Received: 18 May 2021 | Revised: 23 June 2021 | Accepted: 11 July 2021

DOI: 10.1002/cia2.12197

Journal of Cutaneous Immunology and Allergy

WILEY

CORRESPONDENCE

A pediatric case of cellulitis caused by *Stenotrophomonas maltophilia* with subcutaneous microvascular thrombosis and diffuse hemorrhage

Dear Editor,

A Japanese child aged 4 years 2 months developed an erythema with subcutaneous swelling on the right thigh and extensive tenderness widely around the erythema (Figure 1A). The patient had been diagnosed with T lymphoblastic leukemia at the age of 2 years and had underwent multiple remission induction therapies. After pretreatment, bone marrow transplantation was received 16 days before the onset. He had been receiving intermittent empiric antibiotic therapy, including carbapenems, due to febrile neutropenia for 2 years. Multiple immunosuppressive agents for graft-vs-host disease prophylaxis and antibiotics had been administered. After the presentation of high fever, C-reactive protein level elevated to 20 mg/dl. The patient's leukocyte count had been decreased to 250/μl with 12% neutrophils (Figure 1B). His platelet count was 50×10^3/μl, fibrin degradation product was 0.86 μg/ml, fibrinogen was 449 mg/ml, PT-INR was 1.02%, and there was no evidence of disseminated intravascular coagulation. One day after onset, computed tomography showed localized opacity of the subcutaneous adipose tissue inside the right thigh, suggesting cellulitis. A skin biopsy was performed on the third day of onset. *Stenotrophomonas maltophilia* (*S. maltophilia*) was solely detected from the tissue culture and was also subsequently detected alone from several swab cultures (Figure 1B). Histology showed subcutaneous multiple microvascular thrombi and diffuse hemorrhage in the subcutaneous tissue (Figure 1C). On day 10 (Figure 1D), fat-suppressed T2-weighted magnetic resonance imaging demonstrated hyperintensity of subcutaneous adipose tissue (Figure 1E, i) and fluid signal intensity tracking along the peripheral (i, ii) and intermuscular deep fascia (ii) along with thickening of these fasciae. This may reflect subcutaneous inflammation and bleeding. Because antimicrobial susceptibility testing showed minocycline minimum inhibitory concentration (MIC) ≤ 1 μg/ml, levofloxacin MIC 2 μg/ml, trimethoprim-sulfamethoxazole MIC ≤ 1 μg/ml, in addition to levofloxacin, minocycline and a prophylactic dose of trimethoprim-sulfamethoxazole were administered. The patient's symptoms gradually improved, and the subsequent tissue culture was negative on day 17 (Figure 1B,F).

Stenotrophomonas maltophilia is a gram-negative aerobic nonfermentative bacillus and emerged as an opportunistic infection with high mortality rates.[1] Twenty-four cases of the skin infection have been reported so far, nine of which present symptom suggestive of vascular damage. Seven of them had ecthyma gangrenosum or purpura, and two had gangrene of the digits.[2] The cases of ecthyma gangrenosum or purpura and one case of gangrene all had underlying hematologic malignancies. While, Thirty patients with life-threatening hemorrhagic pneumonia caused by *S. maltophilia* have been reported, and all of them also suffering from hematological malignancies.[3] On the other hand, there is only one report of a patient with triple-positive antiphospholipid antibodies who developed a dorsolateral medullary infarction during cutaneous infection with *S. maltophilia*.[4] Therefore, this is the first report to pathologically demonstrate that thrombus formation and hemorrhage occur simultaneously in skin *S. maltophilia* infections. StmPr1, a protease of *S. maltophilia*, has been reported to be a candidate molecule that can damage microvessels.[5] Vascular damage by such bacterial proteases may contribute to thrombus formation and hemorrhage. Elucidating the mechanism of thrombus formation by *S. maltophilia* may lead to prevention of fatal hemorrhage caused by *S. maltophilia*.

