

# Progressive rash as the first sign of *Listeria* meningitis and bacteremia



Alli J. Blumstein, BS, Anjani Pranav Sheth, BA, Alyce J. Anderson, MD, PhD, and Ahmad Amin, MD  
Chicago, Illinois

**Key words:** anti-TNF therapy; infliximab; *Listeria* meningitis; methotrexate; psoriasis.

## INTRODUCTION

*Listeria monocytogenes* is an intracellular, gram-positive bacillus that is most commonly transmitted through foods, including unpasteurized milk products, deli meats, and soft cheeses. The majority of immunocompetent individuals are able to avoid serious infection. However, those with impaired T-cell immunity, including the elderly, pregnant women, neonates, and patients on immunosuppressive medications, are at risk for invasive *Listeria* infections, including sepsis and meningitis.<sup>1</sup>

In the initial placebo-controlled trials of anti-tumor necrosis factor (anti-TNF) therapy, an increased risk of listeriosis was not identified.<sup>2</sup> However, since its more widespread use, there have been limited reports of listeriosis occurring in patients treated with immunosuppressive agents, including anti-TNF agents—especially when used in conjunction with other disease-modifying antirheumatic drugs.<sup>3</sup> Listeriosis typically presents with altered mental status and is rarely identified through cutaneous manifestations of the infection.<sup>4</sup> Here, we present a case of a 55-year-old man on infliximab and methotrexate who presented with a maroon-colored rash on his trunk and upper extremities prior to experiencing altered mental status in the setting of *Listeria* meningitis and bacteremia.

## CASE DESCRIPTION

A 55-year-old man with a past medical history significant for pustular psoriasis and ulcerative colitis presented to the emergency department with altered mental status, fever, and headache. He reported subjective fevers and rash 5 days prior to presentation. The rash initially appeared after a period of prolonged sun exposure, as a patchy,

### Abbreviation used:

TNF: tumor necrosis factor

erythematous-to-violaceous exanthem on his flanks, lower portion of the abdomen, and buttocks and the volar surface of his both arms (Fig 1). The patient described the rash as sensitive to the touch, but it was not painful or pruritic. There was no mucous membrane involvement and no bullae or vesicles.

The patient had trialed a number of systemic medications, including ustekinumab, etanercept, cyclosporine, and secukinumab, for his pustular psoriasis. While on secukinumab, he had been diagnosed with ulcerative colitis, which was minimally responsive to oral steroids. His gastroenterology and dermatology providers agreed to start infliximab in combination with methotrexate for durability of response, which ultimately led to the remission of his ulcerative colitis and moderate control of his pustular psoriasis. Prior to his presentation to the emergency department, the patient's psoriasis and ulcerative colitis were relatively well controlled on 700 mg infliximab every 6 weeks (8.64 mg/kg) and 20 mg methotrexate weekly, although he occasionally experienced psoriasis flares the week before infliximab infusions.

The patient attributed his subjective fevers at the time of presentation to a pustular psoriasis flare, as he had previously experienced low-grade fevers and vigorous chills in the setting of psoriasis exacerbation. He initiated 0.1% triamcinolone ointment to the affected areas twice daily and ibuprofen for fever. Over the next 5 days, the rash intensified in color and

From the Department of Dermatology, Northwestern University Feinberg School of Medicine, Chicago.

Funding sources: None.

IRB approval status: Not applicable.

