Acne Fulminans Induced by Lymecycline in a Patient with Hidradenitis Suppurativa: A Case Report

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Abstract
Acne fulminans (AF) is a rare and severe form of inflammatory acne that typically occurs in male adolescents with acne vulgaris and is characterized by the sudden onset of painful, bleeding, and ulcerated lesions. It has been described very rarely in association with hidradenitis suppurativa (HS). Its onset may be induced by drugs, particularly isotretinoin. We present a case of a 16-year-old patient with HS who developed AF following initiation of antibiotic therapy with lymecycline. In the literature, only 2 patients who developed a coexistence of AF and HS have been reported, and there are only 2 other similar cases of AF induced by doxycycline and lymecycline. We consider our case to be of particular interest not only because of the very rare concomitant presence of AF and HS but also because AF was induced by lymecycline, a drug commonly used to treat both acne and HS, and described only once as a drug responsible for AF, so it is an aspect that deserves to be considered by the clinician dealing with similar conditions.
Introduction

Acne fulminans (AF) is a rare and severe form of inflammatory acne that typically occurs in male adolescents with acne vulgaris and is characterized by the sudden onset of painful, bleeding, and ulcerated lesions. It may or may not occur in association with systemic symptoms and has been described very rarely in association with hidradenitis suppurativa (HS). Its onset may be induced by drugs, particularly isotretinoin [1, 2]. We present a case of a patient with HS who developed AF following initiation of antibiotic therapy with lymecycline.

Case Report

A 18-year-old man was admitted to our Department presenting with an exacerbation of acne lesions associated with fever and malaise. His medical history was remarkable for a 2-year history of draining sinuses linking inflammatory lesions on his groins and scrotum suggesting for HS, for whom he had started a short oral course of tetracyclines (lymecycline) 3 weeks prior. The patient also reported from about a year mild to moderate papular and pustular acne of the face treated with topical antibiotics with little benefit.

Physical examination revealed draining sinuses and abscesses (Hurley stage 3 HS) with peripheral hypertrophic and atrophic scars on his groins and perianal region. Inflammatory and ulcerated nodular acne were observed on the face, chest, and back associated with bleeding crusts over the ulcers on upper trunk (Fig. 1a–c). He denied painful joints. Routine blood analysis was within normal ranges, except for a modest elevation of inflammatory

Fig. 1. AF on the back (a), chest (b), and face (c) before the treatment. Clinical improvement after 12 months of treatment on the back (d), chest (e), and face (f).
markers. X-rays also resulted unremarkable. A diagnosis of AF induced by lymecycline was made. Lymecycline was promptly discontinued, and the patient began a treatment with isotretinoin that was introduced at an escalating dose starting from 5 mg/day up to 30 mg/day, associated with low-dose (0.3 mg/kg/die) prednisone which was gradually reduced over a 16-weeks period. The cutaneous lesions resolved with scarring in 12 weeks; after 12 months, the therapy was interrupted without relapses (Fig. 1d–f). Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Discussion

To the best of our knowledge, 2 patients who developed a coexistence of AF and HS have been reported in the literature. One patient had Hurley stage 3 HS lesions in the axillae, inguinal, and perianal region [2], and the other one had Hurley stage 3 HS in one axilla and Hurley 2 lesions in all other HS area [3]. Both of patients have suffered from concomitant AF and HS for 2 and 3.5 years [2, 3]. In 1 case, AF appeared after 1-month isotretinoin treatment [3], while other patient developed AF after a treatment with oral clindamycin and rifampicin [2]. Both of patients lost weight, had a low-grade fever, and referred joint pain [2, 3] with one of the 2 patients affected by a seronegative undifferentiated spondyloarthropathy [2]. Patients were treated in a different way; 1 patient started adalimumab, a fully human monoclonal IgG1 antibody directed toward membrane-bound TNF alfa on dosing regimen of 160 mg at week 0, 80 mg at week 2, followed by 40 mg weekly starting at week 4 [2]. The other patient was treated with ertapenem followed by oral rifampin plus moxifloxacin plus metronidazole for 6 weeks then rifampin plus moxifloxacin for 8 weeks; a maintenance treatment with cotrimoxazole was continued [3]. The HS and AF lesions improved in 3–12 months [2, 3].

