, although the child had undetectable levels of vitamin A.

Based on a diagnosis of phrynoderma due to vitamin A deficiency associated with anemia and other vitamin deficiencies, treatment was started with supplements of



**Figure 1** Erythematous follicular papules with central hyperkeratosis on the legs.



**Figure 2** Dilation of the follicular infundibulum and central keratotic plug (Hematoxylin-eosin, original magnification  $\times 10$ ).