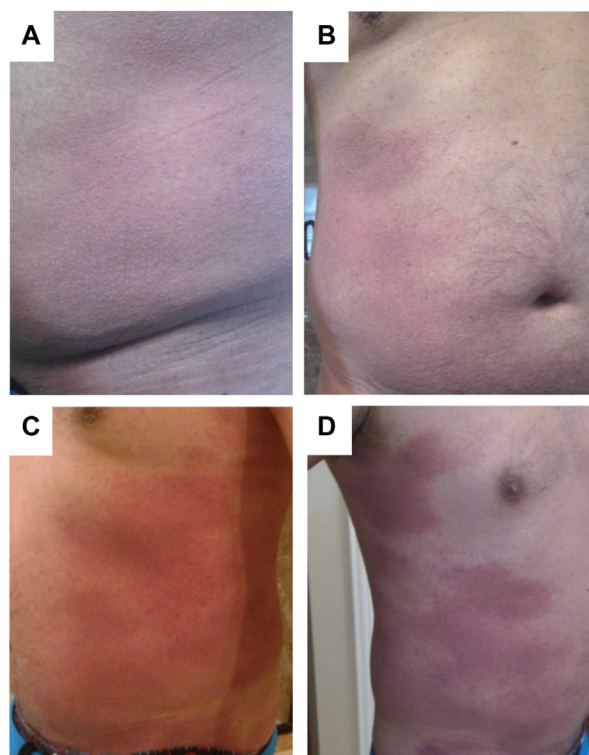
Correspondence to: Alyce J. Anderson, MD, PhD, Department of Dermatology, Northwestern University Feinberg School of Medicine, 676 N St. Clair Street, Suite 1600, Chicago, IL 60611. E-mail: [alyce.anderson@northwestern.edu](mailto:alyce.anderson@northwestern.edu).

JAAD Case Reports 2022;28:130-2.

2352-5126

© 2022 by the American Academy of Dermatology, Inc. Published by Elsevier, Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

<https://doi.org/10.1016/j.jidcr.2022.03.021>



**Fig 1.** Patient-submitted photos of evolving rash. **A**, Day 2, lateral aspect of the right side of the flank. **B**, Day 3, right side of the abdomen. **C**, Lateral aspect of the left side of the thoracic chest. **D**, Lateral aspect of the right side of the thoracic chest and axilla. The rash involving both the flanks consisted of pinpoint, skin-colored-to-erythematous papules on a background of ill-defined, red-to-lilac erythematous patches and thin, coalescing plaques.

spread over his torso, and the fever and chills persisted. On day 5, the patient's wife noticed he was difficult to arouse, prompting emergency care. In the emergency department, he was febrile (101.7 °F), his blood pressure was 124/69 mmHg, and he had a respiratory rate of 20 breaths per minute. A physical examination in the emergency room revealed "a reddish, ruddled colored diffuse macular rash with overlying desquamation on the anterior and posterior torso and proximal thighs with papules at the edges of the rash." A complete blood cell count, comprehensive metabolic panel, C-reactive protein, erythrocyte sedimentation rate, and procalcitonin were obtained in addition to blood cultures and a lumbar puncture. The laboratory tests were within normal limits except for procalcitonin (elevated to 1.3 ng/mL; reference range  $\leq 0.5$  ng/mL) and erythrocyte sedimentation rate (elevated to 41 mm/hr; reference range 0-20 mm/hr). His cerebral spinal fluid was notable for low glucose (17 mg/dL; reference range 40-70 mg/dL), high protein

(258 mg/dL; reference range 15-45 mg/dL), and white blood cell count of 662/ $\mu$ L, consistent with *L. monocytogenes* meningitis. The blood cultures were also positive for *L. monocytogenes*. The patient's last infliximab infusion had occurred 12 days (<2 weeks) prior to his hospitalization, and the methotrexate was held while he was in the hospital. The patient was treated with intravenous ampicillin (10 g  $\times$  4 weeks) and gentamycin (475 mg  $\times$  12 days). On day 2 of his hospitalization, the patient returned to baseline mental status. He disclosed the consumption of deli meats in the week preceding the onset of his rash.

While hospitalized, the patient experienced a severe flare of his pustular psoriasis, resulting in significant discomfort. Through shared decision making, an earlier, unscheduled infliximab infusion was discussed with the patient and care team. An immediate rescue dose was initially deferred until the patient stabilized. After several doses of antibiotics and no signs of clinical infection, the decision was made to continue infliximab at a 5-week, rather than 6-week, interval.

