

Successful Treatment of Localized Pyoderma Faciale in a Patient with Crohn's Disease

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Inflammatory bowel disease (IBD) is associated with several dermatologic manifestations, of which the most commonly cited are erythema nodosum and pyoderma gangrenosum. Pyoderma faciale (PF) is a dermatologic condition characterized by a fulminant eruption of inflammatory papules, pustules, and nodules on the face. PF is usually diagnosed in young women and is thought by some doctors to be a variant of rosacea. We present a case of a patient with longstanding inflammatory ileal Crohn's disease (CD) with complex perianal fistula who presented with the onset of PF while undergoing fistula treatment.

Case Report

A white man, age 34 years, with a history of inflammatory ileal CD with complex perianal fistula was referred to our institution for further management. He received a diagnosis of CD at age 12 years and was initially treated with sulfasalazine with good results. From age 15–32 years, he was in remission and off medical therapy. At age 32 years, abdominal pain, bloating, obstipation, and nausea developed. He was started on mesalamine and ciprofloxacin, with marked improvement in symptoms. A colonoscopy demonstrated active ileitis and a large polypoid lesion with central ulceration at the ileocecal valve. Biopsies of the polypoid lesion did not reveal dysplasia. Two years later, the abdominal pain recurred. A repeat colonoscopy demonstrated that the polypoid lesion was still present and had increased in size. Biopsies of the mass showed acute and chronic inflammation with atypical cells that were suspicious for intramural adenocarcinoma. A repeat colonoscopy at our

institution confirmed these findings and demonstrated a draining right lateral perianal fistula. The patient had no evidence of macroscopic or microscopic colitis in the distal colon. He underwent a laparoscopic right hemicolectomy and ileal resection. Pathology demonstrated a poorly differentiated mucinous adenocarcinoma. The cecum surrounding the tumor demonstrated transmural inflammation and granuloma formation.

Postoperatively, the patient was continued on oral mesalamine 2.4 g twice daily. A midline perianal abscess developed, which was treated with oral ciprofloxacin and metronidazole 500 mg twice daily. The patient was continued on metronidazole, but recurrent midline pain and swelling developed. He was presumed to have an infected pilonidal cyst because no fistulous connection could be demonstrated on 2 examinations under anesthesia (EUAs). A new lateral fistula developed, which was treated with an increase in dosage of antibiotics. The patient continued to report perianal pain, and multiple draining fistulae subsequently developed. A repeat EUA was performed with the placement of 5 setons. Infliximab (IFX; Remicade, Janssen Biotech) was given at a dose of 5 mg/kg at Weeks 0, 2, and 6 and then every 8 weeks for maintenance. The patient had a partial response to therapy. Subsequently, 1 seton became dislodged, and recurrent perianal symptoms developed. Amoxicillin/clavulanate was added to the therapeutic regimen without significant improvement. IFX was increased to 10 mg/kg every 6 weeks, and azathioprine was started at 2.5 mg/kg/day and escalated to 3 mg/kg/day without significant improvement. Subcutaneous methotrexate 25 mg weekly was initiated. The patient underwent another EUA with multiple fistulotomies. He entered complete remission and has not had recurrent perianal symptoms.

Following 6 months of IFX therapy, a cystic lesion developed on the patient's left ear that was excised by a general surgeon. Subsequently, a similar lesion developed just below the site of the initial cyst. In addition,

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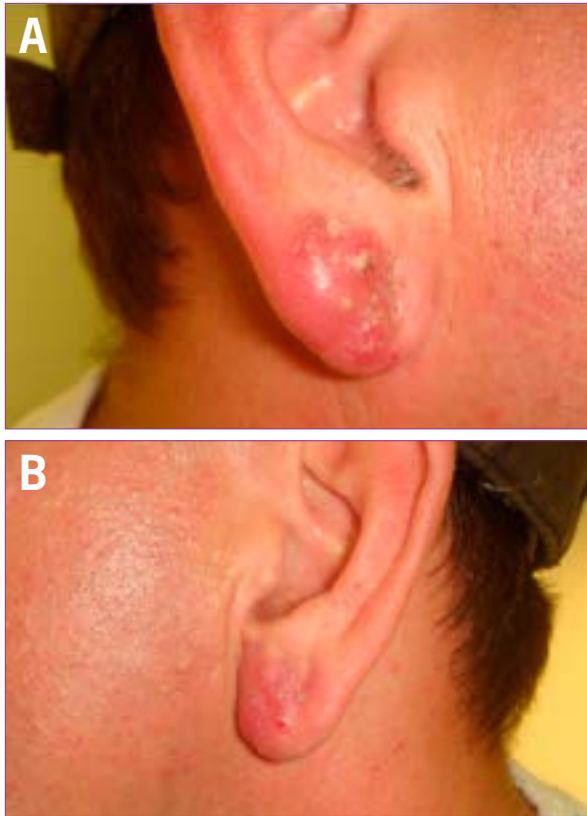


