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Case presentation

Isotretinoin therapy for the treatment of acne in patients with cystic fibrosis: a case series and review of the literature

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Abstract

Background: Cystic fibrosis (CF) is the most common severe autosomal recessive disorder in Caucasians. Viscous secretions typically obstruct the lungs, pancreas, and gastrointestinal tract. As disease management improves, patients will increasingly seek care for conditions such as acne. Isotretinoin therapy for acne in patients with CF is controversial owing to concerns that the medication may exacerbate CF-related hepatic, pulmonary, and ocular complications.

Purpose: We describe two patients with CF treated with isotretinoin from our clinic and also provide a literature review of 11 similar cases. We describe patient outcomes, common complications, and the risks for severe adverse effects.

Materials and methods: The clinical courses of two patients with CF who were treated with isotretinoin for moderate-severe acne are presented. Using PubMed, we analyzed previous case reports of patients with CF who were prescribed isotretinoin and review complications associated with systemic retinoids.

Results: Based on a synthesis of the literature and our own experience, it appears that isotretinoin therapy for CF patients with moderate-severe acne may be an appropriate option when clinically indicated. If dermatologists monitor lab values and adverse effects carefully, patients with CF can benefit from isotretinoin therapy.

Keywords: Acne, cystic fibrosis, isotretinoin

Introduction

Cystic fibrosis (CF) affects approximately one in every 3,700 U.S. births [1] and the disease is the most common severe autosomal recessive disorder in Caucasians [2]. A mutation in the cystic fibrosis transmembranes regulator (CFTR) gene causes a defect in
electrolyte transport in exocrine epithelia, leading to viscous secretions that can obstruct the lungs, pancreas, and gastrointestinal tract [3]. Clinical features include chronic pulmonary infections and pancreatic insufficiency [2].

Advances in medicine have increased survival for patients with CF. Median survival for CF patients born after 2000 exceeds 50 years [4]. As longevity increases, care for conditions such as acne will be increasingly sought. The use of isotretinoin for acne treatment in patients with CF has been used cautiously given concern for worsening of CF-related complications. We describe two cases of patients with CF treated with isotretinoin from our clinic and provide a literature review of 11 similar cases.

Case synopsis

Patient 1 was a 24-year-old woman with CF complicated by CF-related diabetes and a history of depression who presented for acne since age 10. Previous topical treatments included tretinoin 0.05% cream and clindamycin-benzoyl peroxide 1-5% gel. Previous oral medications included tetracycline, minocycline, erythromycin, and an oral contraceptive (3 mg drospirenone/0.02 mg ethinyl estradiol). She noted that none of these treatments were satisfactory. On examination, she had severe comedonal and nodulocystic acne on her face, confluent on the jawline, as well as involvement on her back and chest. We considered spironolactone to target the hormonal aspect of this patient’s acne. The patient’s pulmonologist, however, suggested that isotretinoin would be safer. The patient was subsequently started on isotretinoin 40 mg/day (patient weight 60 kg). She reached a target dose of 153 mg/kg after seven months of therapy. The patient experienced significant improvement of her acne after treatment with isotretinoin.

Adverse effects were limited to cheilitis, xerosis of face and arms, retinoid dermatitis on her arms, and photosensitivity. All of these adverse effects were mild. Of note, the patient received clearance from her psychiatry team to start isotretinoin and she had no mood changes during treatment. Vitamin A was normal prior to starting isotretinoin and readings remained normal during and after treatment. Liver function tests (LFTs) were normal, although a mild elevation of LFTs was seen in the seventh month of therapy. This resolved the following month and was thought to be a consequence of trimethoprim-sulfamethoxazole that the patient was taking for another indication. Triglycerides were mildly elevated throughout therapy but were stable.

Patient 2 was a 16-year-old boy with well-controlled CF who presented for acne. At initial presentation he cited previous treatment with tretinoin cream. We prescribed oral minocycline and clindamycin-benzoyl peroxide 1-5% gel. All of these therapies resulted in minimal benefit. On examination, he had severe comedonal and inflammatory acne on his face, chest, and back. Given the severity of his acne, he was started on isotretinoin 20 mg/kg (patient weight 65 kg) in addition to prednisone 20 mg/day, which was tapered. The patient had improvement but developed diarrhea two months into therapy. Isotretinoin was subsequently stopped due to concern for inflammatory bowel disease (IBD). His symptoms resolved and a gastroenterology consultant ruled out IBD; therefore therapy was resumed after a four-month break in treatment. After four more months of isotretinoin therapy, the patient improved from moderate-severe acne to mild acne. He was satisfied with the results and stopped treatment after achieving 118 mg/kg of isotretinoin, short of the 150 mg/kg target that was set. He did not attribute early termination of therapy to side effects.