## DISCUSSION

This case represents a unique dermatologic presentation of *Listeria* meningitis and bacteremia. Though rare, the development of *Listeria* meningitis in a patient on infliximab has been reported. Among the various anti-TNF agents, infliximab has been most commonly associated with *Listeria* infections, especially when administered with concomitant immunosuppressive therapy.<sup>5</sup> As in our patient, combination immunosuppressive therapy is often used in patients with psoriasis and inflammatory bowel disease to improve efficacy and to reduce of the development of antidrug antibodies.<sup>6</sup> A *Listeria* infection can be acquired by consuming contaminated soft cheeses and deli meats.<sup>1</sup> Thus, our patient's consumption of deli meats prior to presentation was the presumed source of the infection. Infection with *L. monocytogenes* often presents as sepsis and meningitis; cholecystitis and arthritis have also been reported.<sup>7</sup> Thus, to our knowledge, this is the first report of a rash as the presenting symptom of *Listeria* meningitis in a patient on anti-TNF and methotrexate. The findings in this case suggest that a nonpsoriasiform rash in a patient on anti-TNF therapy should raise suspicion for an atypical infection.

Additionally, while data from the Food and Drug Administration's Adverse Events Reporting System suggest that most previous infliximab-related *Listeria* infections occurred within receiving 2.5 doses of medication (with only 2 instances reported

after receiving 6 or more doses), our patient presented with *Listeria* meningitis and bacteremia after 30 infliximab infusions.<sup>3</sup> The awareness of this distinct clinical manifestation and time course of *Listeria* infection is important to ensure that providers encountering new rashes in patients on anti-TNF therapy include *Listeria* infection in their differential diagnoses. This is especially prudent when patients are on infliximab for dermatologic conditions, as differentiating a new rash from the primary process is difficult and can delay diagnosis and treatment. While *Listeria* infection is a rare complication of anti-TNF therapy, it has a high mortality rate, with one study reporting death in up to 26% of patients.<sup>8</sup> Therefore, the early consideration of listeriosis is essential to achieving a timely diagnosis and reduced morbidity and mortality.

#### Conflicts of interest

Dr Amin has served as a consultant and speaker for AbbVie, Eli Lilly, Janssen, Regeneron, Sanofi, UCB, Amgen, and Novartis. Authors Blumstein and Sheth and Dr Anderson have no conflicts of interest to declare.

#### REFERENCES

1. Farber JM, Peterkin PI. *Listeria monocytogenes*, a food-borne pathogen. *Microbiol Rev*. 1991;55(3):476-511. <https://doi.org/10.1128/mr.55.3.476-511.1991>
2. Bodro M, Paterson DL. Listeriosis in patients receiving biologic therapies. *Eur J Clin Microbiol Infect Dis*. 2013;32(9):1225-1230. <https://doi.org/10.1007/s10096-013-1873-1>
3. Slifman NR, Gershon SK, Lee JH, Edwards ET, Braun MM. *Listeria monocytogenes* infection as a complication of treatment with tumor necrosis factor alpha-neutralizing agents. *Arthritis Rheum*. 2003;48(2):319-324. <https://doi.org/10.1002/art.10758>
4. Kesteman T, Yombi JC, Gigi J, Durez P. *Listeria* infections associated with infliximab: case reports. *Clin Rheumatol*. 2007; 26(12):2173-2175. <https://doi.org/10.1007/s10067-007-0660-8>
5. Parihar V, Maguire S, Shahin A, et al. *Listeria* meningitis complicating a patient with ulcerative colitis on concomitant infliximab and hydrocortisone. *Ir J Med Sci*. 2016;185(4):965-967. <https://doi.org/10.1007/s11845-015-1355-9>
6. Hsu L, Snodgrass BT, Armstrong AW. Antidrug antibodies in psoriasis: a systematic review. *Br J Dermatol*. 2014;170(2): 261-273.
7. Abreu C, Magro F, Vilas-Boas F, Lopes S, Macedo G, Sarmiento A. *Listeria* infection in patients on anti-TNF treatment: report of two cases and review of the literature. *J Crohns Colitis*. 2013; 7(2):175-182. <https://doi.org/10.1016/j.crohns.2012.04.018>
8. Thønnings S, Knudsen JD, Schønheyder HC, et al. Antibiotic treatment and mortality in patients with *Listeria monocytogenes* meningitis or bacteraemia. *Clin Microbiol Infect*. 2016; 22(8):725-730. <https://doi.org/10.1016/j.cmi.2016.06.006>