Bowel-associated dermatosis-arthritis syndrome (BADAS) in a patient with cystic fibrosis

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INTRODUCTION

Bowel-associated dermatosis-arthritis syndrome (BADAS) is an uncommon neutrophilic dermatosis characterized by arthralgias, fever, myalgias, and malaise as well as cutaneous eruptions on the extremities and trunk. The characteristic skin lesions are erythematous macules that evolve into purpuric papules, papulopustules, or tender subcutaneous nodules within a few days.[1] First described as a consequence of bowel bypass surgery, BADAS has also been associated with diverticulitis, inflammatory bowel disease (IBD), and peptic ulcers.[1] The pathophysiology of BADAS is thought to involve immune complex formation and deposition in response to antigens from intestinal bacterial overgrowth. We present the first reported case of BADAS in a patient with cystic fibrosis (CF).

Abbreviations used:

BADAS:	bowel-associated dermatosis-arthritis syndrome
CF:	cystic fibrosis
CFTR:	cystic fibrosis transmembrane regulator
GI:	gastrointestinal
IBD:	inflammatory bowel disease
SIBO:	small intestine bacterial overgrowth

CASE REPORT

A 47-year-old woman was admitted with diffuse joint pain, fever, night sweats, and a papulopustular eruption involving the arms, upper back, and thighs (Fig 1). Her medical history was significant for culture-negative endocarditis, periodic loose stools, *Clostridium difficile* colitis, and CF (ΔF508 mutation). Laboratory results on admission showed an elevated white blood cell count (23,300/μL), a normal platelet count (426,000/μL), an elevated erythrocyte sedimentation rate (25 mm/h), a mildly elevated C-reactive protein (5.3 mg/L), and a nonelevated rheumatoid factor (11 IU/mL). Transthoracic echocardiography ruled out endocarditis. Blood cultures were negative, but she was treated with empiric antibiotics (vancomycin, ceftolozane-tazobactam and oxacillin).

Dermatology was consulted on the second day of hospitalization when the papulopustular eruption had spread distally to involve the lower legs. A pustule was cultured and three skin biopsy sections were obtained for histology, direct immunofluorescence, and tissue culture. Bacterial culture from the pustule was negative. Tissue culture and direct immunofluorescence (IgG, IgA, IgM, C3, fibrinogen) were also negative. Histology revealed Sweet syndrome-like neutrophilic dermatosis in the dermis (Fig 2, *A* and *B*). Leukocytoclastic vasculitis was present (Fig 2, *C*). Dermal infiltrates were composed of mixed neutrophils, lymphocytes, histiocytes, and few eosinophils (Fig 2). The patient's clinical presentation and histologic findings were consistent with BADAS. Within a few days of treatment with

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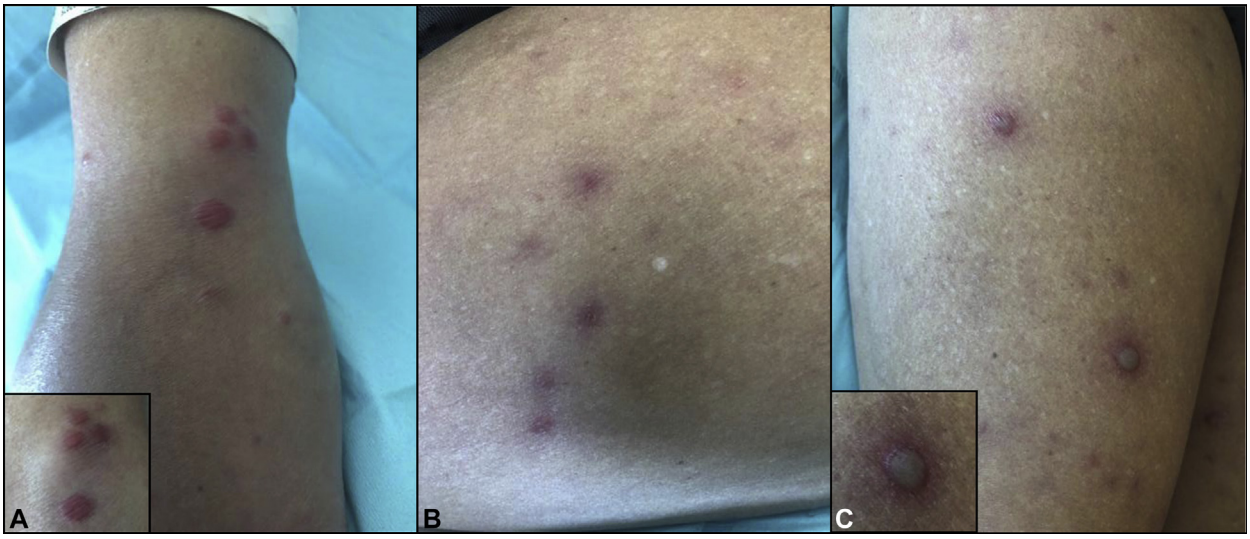

Fig 1. BADAS lesions presented as diffuse papulopustular eruption of the (**A**) arms, (**B**) upper back, and (**C**) thighs in a patient with CF.

