

Severe Acne Fulminans Following Low-Dose Isotretinoin and Testosterone Use

Wioletta Barańska-Rybak, MD, PhD; Dorota Mehrholz, MD; Paulina Flis, MD; Gabrielle Karpinsky, MD; Malgorzata Sokolowska-Wojdyło, MD

PRACTICE POINTS

- Acne fulminans, the most severe form of acne, is characterized by deep ulcerations covered by a hemorrhagic crust. It is commonly associated with fever, polyarthralgia, and myopathy caused by rapid weight loss.
- This rare condition is recognized as a potential complication of oral isotretinoin therapy.

To the Editor:

Acne fulminans (AF), the most severe form of acne, is a rare condition with an incidence of less than 1% of total acne cases.¹ Adolescent boys are the most susceptible group of patients.² Painful inflammatory pustules that transform into deep ulcerations covered by abundant hemorrhagic crust are typical of AF. Commonly affected areas include the face, back, neck, and chest. Additionally, fever and polyarthralgia may be present, and there often is myopathy due to rapid weight loss.^{3,4} Less often, erythema nodosum and splenomegaly may be observed.⁵ Laboratory testing also may reveal markers of systemic inflammation such as leukocytosis with neutrophilia, elevated C-reactive protein levels, increased erythrocyte sedimentation rate, and thrombocytosis. Anemia and elevated hepatic enzyme levels also may be present in AF.² It is suspected that AF may be induced by low doses of isotretinoin therapy with concomitant inherited susceptibility.⁶

We report the case of a 21-year-old man who was referred to the Department of Dermatology by his primary care physician for evaluation of severe hemorrhagic

lesions on the trunk following use of oral isotretinoin (Figure 1). Prior to development of the lesions, the patient had started weekly intramuscular injections of testosterone 500 mg, which he purchased online without consulting a physician, to address muscle mass reduction associated with sudden weight loss from intense physical training. After 8 months of testosterone supplementation along with continued physical training, the patient presented to his primary care physician for treatment of acne vulgaris on the back and trunk of 2 months' duration. Oral isotretinoin 20 mg once daily was initiated; however, the patient reported that the acne lesions showed progression after 1 month of treatment. Isotretinoin was increased to a more weight-appropriate dosage of 60 mg once daily 2 weeks before admission to our dermatology clinic.



FIGURE 1. Acne fulminans. Severe hemorrhagic lesions on the trunk following use of oral isotretinoin.

Drs. Barańska-Rybak, Mehrholz, Sokolowska-Wojdyło are from the Department of Dermatology, Venereology, and Allergology, Medical University of Gdańsk, Poland. Dr. Flis is from the Department of Laboratory Medicine, Division of Clinical Pharmacology, Karolinska University Hospital, Stockholm, Sweden. Dr. Karpinsky is from Children's Hospital Colorado, Aurora.

The authors report no conflict of interest.

Correspondence: Dorota Mehrholz, MD, Mariana Smoluchowskiego 17, 80-001, Gdańsk, Poland (dorota.mehrholz@gmail.com).

At the current presentation, dermatologic examination revealed numerous inflamed ulcerations covered by a hemorrhagic crust on the back and trunk. The patient also reported knee, elbow, and inguinal pain, especially at night. No fever or loss of appetite was reported. The patient was otherwise healthy and had no remarkable family history of acne or other dermatologic diseases.

Laboratory testing showed leukocytosis (11,000/ μ L [reference range, 4500–11,000/ μ L]), an elevated C-reactive protein level (66 mg/L [reference range, 0.08–3.1 mg/L]), and an elevated erythrocyte sedimentation rate (46 mm/h [reference range, 0–20 mm/h]). There were laboratory and clinical signs of a secondary bacterial infection in the affected areas, and a culture of secretions collected from lesions on the back grew *Staphylococcus aureus* with sensitivity to erythromycin, clindamycin, doxycycline, and trimethoprim-sulfamethoxazole and resistance to penicillin. A diagnosis of AF was made based on the clinical presentation and systemic symptoms, and anabolic-androgenic steroids and low-dose isotretinoin were identified as etiologic factors.

Treatment initially included cessation of isotretinoin and administration of prednisone, omeprazole, clindamycin, and doxycycline. Prednisone was given at a dosage of 40 mg once daily for 1 week, then decreased by 5 mg every 7 days. Omeprazole was given concurrently as prophylaxis for the gastrointestinal tract side effects of long-term prednisone use. Clindamycin was given at a dosage of 300 mg 3 times daily. Doxycycline was given for 6 weeks at a dosage of 100 mg twice daily. Topical octenidine dihydrochloride also was given.

Marked improvement was noted after 24 hours (Figure 2) as well as on the third day of treatment (Figure 3A). After 6 weeks, only disfiguring scars were visible (Figure 3B). Oral isotretinoin was reincorporated



FIGURE 2. Marked improvement of acne fulminans was noted after 24 hours of treatment with prednisone, clindamycin, and doxycycline.

after 8 weeks and was subsequently discontinued after 5 months of therapy with a cumulative dose of 150 mg/kg.