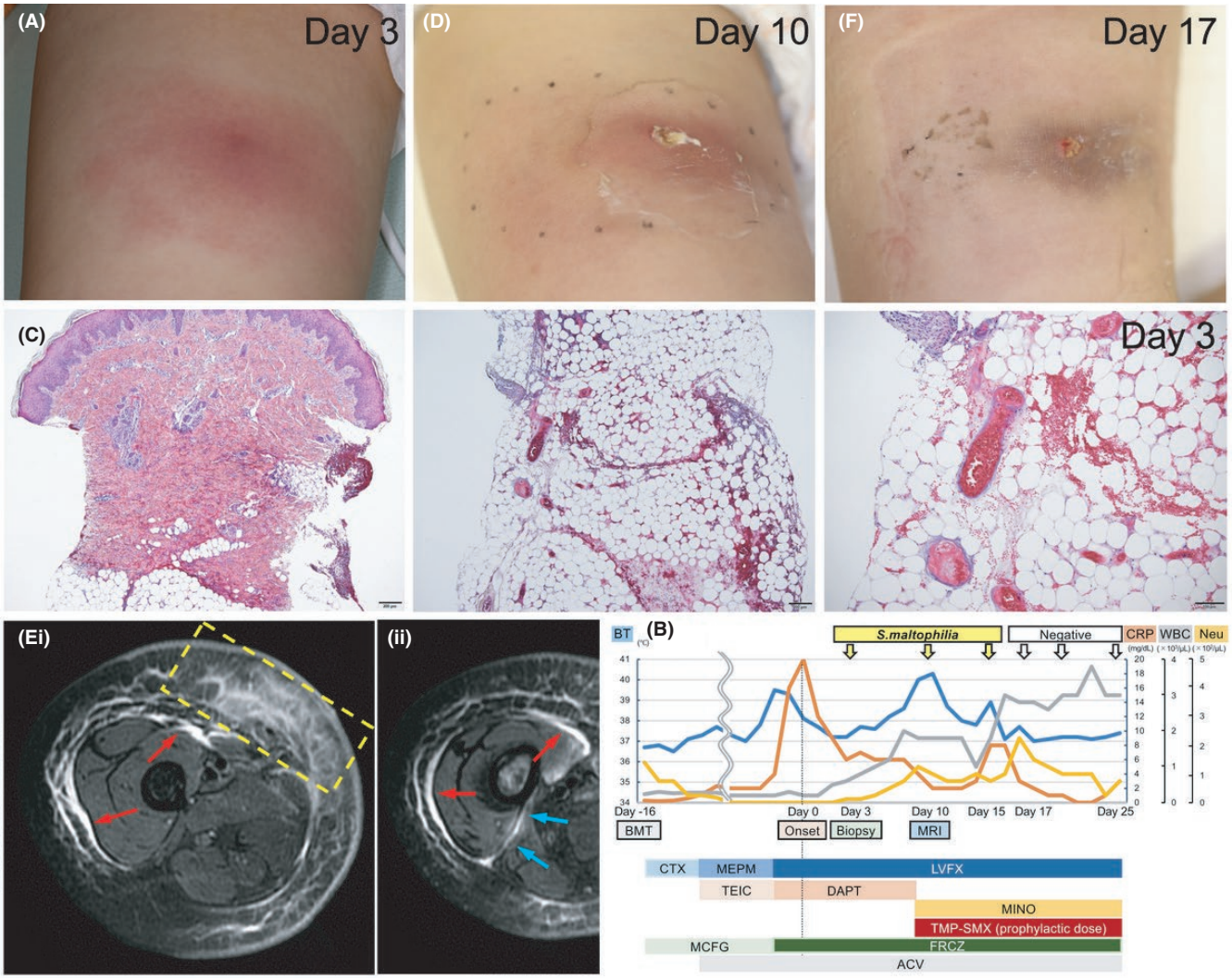

FIGURE 1 (A) A painful erythema 4 cm in diameter (long axis) with subcutaneous swelling on the right thigh, which had extensive tenderness of the surrounding skin at the time of skin biopsy on the third day of onset. (B) Summary of the clinical and laboratory values before and after treatment. ACV, acyclovir; BMT, bone marrow transplantation; BT, blood temperature; CRP, C-reactive protein; CTX, cefotaxime; DAPT, daptomycin; FLCZ, fluconazole; LVFX, levofloxacin; MCFG, micafungin; MEPM, meropenem; MINO, minomycin; Neu, neutrophil; TEIC, teicoplanin; TMP-SMX, trimethoprim-sulfamethoxazole; WBC, white blood cells. (C) Histologically, there were multiple microvascular thrombi and extensive hemorrhage in the lowest dermis and in the subcutaneous tissue. (Hematoxylin and eosin; scale bars: left and center, 200 μm, right, 100 μm). (D) Reduction in erythema and development of skin ulceration after biopsy, on day 10. Dotted line indicating the extent of subcutaneous induration. The tenderness on the surrounding skin was persistent. (E) (i, ii) Axial fat-suppressed T2-weighted magnetic resonance imaging revealed hyperintensity of subcutaneous adipose tissue (yellow square) and fluid signal intensity along of peripheral (red arrows) and intermuscular deep facia (blue arrows) accompanied by thickening of these fasciae to approximately 1 mm. (F) Erythema turned into pigmentation and disappearance of tenderness 17 days after the onset

