Atypical Behçet disease with endocarditis, pyoderma gangrenosum–like ulcers and methicillin-resistant Staphylococcus aureus–positive skin abscesses

Isabelle M. Sanchez, MPH, and Kanade Shinkai, MD, PhD
San Francisco, California

Key words: Behçet disease; cardiac manifestations; endocarditis; methicillin-resistant Staphylococcus aureus–positive abscesses; pyoderma gangrenosum–like ulcers.

INTRODUCTION
Behçet disease (BD) is a neutrophilic dermatosis characterized by relapsing flares of orogenital aphthous ulcers, uveitis, and skin inflammation.1-3 Extracutaneous manifestations involve gastrointestinal, neurologic, pulmonary, and cardiac systems.1 The spectrum of skin manifestations includes erythema nodosum, papulopustular lesions, and pathergy. Skin abscesses, leukocytoclastic vasculitis, bullae, or lesions mimicking Sweet syndrome or pyoderma gangrenosum (PG) are rare.1-3 We describe a patient with atypical BD with endocarditis, PG-like ulcerations, and methicillin-resistant Staphylococcus aureus (MRSA)-positive abscesses, highlighting a unique constellation of infection and immune dysregulation.

CASE REPORT
A 33-year-old man with BD presented with a several-week history of persistent fever, abscesses, and oral and skin ulcers despite escalating his dapsone dose to 100 mg and prednisone dose to 100 mg daily. He was a marijuana farmer with exposure to animals and denied trauma and intravenous drug use. He had discontinued heavy alcohol use 6 weeks before presentation. His prior Behçet flares included fever, orogenital ulcers, and symmetric papulopustular eruptions on his extremities.

Physical examination found an ill-appearing, febrile male with a 3/6 systolic murmur at the lower left sternal border. An extensive hemorrhagic ulcer with undermined violaceous borders and serosanguinous exudate was noted on the right dorsal thumb (Fig 1). Scattered 3- to 4-cm abscesses with surrounding erythema and warmth were present on the abdomen (Fig 2) and left anterolateral leg (Fig 3). Cellulitic plaques were present on the right elbow and dorsal right foot. Multiple 1-cm hyperpigmented macules were observed at the extensor forearms bilaterally, which the patient stated reflected a recent flare more typical of his BD skin disease (Fig 4). There were no signs of uveitis or neurologic deficits.

Diagnostic evaluation found a white blood cell count of 19,000/µL, erythrocyte sedimentation rate of 3 mm/h, C-reactive protein level of 24 µg/mL, and methemoglobinemia of 12% (normal, 0-1.5%). Toxicology screening was positive for opiates and tetrahydrocannabinol. Additional laboratory test results were normal.

The patient was admitted to the surgical service for suspicion of infection or Behçet flare, was treated with vancomycin and ertapenem, and underwent
debridement and incision and drainage. Skin biopsy findings showed a dense neutrophilic dermal infiltrate, edema, and ulceration. Fite and Periodic acid–Schiff diastase stains were negative. Positive Brown-Brenn staining (identifies gram-positive and gram-negative bacteria within tissue) and cultures taken from multiple skin lesions confirmed MRSA. Three blood cultures and a nasal culture, taken after the initiation of antibiotics, were negative.

Transthoracic echocardiogram found a mitral valve vegetation.

After emergent treatment with methylene blue for his methemoglobinemia, the patient was treated with prednisone 1 mg/kg, dapsone 50 mg, and colchicine 1.2 mg, with rapid improvement of his skin lesions, and completed 1 month of vancomycin treatment for his skin lesions and possible infectious endocarditis (IE) without complications.

**DISCUSSION**

The pathophysiology of BD is a complex relationship of genetics, immune dysregulation, and a possible important role for infection. Infectious triggers are suspected to act as auto-antigens in genetically predisposed (HLA-B51+) persons with BD. Herpes simplex virus-1, *Streptococcus*, and oral flora are associated with neutrophilic ulcers and multiorgan disease. Importantly, inflammatory manifestations of BD can also mimic infection, making the diagnosis and definitive treatment challenging. This case illustrates a unique discordance between cultures, transthoracic echocardiogram, and skin findings; his multiple MRSA-positive skin lesions and mitral valve vegetation suggested systemic infection, although negative blood cultures and clinical improvement with corticosteroids supported an equally plausible role for inflammation leading to his presentation.

Typical mucocutaneous presentations of BD occur in 38% to 99% of patients, including orogenital

---

**Fig 1.** Atypical PG-like ulcer at the dorsal aspect of the right proximal first digit. Clinical examination found an extensive hemorrhagic ulcer with undermined violaceous borders and serosanguinous exudate.