It is important to differentiate AF from exacerbation of acne vulgaris because patients typically have mild or moderate acne vulgaris before the onset of acute symptoms.¹ Acne fulminans is characterized by systemic symptoms such as myalgia, polyarthralgia, fatigue, and osteolytic bone lesions.^{1,7} Additionally, hematologic symptoms such as fever, leukocytosis, anemia, splenomegaly, and hepatomegaly may be present.^{1,5,7} Our patient demonstrated the polysymptomatic form of AF. The patient had severe acne with a tendency to scar. There also were some systemic manifestations such as polyarthralgia, weight loss,



FIGURE 3. A, Acne fulminans lesions on the trunk showed clearance after 3 days of treatment. B, After 6 weeks, only disfiguring scars were visible.

leukocytosis, an elevated erythrocyte sedimentation rate, and an elevated C-reactive protein level.

The clinical diagnosis in our patient also was supported by the hypothesis that heredity, overactive immune reactions, bacterial infections, and use of some drugs (eg, isotretinoin, tetracycline, testosterone) can trigger AF.⁸ The most well-known theory is that low doses of isotretinoin induce AF.⁶ The majority of cases are caused by doses of less than 20 mg/kg once daily, but there have been reports of patients using full doses and developing this condition.⁹ The fact that the use of low- and high-dose isotretinoin can provoke AF suggests an idiosyncratic reaction that is not clearly dose related. The most dangerous triggering factor of AF is concomitant usage of testosterone and isotretinoin.¹⁰ Our patient used testosterone injections to increase muscle mass and underwent treatment with isotretinoin for acne.

Treatment of AF is controversial, as there is no standard therapy. Currently, steroids and isotretinoin are the treatments of choice. Antibiotic use is controversial because of a lack of randomized trials.¹¹

In the first stage of treatment, prednisone 0.5 to 1 mg/kg once daily is recommended as an initial anti-inflammatory therapy, with gradual dose reduction. According to evidence-based recommendations, a low dose of isotretinoin can be introduced after crusted lesions have healed. The overlapping therapy with steroids and isotretinoin should be provided for at least 4 weeks. High-potency topical corticosteroids can be used on granulation tissue, which can shorten the systemic treatment with prednisone or can be an alternative treatment for patients with contraindications to systemic corticosteroids.¹¹

Additionally, local care of the lesions including compresses and topical emollients is crucial. There are some case reports in which there is introduction of high doses of isotretinoin, subsequently with systemic steroids.^{7,8,12} Seukeran and Cunliffe⁵ proved that it is beneficial to give acne prophylaxis to prevent further episodes. Our patient was similarly treated with systemic steroids and isotretinoin. Treatment guidelines for AF do not recommend

oral antibiotics,¹¹ but data are limited in the case of isotretinoin-induced AF. Our patient was given doxycycline concomitant with systemic steroids, which was necessary due to signs of secondary infection from a lesion culture. Doxycycline was stopped when isotretinoin treatment was initiated to prevent pseudotumor cerebri. The patient achieved good clinical improvement with no relapse.

Using isotretinoin to treat acne vulgaris has many benefits, despite the possibility of developing AF as an extremely rare complication. Clinicians should be aware of the risk of this complication to make the diagnosis and provide appropriate care, especially in young men. It is particularly important to consider the possibility of concomitant testosterone and isotretinoin when documenting the patient's medical history.

REFERENCES

1. Romiti R, Jansen T, Plewig G. Acne fulminans. *An Bras Dermatol*. 2000;75:611-617.
2. Karvonen SL. Acne fulminans: report of clinical findings and treatment of twenty-four patients. *J Am Acad Dermatol*. 1993;28:572-579.
3. Kelly AP, Burns RE. Acute febrile ulcerative conglobate acne with polyarthralgia. *Arch Dermatol*. 1971;104:182-187.
4. Plewig G, Kligman AM. Vitamin A acid in acneiform dermatoses. *Acta Derm Venereol Suppl*. 1975;74:119-127.
5. Seukeran DC, Cunliffe WJ. The treatment of acne fulminans: a review of 25 cases. *Br J Dermatol*. 1999;141:307-309.
6. Kraus SL, Emmert S, Schön MP, et al. The dark side of beauty: acne fulminans induced by anabolic steroids in a male bodybuilder. *Arch Dermatol*. 2012;148:1210-1212.
7. Jansen T, Plewig G. Acne fulminans. *Int J Dermatol*. 1998;37:254-257.
8. Zanelato TP, Gontijo GM, Alves CA, et al. Disabling acne fulminans. *An Bras Dermatol*. 2011;86:9-12.
9. Azulay DR, Abulafia LA, Costa JAN, et al. Tecido de granulação exuberante. efeito colateral da terapêutica com isotretinoína. *An Bras Dermatol*. 1985;60:179-182.
10. Traupe H, von Mühlendahl KE, Brämwig J, et al. Acne of the fulminans type following testosterone therapy in three excessively tall boys. *Arch Dermatol*. 1988;124:414-417.
11. Greywal T, Zaenglein AL, Baldwin HE, et al. Evidence-based recommendations for the management of acne fulminans and its variants. *J Am Acad Dermatol*. 2017;77:109-117.
12. Honma M, Murakami M, Iinuma S, et al. Acne fulminans following measles infection. *J Dermatol*. 2009;36:471-473.