

CASE REPORT

Recurrent *Paenibacillus* infection

Matthew Alan Szaniawski[†] and Adam Mitchell Spivak^{*}

Department of Medicine, University of Utah School of Medicine, 50 N Medical Drive East, Salt Lake City, UT 84132, USA

^{*}Corresponding address: University of Utah School of Medicine, 50 N Medical Drive, East Salt Lake City, UT 84132, USA. Tel: (801) 587 1964; Fax: (801) 585 3377; E-mail: adam.spivak@hsc.utah.edu

Abstract

The genus *Paenibacillus* includes Gram-positive bacteria that are rarely known to cause infection in humans. Here we report a case of recurrent *Paenibacillus macerans* infection in an otherwise healthy 66-year-old man following environmental exposure decades prior to presentation to our clinic. Despite numerous attempts at surgical debridement, *Paenibacillus* was repeatedly cultured from the soft tissue of the lower extremity wound site over a period of years. Post-operative antibiotic treatment prevented recurrence; however, upon antibiotic discontinuation, *Paenibacillus* was again cultured from the wound. After multiple rounds of debridement and antibiotic therapy, the patient was started on indefinite, low-dose trimethoprim-sulfamethoxazole therapy to suppress infection resulting from transition of *Paenibacillus* spores to vegetative cells. This case adds to the limited number of case reports describing *Paenibacillus* species infection in healthy adults and presents a unique case of bona fide *P. macerans* infection requiring life-long antibiotic therapy.

INTRODUCTION

The genus *Paenibacillus* includes numerous Gram-positive aerobic and facultatively anaerobic bacterial species that are important in plant and animal biology [1]. *Paenibacillus* species are ubiquitous in the environment, particularly in soil, and are often associated with plant roots as rhizobacteria where they are known to promote plant growth through nitrogen fixation, phosphorus solubilization and control of phytopathogens. Most notable among *Paenibacillus* species is *Paenibacllus larvae*, the cause of American Foulbrood, a lethal disease of honeybees that devastates colonies and has been described to persist as spores for decades [1, 2]. In humans, a small number of disease-causing *Paenibacillus* species have been reported. The majority of these *Paenibacillus* infections occur in the setting of immune compromise or secondary to trauma. Here, we describe the recovery of *Paenibacillus macerans* from the soft tissue of a healthy individual requiring life-long antibiotic treatment to suppress recurrent infection resulting from transition of *Paenibacillus* spores to vegetative cells.

CASE REPORT

A 66-year-old man was referred to the University of Utah Infectious Diseases clinic for evaluation of recurrent right thigh soft tissue infection. These symptoms began in 2011 when he underwent left ankle surgery following minor trauma. No indwelling hardware, other than surgical screws, was placed in the ankle. Several weeks after surgery, the patient noted the development of a firm nodule and swelling in the right groin and upper thigh, which he described as 'a pocketful of rocks'. A magnetic resonance imaging (MRI) was performed, which revealed multifocal intermuscular and intramuscular rim-enhancing fluid collections in the proximal anterior lateral thigh. The lesion ulcerated and developed into a chronic, non-healing wound. The patient underwent surgical debridement, followed by several weeks of oral antibiotics targeting Gram-positive coccobacilli recovered from intra-operative tissue culture that were not further specified. Several months after surgery, the wound site became inflamed and ulcerated, requiring repeat surgical debridement and antibiotics. At the time of infectious diseases referral in

[†]<http://orcid.org/0000-0003-1123-3101>

Received: January 10, 2019. Revised: March 12, 2019. Accepted: March 18, 2019

© The Author(s) 2019. Published by Oxford University Press.

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0/>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited.

