CASE REPORT

Identical twins presenting with pyogenic granuloma-like vascular proliferations during isotretinoin therapy

Jaclyn M. Rosenthal, BSN, a Ranon E. Mann, MD, b and Steven R. Cohen, MD, MPHb
Philadelphia, Pennsylvania, and Bronx, New York

Key words: drug reaction; isotretinoin therapy; pyogenic granuloma-like vascular proliferation.

INTRODUCTION

Oral isotretinoin remains the most effective treatment for severe cystic acne, given its ability to reduce sebum production, prevent comedogenesis, decrease Cutibacterium acnes (formerly Propionibacterium acnes) colonization, and induce anti-inflammatory properties.1 Common adverse effects of isotretinoin include xerosis, xerophthalmia, cheilitis, and myalgias.2 Pyogenic granuloma-like vascular proliferations have been reported as a rare adverse effect of oral isotretinoin therapy.3 However, the etiology and appropriate treatment regimen remain poorly understood. We report the first case, to our knowledge, of identical twins presenting with pyogenic granuloma-like vascular proliferations and discuss the possible genetic etiology of this rare skin finding.

CASE

Identical twin boys aged 16 years presented to the Montefiore/Einstein Dermatology Faculty Practice with severe cystic acne of 2 years’ duration. Both boys were treated simultaneously, initially with topical tretinoin. However, there was minimal improvement. An induction regimen of low-dose isotretinoin, 20 mg twice daily, was initiated. Despite improvement of facial acne, after 8 to 9 weeks of isotretinoin therapy the twins developed multiple, irregularly shaped, well-demarcated, red, friable, fleshy, hemorrhagic plaques on the back and chest (Fig 1, A). The plaques varied in size from 1 to 10 cm and formed only in areas of cystic acne. Neither twin had a history of similar lesions or abnormal wound healing. Trephine (punch) skin biopsies were obtained from the upper portion of the torso of both patients. Hematoxylin-eosin–stained tissue specimens (Fig 2) showed extensive proliferation of small blood vessels, fibroblasts, mixed inflammatory cell infiltrates, and edema. These findings were consistent with granulation tissue.

Isotretinoin was discontinued after 12 weeks, and both twins received a 3-month course of oral prednisone, 0.25 to 0.5 mg/kg daily. After discontinuation of isotretinoin, the lesions stopped progressing. Gradual shrinkage of scars and retraction of red fleshy plaques were also observed. During the first month that isotretinoin was discontinued, a trial of topical imiquimod 5%, applied daily to an isolated lesion on one of the twins, was ineffective. Extensive curettage was also performed in 3 stages (Fig 1, B and C). Both twins achieved resolution of lesions. Prednisone was tapered off and the cystic acne and pyogenic granuloma-like vascular proliferative lesions remained in complete remission for 5 years. No additional acne treatments were needed.

DISCUSSION

Pyogenic granuloma-like vascular proliferations are characterized by ulceration, hemorrhagic plaques, and excessive granulation tissue originating from cystic acne lesions.3 Clinically, they resemble pyogenic granulomas, but histologically, they lack the characteristic lobular capillary arrangement. Typically, they present as multiple lesions, but single lesions have also been reported. The eruption most commonly appears on the neck, chest, and back 6 to
9 weeks after initiation of isotretinoin, as observed in our patients.3

The exact frequency, age of onset, and pathogenesis of pyogenic granuloma-like vascular proliferations remain unknown.4 Exner et al4 suggested that isotretinoin may induce vascular proliferation and skin fragility through alterations in connective tissue metabolism and the loss of desmosomes and desmosomal attachments. We postulate that retinoids may not be the only contributing factor. The similarity of plaque severity and presentation observed in these twins suggests a genetic influence may predispose to this adverse effect. Moreover, pyogenic granuloma-like vascular proliferations form only in areas of cystic activity, suggesting that factors unique to cystic acne may play a role in these vascular proliferations. Last, all reported cases of pyogenic granuloma-like vascular proliferations have been restricted to male patients, raising further speculation about a genetic or hormonal component.

There are no standardized guidelines for treatment of pyogenic granuloma-like vascular proliferations. Patients with severe features (ie, pain, numerous lesions, and cosmetic disfigurement) receive systemic steroids to suppress the inflammation.2-5 Secondary treatment with cautery, curettage, and incision and drainage is also effective in treating single lesions. To our knowledge, this is the first case to report the use of imiquimod for topical treatment of pyogenic granuloma-like vascular proliferations. Despite its

Fig 1. Clinical images of pyogenic granuloma-like vascular proliferations. A, Twin B at presentation. B, Twin B immediately after extensive curettage surgery. C, Twin A 3 weeks after the third stage of curettage surgery.

Fig 2. Histopathology of pyogenic granuloma-like vascular lesions. Histologic examination of biopsies from twin A (A and B) and twin B (C and D) showed prominent proliferation of small blood vessels, fibroblasts, mixed inflammatory cell infiltrate, and edema. These findings were consistent with granulation tissue.
antiangiogenic effects, immunosuppressive properties, and success in treating pyogenic granuloma, imiquimod 5% had no effect in our patient.6

Pyogenic granuloma-like vascular proliferations are acute, disfiguring, and rare adverse effects associated with isotretinoin therapy. To our knowledge, this is the first report of identical male twins who experienced pyogenic granuloma-like vascular proliferations after receiving isotretinoin therapy for severe cystic acne, suggesting a possible underlying genetic predisposition. Although our patients achieved complete remission of the proliferations, treatment is complex and variable, underscoring the necessity for further investigations.

REFERENCES
1. Layton A. The use of isotretinoin in acne. Dermatoendocrinol. 2009;1(3):162-169.
2. Figueiras Dde A, Ramos TB, Marinho AK, Bezerra MS, Cauas RC. Paronychia and granulation tissue formation during treatment with isotretinoin. An Bras Dermatol. 2016;91(2):223-225.
3. MacKenzie-Wood AR, Wood G. Pyogenic granuloma-like lesions in a patient using topical tretinoin. Australas J Dermatol. 1998;39:248-250.
4. Exner JH, Dahod S, Pochi PE. Pyogenic granuloma-like acne lesions during isotretinoin therapy. Arch Dermatol. 1983;119:808-811.
5. Hagler J, Hodak E, David M, Sandbank M. Facial pyogenic granuloma-like lesions under isotretinoin therapy. Int J Dermatol. 1992;31(3):199-200.
6. Tritton SM, Smith S, Wong LC, Zagarella S, Fischer G. Pyogenic granuloma in ten children treated with topical imiquimod. Pediatr Dermatol. 2009;26(3):269-272.