Figure. **A:** Erythematous nodules and pustules with overlying crust on the bilateral ear lobes. **B:** Resolution following oral doxycycline, topical antibiotic and corticosteroid preparations, and intralesional triamcinolone acetonide.

multiple tender erythematous nodules and pustules developed on the bilateral ear lobes (Figure A). The patient was evaluated by specialists in the Department of Dermatology due to concern about anti-tumor necrosis factor (TNF)-induced psoriasis. Localized PF limited to the ear lobes was diagnosed. A bacterial culture was obtained from 1 of the pustules and revealed normal skin flora. The patient was given oral doxycycline, topical antibiotic and corticosteroid preparations, and serial intralesional triamcinolone acetonide injections, resulting in slow but progressive improvement of dermatologic symptoms (Figure B).

Discussion

PF, also known as rosacea fulminans, is a rare dermatologic condition that is classically characterized by eruptive inflammatory papules, pustules, nodules, and cysts on the face. Its exact cause is unclear, but it is considered by some doctors to be an acute presentation of rosacea.¹ Facial edema can be associated with the lesions, and draining sinuses are frequently seen.¹ In addition,

the neck, shoulders, chest, and upper arms also can be involved, with lesions typically being asymptomatic.¹ The condition has been almost exclusively reported in women who often have a history of rosacea. The lesions have been successfully treated with a combination approach, including oral and topical corticosteroids in addition to tetracycline antibiotics. Isotretinoin has been used successfully in patients with refractory disease. However, recent studies suggest a possible association between isotretinoin use and IBD.²

PF has been infrequently reported in patients with IBD.³⁻⁶ Two case reports noted successful treatment of the PF lesions with isotretinoin despite concurrent IBD; no exacerbation of IBD was noted.^{4,5} To our knowledge, this is the fifth case of PF reported in a patient with IBD. In our case, the lesions developed while the patient was receiving antibiotic and IFX therapy for treatment of perianal CD. The patient was treated conventionally with both topical corticosteroids and tetracycline antibiotics, with good response. Our case of PF was unusual in that the lesions were limited to the ears and occurred in a male patient.

Our case highlights several key points for clinicians who treat patients with IBD. First, clinicians should be aware of common skin-related extraintestinal manifestations (EIMs), as they occur in 3–8% of patients with CD.⁷ Second, providers should be able to recognize PF because it can be confused with other skin EIMs and adverse effects of IFX therapy. For example, pyoderma gangrenosum would be considered in a patient with draining sinus tracts. Because PF can involve skin surfaces other than the face, both of these disorders would be in the differential diagnosis. Second, although unusual in IBD, Sweet syndrome, characterized by erythematous papules and plaques on the face, neck, and upper extremities, could be confused with PF.^{8,9} Sweet syndrome can be distinguished from PF by the presence of fever and neutrophilia as well as the finding of a dermal neutrophilic infiltration on biopsy. Lastly, a pustular variant of psoriasis that can involve the hands, feet, and scalp can develop in patients on anti-TNF therapy. As mentioned, psoriasiform eruptions associated with anti-TNF use are usually pustular and have a different distribution than PF, which should distinguish most cases of PF from those of psoriasiform lesions.¹⁰ PF should be suspected in young women with a history of rosacea involving the face, neck, chest, and upper arms. Prompt referral to a dermatology specialist is recommended to confirm the diagnosis. If differentiation from other skin EIMs in IBD is difficult, a skin biopsy can be performed.

The authors have no conflicts of interest to disclose.

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Review

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Extraintestinal manifestations of inflammatory bowel disease (IBD) are associated with both ulcerative colitis (UC) and Crohn's disease (CD). These manifestations most commonly involve the dermatologic and musculoskeletal systems but can affect the hepatopancreatobiliary, ocular, renal, and pulmonary systems. Some of the most common dermatologic manifestations of IBD include erythema nodosum (EN) and pyoderma gangrenosum (PG). Other lesions include psoriasis, oral aphthous stomatitis, Sweet syndrome (SS), and metastatic CD.¹ EN is a panniculitis and presents as warm, erythematous, and tender nodules or raised plaques between 1 cm and 5 cm in size usually on both lower extremities.² EN parallels disease activity in IBD. PG is a noninfectious neutrophilic dermatosis that typically starts with sterile pustules and rapidly progresses to painful ulcers.³ PG parallels IBD disease activity in approximately half of all cases, according to most reports.¹ Psoriasis has a greater prevalence in CD than UC. In addition, psoriasis may be induced or exacerbated by tumor necrosis factor inhibitors.⁴ SS, or acute febrile neutrophilic dermatosis, is a rare disorder associated with both CD and UC and is characterized by a sudden onset of painful erythematous papules, nodules, and plaques typically located on the face, neck, arms, hands, and trunk. In addition, patients have fever and neutrophilia.⁵ Metastatic CD is a rare cutaneous disorder characterized by

noncaseating, granulomatous skin lesions that present as papules, plaques, nodules, and ulcerations and involve the face, arms, legs, and genitalia.⁶ One of the most uncommon dermatologic manifestations that may be associated with both UC and CD is pyoderma faciale (PF), which has been described in very few case reports.⁷⁻⁹ However, some doctors believe that the condition may be underdiagnosed.¹⁰ For this reason, there is a need for increased awareness of this skin lesion by gastroenterologists.