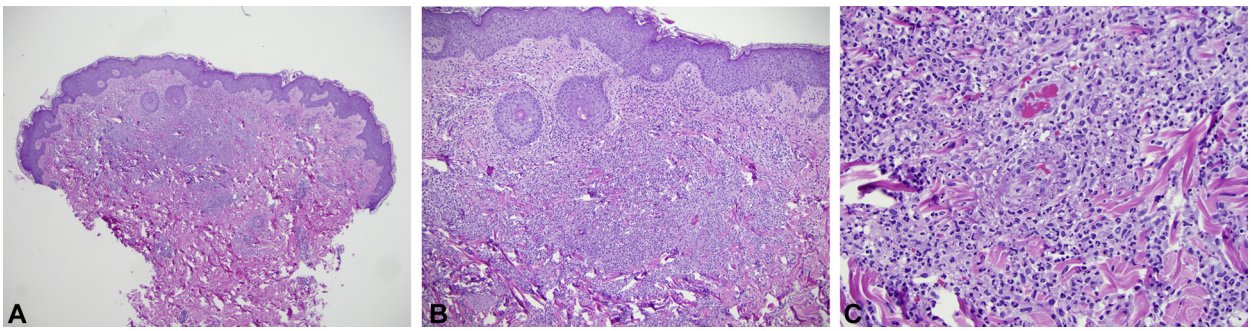

Fig 2. BADAS lesion characterized by neutrophilic dermatosis with mixed dermal infiltrates composed of neutrophils, lymphocytes, histiocytes, and few eosinophils. Overt leukocytoclastic vasculitis is present. (Hematoxylin-eosin stain; original magnifications: **A**, ×2; **B**, ×40, **C**, ×200.)

oxacillin (2 g/d) and ceftolozane-tazobactam (4.5 g/d), the patient's arthralgias and skin lesions improved dramatically. The oxacillin and ceftolozane-tazobactam were continued for an additional 2 weeks after discharge from the hospital.

DISCUSSION

BADAS presents episodically with a prodrome of influenza-like symptoms followed by the development of skin lesions. The cutaneous manifestations initially appear as asymptomatic, painful, or pruritic erythematous macules on the upper extremities and trunk. Within a few days, these lesions transform into purpuric papules or papulopustules, which may persist for up to 4 weeks.[1,2] Complications include diarrhea, liver dysfunction, calcium oxalate renal calculi, hyperuricemia, mood changes, tenosynovitis, and vitamin A or B1 deficiency.[1] In cases related to gastrointestinal (GI) surgery, symptoms may first appear 3 months to 5 years after the procedure.[3] Histologically, BADAS shows superficial dermal edema and neutrophilic perivascular invasion with leukocytoclasia.[1,2,4] Vasculitis is often present in neutrophilic dermatoses, occurring secondary to proteases or other noxious substances released from neutrophils, not as a primary immune-mediated phenomena.[5] All of these histologic features were observed in our patient's skin lesions.

In 1979 Dicken and Seehafer[6] first proposed BADAS, formally known as bowel bypass syndrome, to describe 2 patients who underwent end-to-side jejunocolic bypass or ileal bypass surgery.[6,7] The association of BADAS with bypass procedures has since expanded to include other intestinal or bariatric procedures and IBD.[2] The unifying feature in these conditions appears to be intestinal bacterial

overgrowth (eg, through the creation of blind loops of intestine). Intestinal bacterial overgrowth and the subsequent increases in bacterial antigens (eg, bacterial peptidoglycans) are hypothesized to induce an immune response that results in the formation of immune-antigen complexes. These immune-antigen complexes deposit in the skin and joints resulting in the cutaneous and arthritic manifestations of BADAS.[8]

CF is an autosomal recessive disorder involving the CF transmembrane regulator (CFTR) gene. The *CFTR* gene encodes the CF transmembrane chloride channel, which is widely expressed in the skin, lungs, and GI tract. A high prevalence of small intestinal bacterial overgrowth (SIBO) has been described in patients with CF.[9,10] The clinical presentation in this case report (eg, history of periodic loose stools and CF) could be explained by SIBO. The most common risk factors for the development of SIBO are decreased gastric acid production and reductions in intestinal motility; patients with CF are predisposed to both of these risk factors.[11] For example, patients with CF are more susceptible to gastroesophageal reflux and are frequently prescribed protein pump inhibitors to reduce gastric acid production. Moreover, CFTR receptor dysfunction in the GI tract results in thickened and acidified intestinal secretions.[9] Thickened intestinal secretions reduce intestinal motility and predispose these patients to intestinal obstruction.[9] Overall, these patients are more susceptible to SIBO; however, to our knowledge, BADAS in a patient with CF has not been reported.

In this case report, we recount a patient with CF presenting with arthralgias, fever, night sweats, loose stools, and a papulopustular eruption involving the upper back and proximal extremities. The clinical signs and symptoms as well as the histopathology were consistent with BADAS, presumably caused by SIBO. Alternate etiologies of BADAS, such as GI surgery and IBD, were not present in this case. Until now, the relationship between BADAS and CF was not reported. The incidence of BADAS among patients with CF should be explored further to determine the extent of this relationship. Highlighting the association between these entities will help practitioners recognize BADAS earlier and avoid unnecessary diagnostic testing and treatments. Moreover, a better understanding of the features that predispose individuals to BADAS may aid in the prevention and treatment of this condition.

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