For commercial re-use, please contact journals.permissions@oup.com

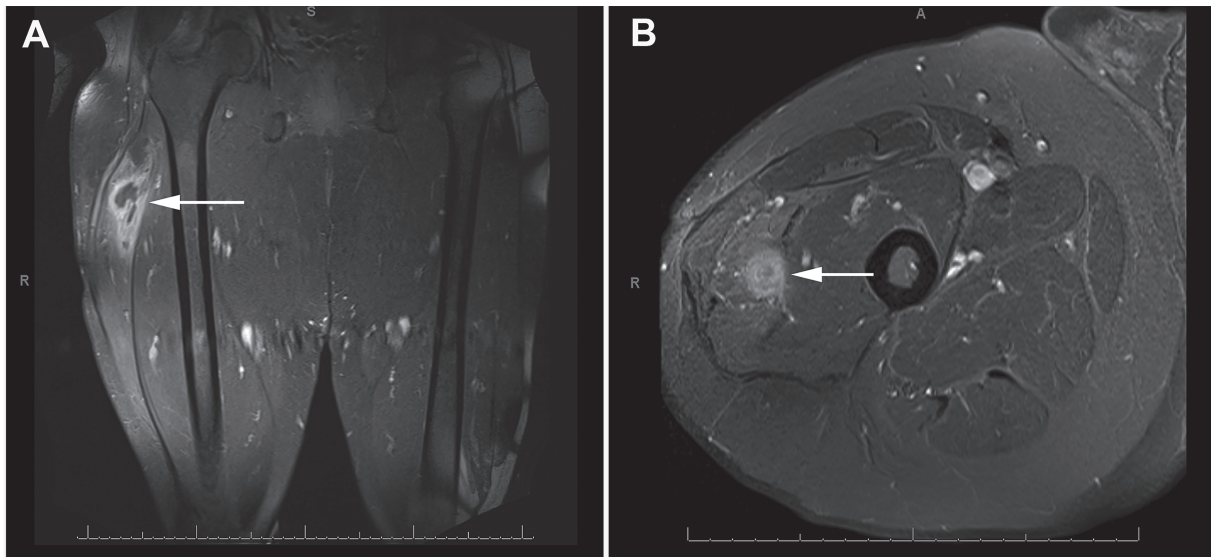


Figure 1: MRI of right thigh cavitation. (A) Coronal T1 sequence showing multifocal intermuscular and intramuscular rim-enhancing fluid collections within and around the vastus lateralis in the proximal anterior lateral thigh. (B) Transverse section of right thigh confirming fluid collection in the anterior compartment.

Table 1: Antibiotic minimal inhibitory concentrations and sensitivities for cold abscess *Paenibacillus* isolate in aerobic tissue culture

Antibiotic	Minimal inhibitory concentration ($\mu\text{g/ml}$)	Sensitivity interpretation
Ceftriaxone	≤ 0.06	-
Clindamycin	2	Intermediate
Doxycycline	≤ 0.12	-
Erythromycin	≥ 8	Resistant
Gentamicin	≤ 0.12	Sensitive
Levofloxacin	≤ 0.25	Sensitive
Linezolid	0.5	-
Meropenem	2	Sensitive
Penicillin	2	Resistant
TMP-SMX	$\leq 0.25/4.8$	Sensitive
Vancomycin	≥ 16	-

late 2016, the patient had undergone 11 episodes of surgical debridement of the right upper groin and thigh followed by short course antibiotics over a 5-year period.

The patient's medical history is significant for well-controlled diabetes mellitus (HbA1c = 5.7%), hypercholesterolemia, hypertension, prostate cancer and West Nile virus (WNV) encephalitis in 2006 from which he recovered without incident. On physical examination, a 2-cm irregularly shaped, well-healed scar was identified immediately adjacent to the surgical site on the anterior right lower extremity. The patient attributed this scar to a distant childhood traumatic injury, when a large stick penetrated his right thigh after he fell from a tree house onto a marshy forest floor. He recalls removing the penetrating foreign body and never sought medical attention for this wound, which healed spontaneously. The wound was never explored for retained foreign bodies, and he denied any history of surgery or invasive procedures prior to the ankle surgery in 2011.