AF and HS could be the warning sign of pyoderma gangrenosum, acne, suppurative hidradenitis, and spondyloarthritis syndrome with pyoderma gangrenosum that can appear at any point after the development of HS lesions. As suggested by some authors, AF could be a facial form of HS [4].

In addition of association between AF and HS, we consider this case interesting because acne was worsened by tetracycline antibiotic treatment. In the literature, there are only 2 other similar cases of AF induced by doxycycline [5] and lymecycline [6] that are in addition to the aforementioned case [2]. The lesions appeared after 4 days [6] and 3 weeks [5], respectively. While the case worsened by doxycycline showed acneiform lesions without fever, musculoskeletal pain, or other systemic symptoms (called AF sine fulminans) [5], the case of AF induced by lymecycline was described with painful, ulcerated nodules associated with mild fever, headache, diffuse arthralgias, and blood count alterations. In both cases, antibiotic discontinuation and the introduction of low-dose oral isotretinoin with corticosteroids led to a significant improvement overall [5, 6].

A crucial pathogenetic step of AF seems to be the alteration of both innate and adaptive immune responses or the autoinflammatory/inflammasome pathway. Briefly, according to the literature, the treatment with doxycycline could promote in AF a massive immune reaction against the P. acnes bacterial antigens with subsequent hypersensitivity reaction of types III and IV, similarly to oral isotretinoin [7]. In addition, a large number of noninflamed macrocomedones may probably represent a “reservoir” of inflammatory mediators that induce acne flare-up after antibiotic treatment [1].

In conclusion, we consider our case to be of particular interest not only because of the very rare concomitant presence of AF and HS but also because AF was induced by lymecycline, a drug commonly used to treat both acne and HS and described only once as a drug responsible for AF, so it is an aspect that deserves to be taken into account by the clinician dealing with similar conditions.
Statement of Ethics

Ethical approval was not required for this study in accordance with local/national guidelines. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Trave Ilaria: conceptualization (equal), data curation (equal), formal analysis (equal), investigation (equal), development or design of methodology (equal), project administration (equal), resources (equal), software (equal), supervision (equal), validation (equal), visualization (lead), and writing – original draft preparation (lead). Micalizzi Claudia: conceptualization (equal), data curation (equal), formal analysis (equal), investigation (equal), development or design of methodology (equal), project administration (equal), resources (equal), software (equal), supervision (equal), validation (equal), visualization (lead), and writing – original draft preparation (lead). Molle Mattia: conceptualization (equal), data curation (equal), formal analysis (equal), investigation (equal), development or design of methodology (equal), project administration (equal), resources (equal), software (equal), supervision (equal), validation (equal), visualization (lead), and writing – original draft preparation (lead). Castelli Riccardo: conceptualization (equal), data curation (equal), formal analysis (equal), investigation (equal), development or design of methodology (equal), project administration (equal), resources (equal), software (equal), supervision (equal), validation (equal), visualization (lead), and writing – original draft preparation (lead). Cozzani Emanuele: conceptualization (equal), data curation (equal), formal analysis (equal), investigation (equal), development or design of methodology (equal), project administration (equal), resources (equal), software (equal), supervision (equal), validation (equal), visualization (lead), and writing – original draft preparation (lead). Aurora Parodi: conceptualization (lead), data curation (equal), formal analysis (equal), investigation (equal), development or design of methodology (equal), project administration (equal), resources (equal), software (equal), supervision (lead), validation (equal), visualization (lead), and writing – original draft preparation (lead).

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.
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