**Fig 2.** MRSA-positive abscess with surrounding cellulitic plaque at the right lower abdominal quadrant.

**Fig 3.** MRSA-positive abscess with surrounding cellulitic plaque at the left anterolateral leg.

**Fig 4.** Hyperpigmented postinflammatory macular eruption on the extensor forearms bilaterally after a recent typical Behçet disease flare of papulopustules.
aphthous ulcers, erythema nodosum, and papulopustular lesions resembling folliculitis. Atypical skin presentations, including abscesses and lesions resembling PG, Sweet syndrome, or necrotizing fasciitis, are rare. Infectious mucocutaneous lesions have also been described, including a BD patient with MRSA-positive gingivae and a second case with methicillin-sensitive *S aureus*-positive necrotizing fasciitis. Our patient presented with MRSA-positive lesions resembling abscesses, PG, and cellulitis. MRSA-positive skin lesions have not been previously reported in BD.

This patient had a mitral valve vegetation with negative blood cultures in the setting of systemic antibiotic treatment, raising the question of whether he had infectious versus inflammatory endocarditis. Aseptic cardiac involvement occurs in 6% to 46% of BD patients; endocardial biopsy shows neutrophilic infiltration. The prognosis of cardiac BD is poor, associated with 15.4% compared with 5.4% BD-related deaths without cardiac involvement. The prevalence of culture-negative endocarditis in BD patients with cardiac lesions is 26.9%. Culture-negative endocarditis in BD may be a result of antibiotics, a result of infection with intracellular organisms difficult to culture, or reflect sterile inflammation. The latter is supported by reports of improvement with corticosteroid treatment alone. Importantly, blood cultures for IE are often negative, with a sensitivity and specificity of 61% and 52%, respectively. Although the literature suggests that valve vegetation in BD is more strongly associated with BD cardiac involvement than with IE, an infectious etiology of a cardiac lesion must be actively excluded.

BD is a clinical diagnosis, classified by an International Criteria for BD score of $\geq 4$; our patient had a calculated score of $5$. This patient’s unique presentation of MRSA-positive skin lesions was distinct from his typical BD acral papulopustules. His cardiac murmur, negative nasal cultures, and MRSA-positive skin cultures from multiple scattered skin lesions prompted a diagnostic evaluation for IE. The role of MRSA in our case is unclear; his presentation may reflect sequelae of IE, an atypical manifestation of his BD with skin and cardiac involvement, or a combination of conditions. We hypothesize that his presentation reflected an interplay of MRSA endocarditis as an infectious trigger in a patient with known immune dysregulation, resulting in his unique systemic and cutaneous presentation. An equally plausible alternative hypothesis is that this patient had sterile endocarditis with multifocal MRSA-positive skin lesions that are rarely seen in BD.

Given the complex interplay of infection, genetics, and immune dysregulation in patients with BD, atypical presentations may pose a diagnostic challenge and may warrant additional evaluation for complicating factors. Currently, to our knowledge, there are no documented cases of severe BD with this unique constellation of concurrent clinical features. Diagnostic evaluation to distinguish infectious versus inflammatory signs, especially in an immunosuppressed patient with BD, is paramount.

REFERENCES
1. Alpsoy E. Behcet’s disease: A comprehensive review with a focus on epidemiology, etiology and clinical features, and management of mucocutaneous lesions. *J Dermatol*. 2016; 43(6):620-632.
2. Demirelli S, Degirmenci H, Inci S, Arisoy A. Cardiac manifestations in Behcet’s disease. *Intractable Rare Dis Res*. 2015;4(2):70-75.
3. Geri G, Wechsler B, Thi Huong du L, et al. Spectrum of cardiac lesions in Behcet disease: a series of 52 patients and review of the literature. *Medicine*. 2012;91(1):25-34.
4. Suga Y, Tsuboi R, Kobayashi S, Ogawa H. A case of Behcet’s disease aggravated by gingival infection with methicillin-resistant *Staphylococcus aureus*. *Br J Dermatol*. 1995;133(2):319-321.
5. Chams-Davatchi C, Shizarpour M, Davatchi F, et al. Extensive pyoderma gangrenosum-like lesion in two cases of Behcet’s disease, responding only to cyclosporin. *Adv Exp Med Biol*. 2003;528:337-338.
6. Joshi A, Mamt. Behcet’s syndrome with pyoderma-gangrenosum-like lesions treated successfully with dapsone monotherapy. *J Dermatol*. 2004;31(10):806-810.
7. Ng F, Chiong FJ, Buchanan R, Burrell LM. A rare case of Behcet disease with generalised myositis, cardiomyositis and necrotising fasciitis. *BMJ Case Rep*. 2016. https://doi.org/10.1136/bcr-2015-219823.
8. Kang HM, Kim GB, Jang WS, et al. An adolescent with aortic regurgitation caused by Behcet’s disease mimicking endocarditis. *Ann Thorac Surg*. 2013;95(6):e147-e149.
9. Shiran A, Zisman D, Karkabi B, et al. Behcet’s aortitis mimicking aortic valve endocarditis with subaortic complications. *J Am Soc Echocardiography*. 2006;19(5):578.e1-4.
10. Brandao TJ, Januario-da-Silva CA, Correia MG, et al. Histopathology of valves in infective endocarditis, diagnostic criteria and treatment considerations. *Infection*. 2017;45(2):199-207.