ACKNOWLEDGMENTS

This study was supported by the Japan Society for the Promotion of Science (JSPS) KAKENHI (grant number JP18K08296).

DECLARATION SECTION

Approval of the research protocol: No human participant was involved in this study.

Informed Consent: Informed consent was obtained from the patient.

Registry and the Registration No. of the study/trial: N/A.

Animal Studies: N/A.

CONFLICT OF INTEREST

The authors declare no conflict of interest. Dr Manabu Fujimoto is the Editor in Chief for the Journal of Cutaneous Immunology and Allergy. Management of the peer review process, and all editorial decision making, for this article was undertaken by an Associate Editor.

Emi Inoue MD[1]
Noriko Arase MD, PhD[1]
Takako Miyamura MD, PhD[2]
Tomohiro Wataya MD[3]

Yusuke Tanaka MD[2]
Nobuo Kashiwagi MD, PhD[4]
Hiroshi Sakai MD[1]
Satoshi Nojima MD, PhD[5]
Manabu Fujimoto MD, PhD[1]

[1]*Department of Dermatology, Osaka University Graduate School of Medicine, Suita, Japan*
[2]*Department of Pediatrics, Osaka University Graduate School of Medicine, Suita, Japan*
[3]*Department of Artificial Intelligence Diagnostic Radiology, Osaka University Graduate School of Medicine, Suita, Japan*
[4]*Department of Future Diagnostic Radiology, Osaka University Graduate School of Medicine, Suita, Japan*
[5]*Department of Pathology, Osaka University Graduate School of Medicine, Suita, Japan*

Correspondence
Noriko Arase, MD, PhD, Department of Dermatology, Osaka University Graduate School of Medicine, 2-2 Yamadaoka, Suita, Osaka 565-0871, Japan.
Email: arase@derma.med.osaka-u.ac.jp

ORCID
Noriko Arase https://orcid.org/0000-0003-3966-3437
Tomohiro Wataya https://orcid.org/0000-0002-1224-6601
Manabu Fujimoto https://orcid.org/0000-0002-3062-4872

REFERENCES

1. Ebara H, Hagiya H, Haruki Y, Kondo E, Otsuka F. Clinical characteristics of *Stenotrophomonas maltophilia* bacteremia: a regional report and a review of a Japanese case series. Intern Med. 2017;56:137–42.
2. Bin Abdulhak AA, Zimmerman V, Al Beirouti BT, Baddour LM, Tleyjeh IM. *Stenotrophomonas maltophilia* infections of intact skin: a systematic review of the literature. Diagn Microbiol Infect Dis. 2009;63:330–3.
3. Mori M, Tsunemine H, Imada K, Ito K, Kodaka T, Takahashi T. Life-threatening hemorrhagic pneumonia caused by *Stenotrophomonas maltophilia* in the treatment of hematologic diseases. Ann Hematol. 2014;93:901–11.
4. Chen Y-L, Yang H-T, Liu L-X, Chen C-H, Huang Q, Hong X-P, et al. Dorsolateral medullary infarction during skin infection by *Stenotrophomonas maltophilia* in a patient with triple antiphospholipid antibody positivity: a case-based review. Clin Rheumatol. 2021;40:2965–71.
5. Windhorst S, Frank E, Georgieva DN, Genov N, Buck F, Borowski P, et al. The major extracellular protease of the nosocomial pathogen *Stenotrophomonas maltophilia*: characterization of the protein and molecular cloning of the gene. J Biol Chem. 2002;277:11042–9.

How to cite this article: Inoue E, Arase N, Miyamura T, Wataya T, Tanaka Y, Kashiwagi N, et al. A pediatric case of cellulitis caused by *Stenotrophomonas maltophilia* with subcutaneous microvascular thrombus formation and diffuse hemorrhage. J Cutan Immunol Allergy. 2021;4:181–183. https://doi.org/10.1002/cia2.12197