A case of chronic granulomatous disease and acne: is isotretinoin a safe treatment?

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Abstract

We report the case of a patient with chronic granulomatous disease and acne treated with isotretinoin, who developed a diffuse staphylococcal skin infection during the therapy. Chronic granulomatous disease is a rare genetic disorder characterized by an altered innate immunity with an increased risk of potentially lethal bacterial and fungal infections. Although chronic granulomatous disease is rare, acne is a common manifestation in these patients, but there are no data about the gold standard therapy.

Introduction

Chronic granulomatous disease (CGD) is a rare genetic disorder characterized by a deficit of NADPH oxidase that leads to an impaired phagocytosis with potentially lethal bacterial and fungal infections. Skin is one of the most affected organs, with *Staphylococcus aureus* (SA) as the major isolated pathogen.[1,2] Moreover, due to altered immunity, patients are more prone to inflammatory diseases, such as autoimmune and inflammatory bowel diseases.[1,2] Acne is the most frequently reported inflammatory skin disorder,[1,2] but data about the severity and gold standard therapy are lacking.

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Key words: chronic granulomatous disease, acneiform eruption, acne vulgaris, isotretinoin, staphylococcal skin infection.

Contributions: all authors contributed equally.

Conflict of interest: the authors declare no potential conflict of interest, and all authors confirm accuracy.

Patient consent for publication: written informed consent was obtained from the patient.

Availability of data and materials: data and materials are available from the corresponding author upon request.

Received for publication: 18 November 2022.
Accepted for publication: 27 November 2022.
Early view: 29 December 2022.

Dermatology Reports 2023; 15:9361
doi:10.4081/dr.2023.9631

Case Report

We report the case of a 25-year-old Caucasian man affected by CGD and chronically treated with oral co-trimoxazole (CTX) and itraconazole, referring to us for a chronic-relapsing acneiform rash occurring for several years. Clinically, the patient showed diffuse inflammatory papules and pustules, localized in seborrheic areas of the face and trunk (Figure 1 a,b). Because of the large extension of the rash and the chronic antibiotic therapy, we decided to start low-dose isotretinoin (0.25 mg/kg/die) in association with an antiseptic soap. During the following weeks, we observed a progressive resolution of the lesions (Figure 1 c,d), but after three months of treatment, the patient developed diffuse furuncles and abscesses on the face, trunk, and limbs (Figure 1 e,f). We performed nasal and abscess swabs, respectively positive for a CTX-resistant and a CTX-sensitive SA. The infection was successfully treated with topical fusidic acid and oral clindamycin; nevertheless, we decided to stop isotretinoin with progressive relapsing of the acneiform rash during the next months. Nowadays, the manifestation is partially controlled with salicylic acid spray and antiseptic soap, with recurrent flare-ups.

Discussion

Isotretinoin is a well-known retinoid that is widely used in the treatment of moderate-to-severe and extensive acne, directly acting on follicular hyperkeratosis, hyperseborrhea, and inflammation. About infection, the inhibition of sebum excretion indirectly reduces the number of *Cutibacterium acnes* and gram-negative bacteria regardless of isotretinoin dosage.[3] On the other hand, isotretinoin increases cutaneous colonization by SA in all body sites, especially in the nasal mucosa.[4] This change in cutaneous microflora causes SA infections only in a small percentage of patients,[5] but could be a great concern in CGD patients. In the literature, 5 subjects with CGD and acne treated with isotretinoin are reported (Table 1).[6-10]

Three patients were treated with isotretinoin at different dosages (ranging 0.5-1 mg/kg/die) without any adverse event,[6-8] while one patient had to promptly interrupt the treatment because of hypertriglyceridemia.[9] Conversely, the last one reported an episode of invasive pulmonary aspergillosis after only two weeks of treatment.[10] The authors explained this adverse event with a

decrease in blood levels of itraconazole, due to isotretinoin induction of cytochrome P450. However, this conclusion is questionable, and this effect is being debated *in vivo*.[11] To our knowledge, this is the first reported SA infection during isotretinoin treatment in a patient with CGD. Even in the absence of nodular lesions or scars, we decided to start isotretinoin because of the large extension of skin lesions and the great impairment of the patient's quality of life. Unfortunately, after three months of treatment, he developed numerous furuncles and abscesses positive for SA. Even if the infection was not life-threatening, we decided to stop isotretinoin to avoid more severe consequences. We cannot exclude *a priori* an increased metabolism of co-trimoxazole due to the retinoid, but in our opinion, the finding of two different strains of SA (CTX-sensitive in the skin and CTX-resistant in the nose) is more likely a consequence of the altered cutaneous microflora.

Conclusions

Although effective, isotretinoin is a treatment that should be given with extreme caution in patients suffering from CGD and requires strict clinical monitoring to promptly identify possible SA cutaneous infections.

