involution of the lymphangioma. Local inflammatory reactions, such as posttreatment fever, swelling, or tenderness, may develop.[5] However, the reactions do not appear to cause any damage to the overlying skin and do not lead to scar formation.[5] In addition, the medication is grown in calf serum and concerns have been raised about the theoretical potential of transmitting "mad cow disease" if coming from countries where this prion-related disease is present in cattle stock. In our patient, there was an obvious reduction in the size of the lesions and the amount of oozing fluid, without any scarring, change of the surface texture, or ulceration. Spontaneous improvement seemed unlikely in light of the close temporal correlation between beginning of treatment and resolution of the lesions. Although long-term follow-up will be needed to evaluate the efficacy and side effects of our therapy, it was very effective in the short term. Most of the previous OK-432 treatments have been utilized on macrocystic lymphangiomas, and microcystic or mixed lymphangiomas have not shown encouraging results. We believe that OK-432 could be considered as a therapeutic option for unresectable microcystic lymphangioma circumscriptum of the vulva in childhood.

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REFERENCES

1. Vlastos AT, Malpica A, Follen M. Lymphangioma circumscriptum of the vulva: a review of the literature. Obstet Gynecol 2003;101:946-54.
2. Abu-Hamad A, Provencher D, Ganjei P, Penalver M. Lymphangioma circumscriptum of the vulva: case report and review of the literature. Obstet Gynecol 1989;73:496-9.
3. Orford J, Barker A, Thonell S, King P, Murphy J. Bleomycin therapy for cystic hygroma. J Pediatr Surg 1995;30:1282-7.
4. Rautio R, Keski-Nisula L, Laranne J, Laasonen E. Treatment of lymphangiomas with OK-432 (Picibanil). Cardiovasc Intervent Radiol 2003;26:31-6.
5. Ogita S, Tsuto T, Nakamura K, Deguchi E, Tokiwa K, Iwai N. OK-432 therapy for lymphangioma in children: why and how does it work? J Pediatr Surg 1996;31:477-80.

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Pyoderma gangrenosum associated with isotretinoin therapy

To the Editor: We describe a case of a pyoderma gangrenosum (PG) associated with isotretinoin therapy. A 38 year-old woman with HAIR-AN syndrome (*h*yper*a*ndrogenism, *i*nsulin *r*esistance, and *a*canthosis *n*igricans) treated with aldactone had nodulocystic acne of 1 year's duration predominantly involving her back. She was started on a regimen of isotretinoin therapy (0.5 mg/kg/d) after a 3-month course of minocycline had failed. The patient initially responded well to treatment, with resolution of most lesions. However, 1 month into therapy, painful ulcerations developed on her back, mostly outside the previous acne lesions. Isotretinoin was stopped, and the patient was then referred to our clinic.

On presentation, she had multiple extensive ulcerations with violaceous borders and yellow discharge on her back (Fig 1). Two deep punch biopsies of the ulcers' borders were performed, revealing sterile neutrophilic inflammation, without evidence of primary vasculitis or folliculitis. Bacterial, fungal, and mycobacterial cultures were negative. Other than pain in the lesions, the patient did not complain of other systemic symptoms, such as arthralgias or gastrointestinal symptoms. Results and findings of additional investigations, including complete blood cell count, serum protein electrophoresis, liver function tests, urinalysis, and chest radiography, were within normal limits.

With the clinical diagnosis of PG, the patient was treated with nonadherent dressings, topical tacrolimus 0.1% ointment, and systemic prednisone 30 mg daily, resulting in re-epithelialization of the lesions, some with cribriform scarring, over a 2-month course. However, she became hyperglycemic and agitated with prednisone, and as sterile pustules persisted within epithelialized areas, mycophenolate mofetil (3 gm/d) was initiated as a steroid-sparing agent, leading to resolution of the lesions.

