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ID CASE

Lysinibacillus massiliensis Panniculitis Masquerading as Erythema Nodosum: A Case Report

Jay J. Jin,[1] Phillip J. Keith,[2] Nathan W. Cummins,[3] Sunanda V. Kane,[4] Bobbi S. Pritt,[3,5] and Joyce L. Sanchez[3]

[1]Division of Allergy and Immunology, [2]Department of Dermatology and Divisions of [3]Infectious Diseases, [4]Gastroenterology, and [5]Clinical Microbiology, Mayo Clinic, Rochester, Minnesota

Lysinibacillus massiliensis, formerly *Bacillus massiliensis*, is an environmental Gram-positive bacillus that is generally non-pathogenic. Rare case reports in immunosuppressed patients have described sepsis with this organism. In this study, we report a case of *L massiliensis* as a cause of infectious panniculitis mimicking erythema nodosum after infusion of autologous adipose-derived stem cells in an immunosuppressed patient with refractory Crohn's disease. This case highlights the importance of care providers to consider exposures and host factors when interpreting culture results with otherwise benign organisms.

Keywords. adipose-derived stem cell treatment; erythema nodosum; *Lysinibacillus massiliensis*; panniculitis.

CASE REPORT

A 44-year-old woman with Crohn's disease underwent ileal pouch-anal anastomosis. She developed recurrent perianal abscesses and fistulas for 6 years requiring multiple incision and drainage procedures and Seton and plug placements. She could not taper from steroids despite the use of various steroid sparing agents. She underwent an experimental autologous adipose-derived stem cell procedure at an outside facility, with cells injected directly into the perianal region. She remained free of perianal complications for one and half years before redeveloping new perianal fistulas. She underwent a second autologous adipose-derived stem cell injection to the perianal region. Cells were also infused intravenously. Within 24 hours, she developed painful, indurated, erythematous nodules on her lower extremities. The lesions grew rapidly in size reaching up to 5 cm in diameter. The skin overlying the nodules eventually blistered. The clinical appearance of these lesions resembled erythema nodosum, which seemed to be the likely diagnosis given the patient's history of inflammatory bowel disease (IBD) (Figure 1).

Punch biopsies from the left superior shin and left thigh revealed periseptal acute and granulomatous inflammation (Figure 2). The acid-fast bacilli, Fite, Giemsa-Wright, and Gram stains for microorganisms were negative; however, the tissue culture grew 4+ *Lysinibacillus massiliensis*, which was confirmed by 16S ribosomal deoxyribonucleic acid sequencing. The isolate was susceptible to penicillin (minimum inhibitory concentration [MIC] ≤0.06), cefazolin (MIC ≤2), levofloxacin (MIC ≤1), clindamycin (MIC ≤0.5), trimethoprim-sulfamethoxazole (MIC ≤0.5/9.5), and vancomycin (MIC ≤0.5), by agar dilution. Fungal and mycobacterial cultures from this tissue culture were negative. Blood cultures were negative. Serologic testing for endemic fungi, syphilis, and human immunodeficiency virus were negative.

Upon presentation to the Infectious Disease clinic, the patient had persistent skin lesions for 4 weeks. She was started on cefadroxil for 14 days. Within 1 week, the skin lesions showed signs of healing with desquamation of the overlying affected skin and improvement in pain. The final assessment from Dermatology determined the skin lesions to be an infectious panniculitis masquerading as erythema nodosum.

We obtained informed consent from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review.

DISCUSSION

Our report describes *L massiliensis*, an atypical organism associated with infectious panniculitis in an immunocompromised host. Infectious panniculitis is commonly a consequence of disseminated infection. Treatment is directed at the causative organism, which is best identified by tissue culture from a lesional biopsy. *Lysinibacillus* species have been identified in cases of bacteremia in pediatric cancer patients undergoing bone marrow transplantation and in a patient with a history of intravenous drug use and splenectomy [1, 2]. The temporal association of skin lesion onset with the stem cell procedure suggests that this process may have been due to the infusion. *Lysinibacillus* species from air samples in a medical practice as well as catheters and tubing in hospital settings renders this explanation plausible [3]. It is unfortunate that the product was not available for culture to confirm our suspicion.

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Correspondence: J. L. Sanchez, MD, Division of Infectious Diseases, Mayo Clinic, 200 First Street SW, Rochester, MN 55905 (sanchez.joyce@mayo.edu).

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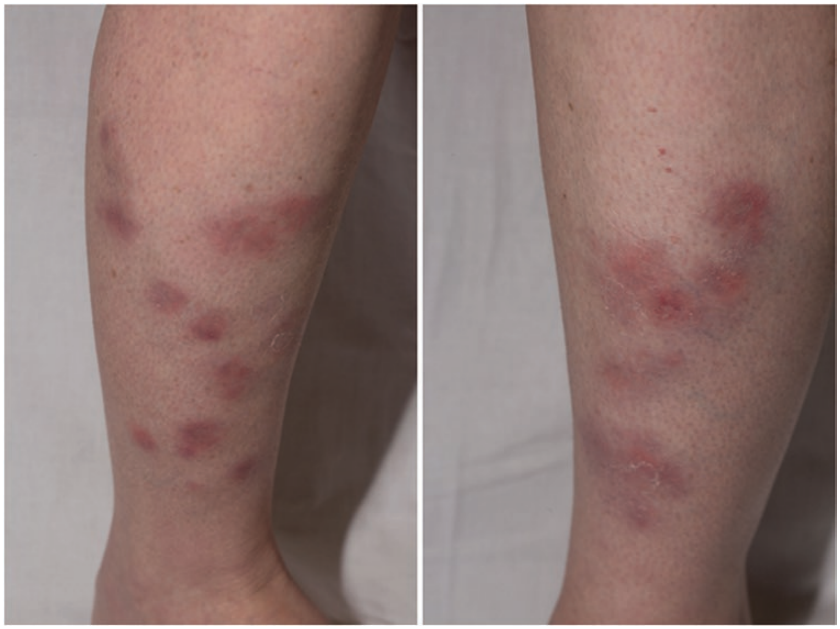

Figure 1. Warm, painful erythematous, violaceous, subcutaneous nodules with smooth, rolled, borders seen on the anterior lower extremities.