Table 1. Reported cases of patients with chronic granulomatous disease and acne treated with isotretinoin.

Author	Sex and age (years)	Isotretinoin dosage	Duration	Adverse event
Alonso-de-Celada *et al.*[6]	M 13	0.85 mg/kg/day	5 months	None
Barbi *et al.*[7]	M 30	0.5 mg/kg/day	3 months	None
Spillane *et al.*[8]	M 14	1 mg/kg/day	4 months	None
Kempet *al.*[9]	F 13	0.66 mg/kg/day	3 weeks	Hypertriglyceridemia
von Bernuth *et al.*[10]	M 20	Not reported	2 weeks	Invasive pulmonary aspergillosis
Our case	M 25	0.25 mg/kg/day	3 months	*Staphylococcus aureus* skin infection

F, female; M, male.

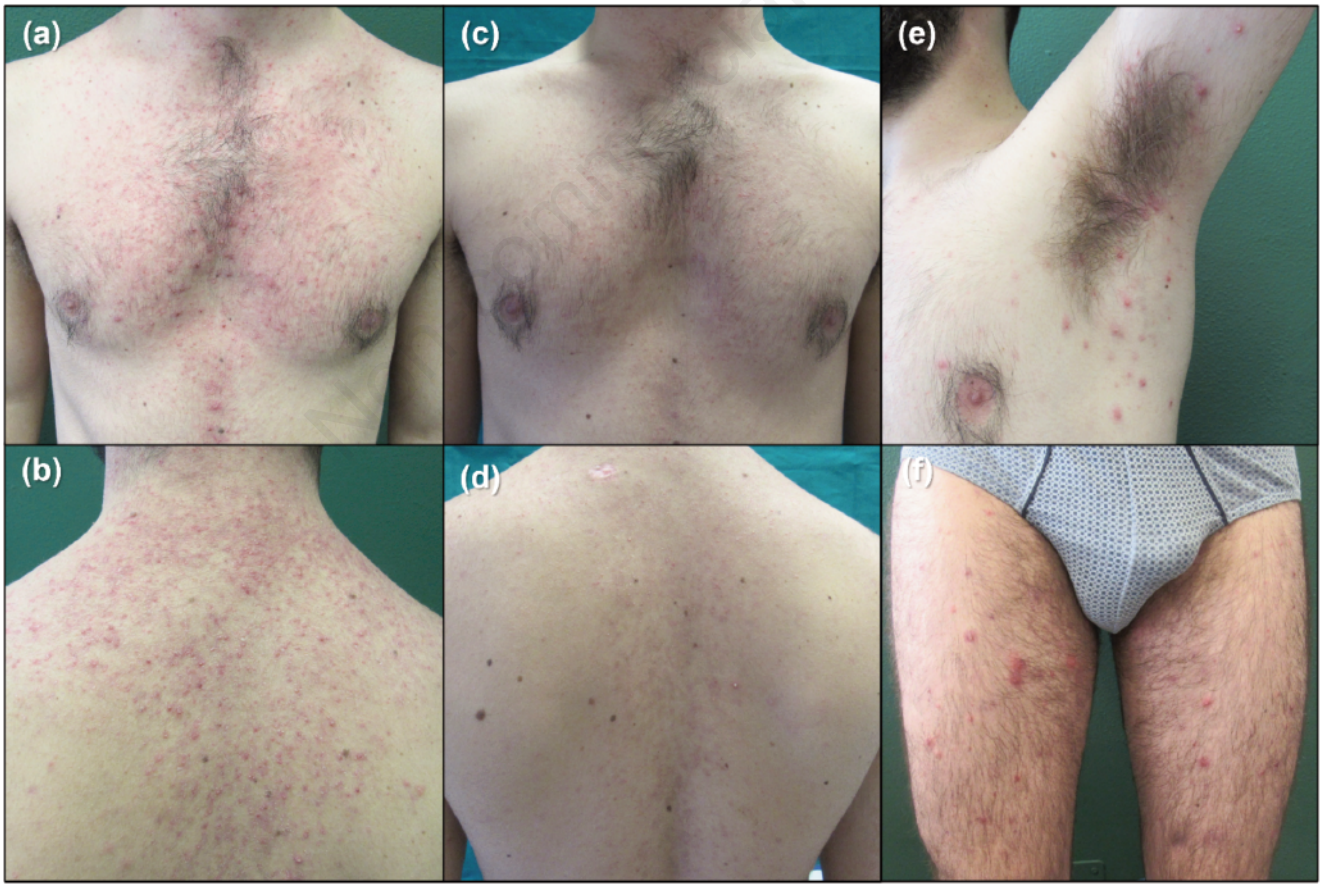

Figure 1. Acneiform rash at the beginning (a, b) and after ten weeks of therapy with isotretinoin (c, d); diffuse furuncles and abscess after three months of therapy (e, f).

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