The following features of the case were consistent with the clinicopathologic PG criteria recently proposed by Su et al[1]: rapid onset of painful ulcers with violaceous borders, cribriform scarring, sterile dermal neutrophilia, relatively rapid response to therapy, and exclusion of other causes of ulcers. Considering the latter, the main differential diagnosis

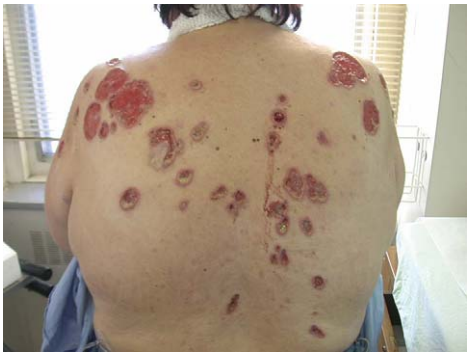

Fig 1. Extensive ulcerations on the back after isotretinoin therapy.

of the case includes acne fulminans, which has been reported to result, paradoxically, from isotretinoin therapy.[2] Characterized by the sudden onset of severe, ulcerative acne, acne fulminans is associated with fever and systemic symptoms, which were absent in our patient. Of note, the ulcers in our patient mostly occurred outside her previous acne lesions.

PG associated with isotretinoin acne therapy is rare. To our knowledge, only 3 cases have been reported in the literature, all in adolescent males and none of such severity. In one, a 19-year-old man with severe acne developed folliculitis and superficial PG on the scalp after a course of isotretinoin. Associated myelodysplastic syndrome was diagnosed during subsequent work-up.[3] In a series of 49 patients with severe nodulocystic acne treated with isotretinoin, Exner, Dahod, and Pochi[4] described 3 male patients in whom inflammatory hemorrhagic lesions had formed in preceding crusted acne nodules, with PG developing in one patient on the thigh 2 weeks after discontinuation of isotretinoin (1 mg/kg/d). In another case, PG developed over the mid chest of a 17-year-old boy 2 weeks into acne therapy with isotretinoin (0.5 mg/kg/d).[5] Oral prednisone was used to treat PG in all cases, resulting in resolution of the lesions. Parenthetically, PG has been associated with acne conglobata[6] and PAPA syndrome, consisting of pyogenic sterile arthritis, PG and acne, has been characterized.[7] The precise mechanism of PG developing with isotretinoin therapy is not clear. Increased skin fragility and vascular proliferation induced by isotretinoin may play a role.[4,8] With a series of reports of PG associated with isotretinoin therapy, clinicians should be aware of this potential complication and counsel their patients accordingly.

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REFERENCES

1. Su WPD, Davis MD, Weenig RH, Powell FC, Perry HO. Pyoderma gangrenosum: clinicopathologic correlation and proposed diagnostic criteria. Int J Dermatol 2004;43:790-800.
2. Choi EH, Bang D. Acne fulminans and 13-cis-retinoic acid. J Dermatol 1992;19:378-83.
3. Hughes BR, Cunliffe WJ. Development of folliculitis and pyoderma gangrenosum in association with abdominal pain in a patient following treatment with isotretinoin. Br J Dermatol 1990;122:683-7.
4. Exner JH, Dahod S, Pochi PE. Pyogenic granuloma-like acne lesions during isotretinoin therapy. Arch Dermatol 1983;119:808-11.
5. Gangaram HB, Tan LP, Gan AT, Suraiya HH, Ganesapillai T. Pyoderma gangrenosum following treatment with isotretinoin. Br J Dermatol 1997;136:636-7.
6. Birnkrant MJ, Papadopoulos AJ, Schwartz RA, Lambert WC. Pyoderma gangrenosum, acne conglobata, and IgA gammopathy. Int J Dermatol 2003;42:213-6.
7. Yeon HB, Lindor NM, Seidman JG, Seidman CE. Pyogenic arthritis, pyoderma gangrenosum, and acne syndrome maps to chromosome 15q. Am J Hum Genet 2000;66:1443-8.
8. Holmes SC, Thomson J. Isotretinoin and skin fragility. Br J Dermatol 1995;132:165.

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Zinc deficiency associated with necrolytic acral erythema

To the Editor: Necrolytic acral erythema (NAE) is a cutaneous sign of hepatitis C virus (HCV) infection. The clinical and histologic features of NAE have led to its classification within a group of diseases called necrolytic erythemas, which are all linked to nutrient deficiencies (Table I).[1-4] However, the physiological reason NAE presents in patients with HCV infection remains unknown. It has been asserted that zinc deficiency is not associated with NAE, but responses of NAE to empiric zinc therapy suggest that zinc deficiency is indeed associated with NAE.[1,2,4,5] We describe what, to our knowledge, is the first case of a patient with NAE who was found to have zinc deficiency by peripheral blood examination, and this case corroborates a link between zinc deficiency and NAE.

A 48-year-old woman presented with an acral dermatitis that began in December 2003. She had a history of untreated infection by HCV type 1a. In 2003 her viral load was 5,060,000 IU/mL, and