Although the US Food and Drug Administration has not approved adipose-derived stem cell products, private clinics are offering this option in the United States [4]. It is thought that the immunomodulatory and regenerative properties of mesenchymal stem cells can be useful in treating patients with IBD refractory to traditional immunosuppressive therapy [5]. Phase I and II studies using autologous stem cells have been published in recent years on the treatment of IBD. To date, bloodstream and disseminated infections have not been described. Two of seven studies reported serious adverse effects after local stem cell administration to tissues, including fever and perianal abscess; however, both were thought to be related to the underlying disease rather than the stem cell treatment [6]. A study of systemically infused autologous bone marrow-derived stem cells also reported no serious adverse effects in the 6-month follow-up period. All minor adverse reactions were considered unrelated

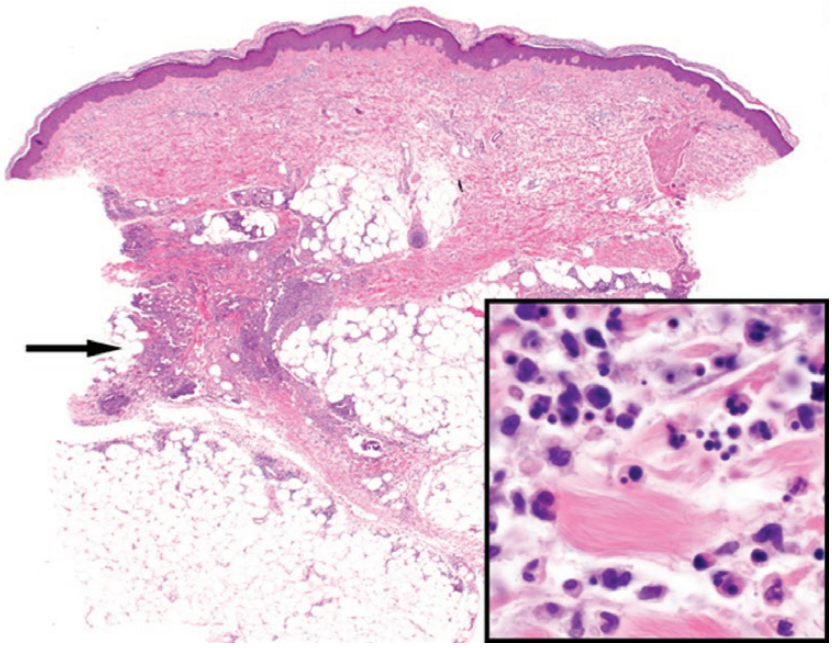

Figure 2. Left superior shin skin punch biopsy demonstrating deep dermal periseptal acute and granulomatous inflammation (arrow, hematoxylin and eosin stain, ×20). Higher magnification (inset, ×1000) demonstrates the neutrophilic component of the inflammation.

to the stem cell infusion [7]. Further studies describing the outcomes and infectious complications are needed. In addition, standardization of stem cell collection, processing, and injection is warranted.

CONCLUSIONS

To our knowledge, this is the first case reporting *L massiliensis* as a potential pathogen and associated with infectious panniculitis. Had this patient not (1) been immunosuppressed, (2) recently received an intravenous infusion of autologous stem cells, or (3) had clinical response to tailored antimicrobial therapy, this isolate may have been considered a contaminant. This case highlights the need for further studies surrounding the potential adverse effects of stem cell therapy for IBD.

Acknowledgments

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References

1. Wenzler E, Kamboj K, Balada-Llasat JM. Severe sepsis secondary to persistent *Lysinibacillus sphaericus*, *Lysinibacillus fusiformis* and *Paenibacillus amylolyticus* bacteremia. Int J Infect Dis **2015**; 35:93–5.
2. Castagnola E, Fioredda F, Barretta MA, et al. *Bacillus sphaericus* bacteraemia in children with cancer: case reports and literature review. J Hosp Infect **2001**; 48:142–5.
3. Seiler H, Scherer S, Wenning M. *Lysinibacillus meyeri* sp. nov., isolated from a medical practice. Int J Syst Evol Microbiol **2013**; 63:1512–8.
4. Turner LG. Federal regulatory oversight of US clinics marketing adipose-derived autologous stem cell interventions: insights from 3 new FDA draft guidance documents. Mayo Clin Proc **2015**; 90:567–71.
5. Martínez-Montiel Mdel P, Gómez-Gómez GJ, Flores AI. Therapy with stem cells in inflammatory bowel disease. World J Gastroenterol **2014**; 20:1211–27.
6. Dave M, Mehta K, Luther J, et al. Mesenchymal stem cell therapy for inflammatory bowel disease: a systematic Review and Meta-analysis. Inflamm Bowel Dis **2015**; 21:2696–707.
7. Duijvestein M, Vos AC, Roelofs H, et al. Autologous bone marrow-derived mesenchymal stromal cell treatment for refractory luminal Crohn's disease: results of a phase I study. Gut **2010**; 59:1662–9.