Similar to Patient 1, complications were mild and included cheilitis, xerosis of face and arms, retinoid dermatitis on arms, and photosensitivity. Vitamin A levels were stable, although alkaline phosphatase (ALP) was elevated for several months. The ALP elevation was attributed to the patient’s growth spurt. Triglycerides spiked one month into isotretinoin therapy but returned to within normal limits by the next month.

Patient 2 followed up for a moderate-severe cystic acne flare seven months after stopping isotretinoin. Though the patient relapsed, he returned with less severe disease than his initial presentation. The patient was encouraged to restart isotretinoin but declined.

Discussion

Isotretinoin, which is a chemically modified form of vitamin A, can provide permanent cure of acne vulgaris [5]. It is considered standard therapy in cases of severe nodulocystic acne [5]. Isotretinoin use in CF patients is controversial because of concerns that the medication may exacerbate certain complications.

Our literature review revealed 11 previous cases of patients with CF treated with isotretinoin for acne (TABLE 1) [2,6,7]. Including Patients 1 and 2, all 13 patients experienced significant improvement in their acne. The most common complications were mucocutaneous (13/13), and lab changes were often transient. However, providers may worry about hepatic, pulmonary, and ocular complications in CF patients treated with isotretinoin.
Since patients with CF may have underlying liver disease, there is concern that isotretinoin may lead to increased risk of hepatobiliary complications given that severe hepatic toxicity is a rare adverse effect of synthetic retinoids [2,8]. More commonly, isotretinoin is linked only to a mild elevation in liver enzymes, a finding observed in approximately 5-35% of patients [8]. Although vitamin A is stored in the liver, extensive storage of synthetic retinoids in the liver has not been demonstrated [8]; therefore, the mechanism of liver toxicity is not clear and may be idiosyncratic or pharmacologic [9]. In our review, only Patient 1 developed LFT elevations. This was attributed to her antibiotics and subsequently resolved. Three patients developed a transient increase in alkaline phosphatase (ALP) [2]. One patient had an elevated gamma-glutamyl transferase (GGT) and this was thought to be a consequence of his CF rather than isotretinoin [6].

Worsening pulmonary function is a theoretical concern in patients with CF on isotretinoin. Since isotretinoin can dry skin and mucous membranes, there is concern the drug may dry lung secretions [2]. If true, isotretinoin could increase the risk of pulmonary infection since mucus plugs would be fixed in the lungs [2]. This blockage could exacerbate bacterial infection, but no patients reported worsening lung function while on isotretinoin. Rather, one patient experienced improvement [7]; this patient had no lung infections requiring antibiotics during isotretinoin therapy [7].

Isotretinoin is linked to night blindness and the drug has been shown to competitively inhibit ocular retinol dehydrogenases in vitro [10]. Ocular retinol dehydrogenases carefully process vitamin A to promote vision [6]. Additionally, CF patients often suffer from pancreatic insufficiency, which would promote hypovitaminosis A [6]. Isotretinoin’s potential to inhibit ocular retinol dehydrogenases in the context of pancreatic insufficiency would raise the concern for nyctalopia in CF patients treated with the drug. However, in our literature review, we found only one patient who experienced nyctalopia, and this resolved with increased vitamin A supplementation [6].

Of note, most isotretinoin-related side effects mimic hypervitaminosis A, which is not unexpected given the drug’s chemical structure [11]. However, the exception is nyctalopia, which is secondary to relative hypovitaminosis A (TABLE 2) [11].
Table 2. Potential complications from isotretinoin therapy

<table>
<thead>
<tr>
<th>Findings mimicking hypervitaminosis A</th>
<th>Cheilitis, xerosis, epistaxis, alopecia, dry eyes, blepharitis, papilledema, arthralgia, myalgia, headache, fatigue, nausea, abdominal pain, cirrhosis, elevated labs (e.g., triglycerides, cholesterol, LFTs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Finding mimicking hypovitaminosis A</td>
<td>Nyctalopia</td>
</tr>
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</table>

Conclusion

Based on the literature and our experience, isotretinoin therapy could serve as an effective option in CF patients with moderate-severe acne. Standard monitoring for isotretinoin including baseline then monthly LFTs, fasting lipids, and vitamin A should be performed to monitor the drug’s potential to affect these measures. Pregnancy tests in females of child-bearing age are also necessary. In addition, we recommend collaboration with the patient’s pulmonologist to consider vitamin supplementation to thwart nyctalopia. In conclusion, dermatologists may want to consider isotretinoin therapy when clinically indicated for any CF patients with acne for whom they provide care.

References