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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 an altered immunity, the patients are more prone also to inflammatory diseases, such as autoimmune and inflammatory bowel diseases[1,2]. Acne is the most frequently reported inflammatory skin disorder[1,2], but lacking data about severity and gold standard therapy.

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 since several years. Clinically the patient showed diffuse inflammatory papules and pustules, localized in seborrheic areas of face and trunk (Fig. 1a, 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 progressively resolution of the lesions (Fig. 1c, d), but after three months of treatment the patient developed diffuse furuncles and abscesses at face, trunk and limbs (Fig. 1e, 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 a 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.

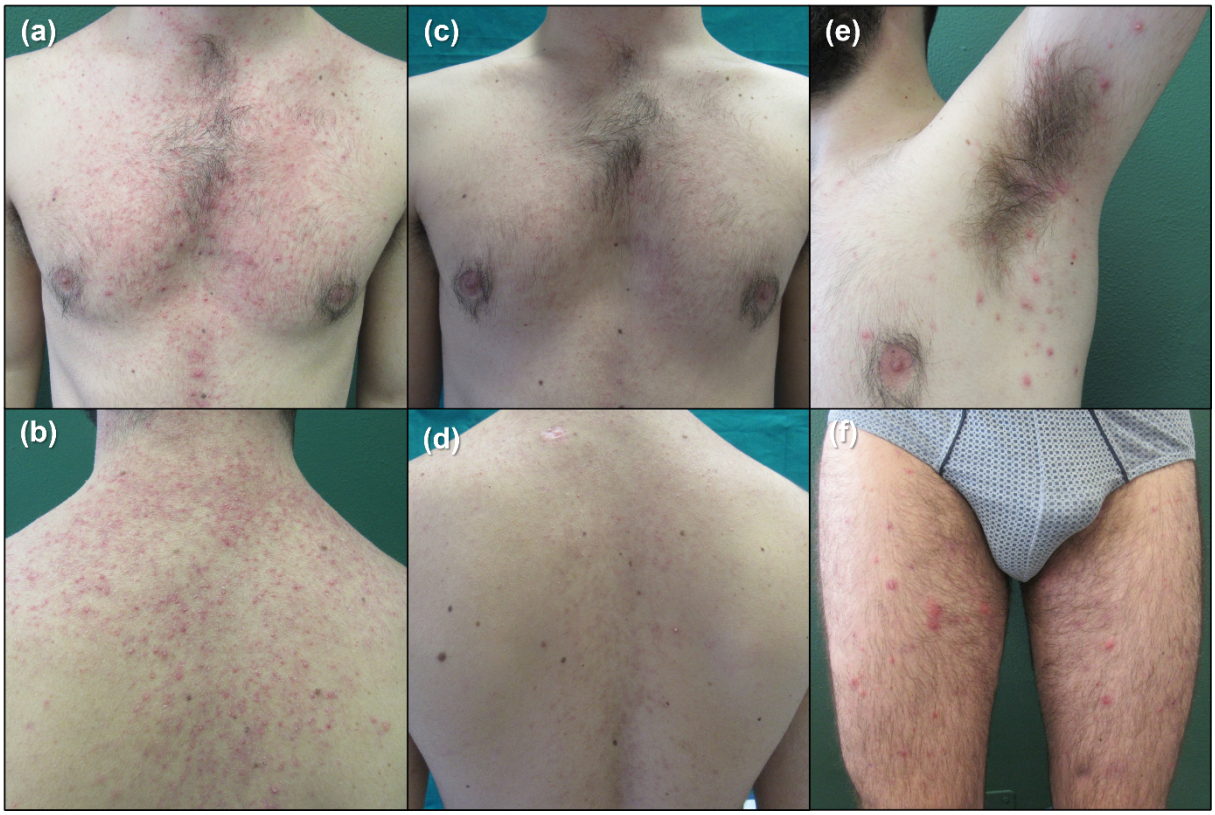

Figure 1. Acneiform rash at the beginning (a, b) and after ten weeks of therapy with isotretinoin (c, d). Diffuse furuncles and abscess after three months of therapy (e, f).

Discussion

Isotretinoin is a well-known retinoid 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 the cutaneous colonization by SA in all body sites, especially in nasal mucosa[4]. This change in cutaneous microflora cause SA infections only in a small percentage of patients[5] but could be a great concern in CGD patients.

In literature are reported five subjects with CGD and acne treated with isotretinoin (Table 1).

Table 1. Reported cases of patients with CGD and acne treated with isotretinoin

Author	**Sex-Age (years)**	**Isotretinoin Dosage**	**Duration**	**Adverse event**
Alonso-de-Celada et al.[5]	M 13	0.85 mg/kg/day	5 months	None
Barbi et al.[6]	M 30	0.5 mg/kg/day	3 months	None
Spillane et al.[7]	M 14	1 mg/kg/day	4 months	None
Kemp et al.[8]	F 13	0.66 mg/kg/day	3 weeks	Hypertriglyceridemia

von Bernuth et al.[9]	M 20	Not reported	2 weeks	Invasive pulmonary aspergillosis
Our case	M 25	0.25 mg/kg/day	3 months	Staphylococcus aureus skin infection

Three patients[6-8] were treated with isotretinoin at different dosages (ranging 0.5-1 mg/kg/die) without any adverse event, while one patient[9] had to promptly interrupt the treatment because of hypertriglyceridemia. Conversely, the last one[10] reported an episode of invasive pulmonary aspergillosis after only two weeks of treatment. Authors explained this adverse event with a decrease of blood levels of itraconazole, due to isotretinoin induction of cytochrome P450. However, this conclusion is questionable, being debated this effect in vivo[11].

To our knowledge this is the first reported SA infection during isotretinoin treatment in a patient with CGD. Even in absence of nodular lesions or scars, we decided to start isotretinoin because of the large extension of skin lesions and the great impairment of patient's quality of life. Unfortunately, after three months of treatment he developed numerous furuncles and abscess positive for SA. Even if the infection was not life threating, 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 skin and CTX-resistant in nose) is more probably 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 that requires strict clinical monitoring to promptly identify possible SA cutaneous infections.

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