The case by Razeghi and colleagues describes PF localized to the ear lobes in a man with a history of inflammatory ileal CD with complex perianal fistula.¹¹ A cystic lesion initially developed on the patient's left ear. When the lesion was excised, a similar cyst developed below the site of the first lesion along with multiple tender erythematous nodules and pustules on the bilateral ear lobes. Treatment with oral doxycycline, topical antibiotics and corticosteroids, and intralesional corticosteroid injections led to progressive improvement.

PF, also known as rosacea fulminans, is a rare cutaneous disorder that affects women in their 20s and 30s.¹² It was first described by O'Leary and Kierland in 1940.¹³ Plewig and colleagues reported 20 cases in 1992 and proposed the term rosacea fulminans.¹⁴ The disorder typically involves the face and is characterized by the sudden eruption of edema, nodules, pustules, and cystic swellings often interconnected by sinuses. The condition has been noted in patients with a prior history of acne rosacea and distinguishes itself from acne vulgaris by the absence of comedones, sudden onset, and a fulminating course, although patients with PF may have acne vulgaris at the same time. In 2 case reports, PF was described as being accompanied by EN.^{15,16} The pathogenesis of PF is poorly understood but believed to be immune-mediated, with the inflammatory cell infiltrate sharing some characteristics of hypersensitivity reactions.¹⁷

The diagnosis of PF is often made based on clinical findings, but early diagnosis may be aided by biopsy.¹⁸

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Biopsy often shows evidence of marked inflammation with lymphocytes, leukocytes, histiocytes, and perifollicular and perisebaceous gland abscesses. Mild anemia, leukocytosis, or an elevated erythrocyte sedimentation rate may also be found in these patients.¹⁹ Cultures from the lesions are generally negative. Treatment of PF consists of topical and oral corticosteroids, often in combination with isotretinoin.²⁰ It has been suggested that treatment should start with potent topical corticosteroids for no more than 2 weeks, oral prednisolone at 1.0 mg/kg daily for 1–2 weeks followed by a slow taper, and oral isotretinoin at 0.2–0.5 mg/kg daily for 3–4 months until complete epithelialization occurs.¹⁴ Dapsone has been described as effective in some case reports.^{16,19,21} The case presented by Razeghi and colleagues was clinically diagnosed as PF.¹¹ However, in the absence of a tissue diagnosis, PG, which presents as erythematous pustules or nodules, also should be considered. As PG progresses, it develops into burrowing ulcers with irregular, violaceous edges.²²

Razeghi and colleagues note that recent studies have suggested a possible association between isotretinoin and IBD.¹¹ The link between isotretinoin and IBD remains unclear. More recently, a population-based nested case-control study showed no association.²³ Another case-control study showed that UC (odds ratio [OR], 4.36; 95% confidence interval [CI], 1.97–9.66), but not CD (OR, 0.68; 95% CI, 0.28–1.68), was strongly associated with previous isotretinoin exposure.²⁴ In a large retrospective population-based cohort study in British Columbia, Canada, patients who were newly treated with isotretinoin or topical acne medications were studied.²⁵ In this study, almost 50,000 patients were compared with more than 1.5 million untreated persons. No association between IBD and isotretinoin use was found (rate ratio, 1.14; 95% CI, 0.92–1.41). In the same study, the authors found that patients with IBD who were treated with isotretinoin did not have increased hospital admission rates when compared with patients who were not on isotretinoin treatment. Given that the risk for development of IBD with isotretinoin use is doubtful and that patients with IBD who take isotretinoin are not at increased risk for being hospitalized, according to this study²⁵ isotretinoin should be used in patients with IBD and PF if other therapies have failed. Razeghi and colleagues reported that their patient had progressive response to oral doxycycline, topical antibiotics and corticosteroids, and intralesional corticosteroid injections and were, therefore, justified in not using isotretinoin.¹¹

The case described by Razeghi and colleagues is interesting in that PF, a female-predominant disease, occurred in a male patient.¹¹ Furthermore, PF is typically described as involving the face, but in the case report, the lesions

were restricted to the ears. It has been suggested that PF is more common than is actually reported, with the theory that more severe cases have been described in case reports.¹⁰ With increased awareness about PF, the lesion will likely be diagnosed more frequently, resulting in more appropriate treatment of PF in patients with IBD.

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