

# A case of bowel-associated dermatosis-arthritis syndrome treated with ustekinumab: The importance of targeting underlying gastrointestinal disease



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**Key words:** bowel-associated dermatosis-arthritis syndrome; Crohn's disease; inflammatory bowel disease; neutrophilic dermatoses; ulcerative colitis; ustekinumab.

## INTRODUCTION

Bowel-associated dermatosis-arthritis syndrome (BADAS) is a condition in the family of neutrophilic dermatoses. It presents with constitutional symptoms including fever, arthritis, arthralgia, and myalgia preceding an inflammatory skin eruption.<sup>1</sup> Originally thought to be associated with bowel bypass surgery, Jorizzo et al<sup>2</sup> in 1983 described an identical array of symptoms in patients who had not undergone a bowel bypass but had other gastrointestinal diseases. Thus, bowel bypass syndrome was renamed BADAS. We present a patient with BADAS secondary to Crohn's proctitis who had complete resolution of cutaneous lesions and improvement of gastrointestinal symptoms with ustekinumab.

## CASE REPORT

A 49-year-old woman was admitted with fever, diarrhea, rectal bleeding, dehydration, multiple syncopal episodes, arthralgia, and several lesions on the skin and oral mucosa. Her medical history was significant for Crohn's proctitis previously treated with mesalamine, reflux, mitral valve prolapse, stroke, anxiety and depression.

Physical examination found several erythematous vesiculopustules and erosions on both axillae, thighs, and the trunk as well as the oral mucosa (Figs 1-3). The lesions were painful and had been coming and going for months before admission.

### Abbreviations used:

BADAS: bowel-associated dermatosis-arthritis syndrome  
 IBD: inflammatory bowel disease

On admission, her temperature was 38.4°C. Hemoglobin and albumin levels were low in the setting of an otherwise unremarkable complete blood count and comprehensive metabolic panel. Blood cultures were negative, and cultures of the pustules grew only coagulase-negative *Staphylococcus*. A colonoscopy was performed that found severe ulcerations in both the rectum and sigmoid colon.

Papillary edema and a dense neutrophilic infiltrate consistent with a sterile neutrophilic dermatosis were seen on punch biopsy of a lesion on the right axilla (Fig 4). The diagnosis of BADAS in the setting of Crohn's proctitis was made based on clinicopathologic correlation.

The patient received empiric piperacillin-tazobactam in the hospital. She was started on a ustekinumab loading dose, 260 mg intravenous, in the hospital and was discharged on a maintenance dose of 90 mg subcutaneously every 8 weeks. The patient had significant improvement of skin and oral lesions at 2-week follow-up and complete resolution at 3-month follow-up as well as improvement in gastrointestinal symptoms.

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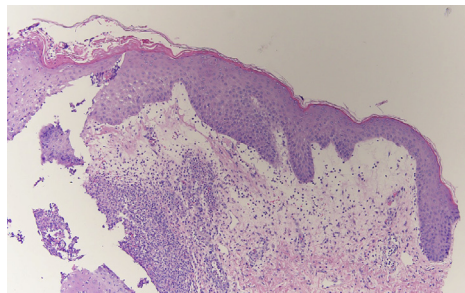
**Fig 1.** BADAS. Vesiculopustules and erosions on lower back and buttocks.



**Fig 3.** BADAS. Aphthae on the oral mucosa.



**Fig 2.** BADAS. Eroded vesiculopustule on the right axilla that was biopsied.



**Fig 4.** BADAS. Histologic findings of papillary edema and dense neutrophilic infiltrate.

## DISCUSSION

Neutrophilic dermatoses are a heterogeneous group of skin disorders classified by a sterile, predominantly neutrophilic dermal infiltrate.<sup>1</sup> Although they can appear similar histologically, the clinical features of the cutaneous lesions and associated symptoms allow clinicians to distinguish between them. Inflammatory bowel disease can be associated with several neutrophilic dermatoses including BADAS.

BADAS presents with skin lesions, nondeforming arthralgia, and fever in patients with surgical or

medical gastrointestinal disease. The cutaneous lesions commonly begin as erythematous macules and papules that become vesiculopustular. On histology there is papillary dermal edema and a dense, often perivascular, neutrophilic infiltrate; leukocytoclasia can also be seen, but primary vasculitis and fibrinoid necrosis are absent.<sup>2</sup> The mechanism is thought to involve immune complexes related to bacterial overgrowth in the bowel that enter the circulation and deposit in the skin and synovium. Immune complexes also play a role in inflammatory bowel disease (IBD).<sup>3</sup>

Treatment for BADAS is focused on reducing neutrophilic inflammation, reducing bacterial overgrowth, and treating the underlying gastrointestinal condition. Jorizzo et al<sup>4</sup> in 1988 postulated that a reduction in bowel flora overgrowth and circulating immune complexes explains the clinical benefit of these therapies in BADAS, leading to resolution of both gastrointestinal and skin disease. Additionally, Letsinger et al<sup>5</sup> noted that in IBD, oral aphthae may

“antedate, coexist with, and/or reflect the activity of bowel inflammation” and these lesions typically respond to treatment of the bowel disease. These aphthae can classically present as solitary or multiple recurring lesions in the setting of Crohn’s disease.<sup>4,5</sup> Thus, therapy should focus on underlying gastrointestinal disease as the cause of cutaneous eruptions. A combination of appropriate wound care with local and systemic therapies appear to be adequate treatment.<sup>1</sup> Systemic corticosteroids, steroid-sparing immunosuppressants such as cyclosporine and tumor necrosis factor- $\alpha$  inhibitors, and antibiotics such as tetracycline have all been used.<sup>6</sup>

To our knowledge, ustekinumab for BADAS has not been reported in the literature, but it has been used for other neutrophilic dermatoses. Guenova et al<sup>7</sup> described the overexpression of interleukin 23 in affected skin in several cases of pyoderma gangrenosum that were subsequently treated with ustekinumab, an interleukin 12 and interleukin 23 antagonist. A multicenter retrospective study performed in France assessed use of ustekinumab as a treatment for neutrophilic dermatoses—most commonly pyoderma gangrenosum—associated with Crohn’s disease. A complete remission of Crohn’s disease and neutrophilic dermatosis was seen in 4 of 7 patients.<sup>8</sup> Additionally, ustekinumab can be an effective treatment for IBD, adding to its benefit in treating BADAS associated with IBD.<sup>9,10</sup>

This case and the trials presented suggest cutaneous manifestations of IBD may resolve by targeting the gastrointestinal disease. Ustekinumab

appears to be an efficacious treatment for multiple inflammatory conditions involving the gastrointestinal tract and skin.

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