Upon examination, the patient was oriented and in no distress. The blood pressure was 116/64 mm Hg, pulse was 76 beats per minute, respirations were 16 per minute, oxygen saturation was 93% on room air and temperature was 36.4°C. Examination of the right anterior thigh revealed a serpiginous, well-healed surgical scar that was non-tender and non-erythematous. Two well-healed irregularly shaped scars were noted adjacent to the

surgical site. There was full range of motion and no tenderness over the hip joint or lumbar spine. He exhibited normal gait and had no inguinal lymphadenopathy. Laboratory results showed no abnormalities in blood counts, complete metabolic panel or inflammatory markers. The patient's blood work was negative for human immunodeficiency virus, Hepatitis B and Hepatitis C.

Multiple intra-operative tissue cultures from surgical debridement recovered either *Paenibacillus* species or Gram-positive coccobacilli not further speciated, including the most recent debridement in 2016. He had been prescribed a variety of post-operative antibiotic regimens and reported that trimethoprim-sulfamethoxazole (TMP-SMX) treatment brought symptom relief, with no recurrence during the antibiotic course. At the time of infectious diseases consultation, the patient was taking TMP-SMX after the most recent surgical debridement. A repeat MRI was scheduled. Five days prior to repeat imaging, the patient discontinued TMP-SMX treatment. MRI revealed no fluid accumulation or recurrence of infection, and the patient was advised to remain off TMP-SMX.

The patient remained healthy and pain-free for 3 months following TMP-SMX interruption, when fatigue and weakness returned, as well as tenderness and swelling at the surgical site. A superficial abscess at the site of debridement was drained, and tissue cultures grew *P. macerans*. An MRI was performed, with

multifocal intermuscular and intramuscular rim-enhancing fluid collections within and around the vastus lateralis (Fig. 1). The patient underwent right thigh surgical debridement and wash out. Antibiotic susceptibility testing of intra-operative tissue culture identified TMP-SMX-susceptible *P. macerans* (Table 1); fungal and mycobacterial cultures were negative. Pathology showed focal necrobiotic granulomatous inflammation in soft tissues. The patient was continued on a regimen of 360 mg oral TMP-SMX BID indefinitely and has remained afebrile and clinically stable since reintroduction of therapy.

DISCUSSION

Our working hypothesis is that remote childhood trauma resulted in soft tissue inoculation of *P. macerans* spores, which remained dormant over five decades until reverting to active infection in 2011 following an elective orthopedic procedure on the right ankle. Several conditions may have contributed to the development of active *Paenibacillus* infection several decades after initial exposure, including WNV encephalitis, diabetes mellitus or the stress of elective ankle surgery. Though it is impossible to pinpoint what caused *Paenibacillus* spores to transition to vegetative cells, mechanisms employed by bacterial spores to evade immune responses and persist indefinitely have been described [3, 4, 5]. Given the patient's extensive surgical history related to deep soft tissue *Paenibacillus* infection and recurrence after antibiotic cessation, we initiated indefinite antibiotic suppression with low-dose TMP-SMX. This has suppressed recurrent *P. macerans* infection to date (20 months), and we anticipate life-long secondary prophylaxis. The surgical wound has healed completely, and he follows up regularly to monitor for antibiotic toxicity or recurrence of infection.

ACKNOWLEDGEMENTS

We wish to acknowledge the patient described for allowing us to share the details contained within this report.

CONFLICT OF INTEREST STATEMENT

None declared.

FUNDING STATEMENT

There are no sources of funding for this manuscript.

ETHICAL APPROVAL

This case report was approved by the institute's institutional review board as per its policy.

CONSENT

Consent was obtained from the patient described to publish his case report without identifying information.

GUARANTOR

Adam M. Spivak, M.D., University of Utah School of Medicine, 50 N Medical Drive East, Salt Lake City, UT 84132, USA.

REFERENCES

1. Grady EN, MacDonald J, Liu L, Richman A, Yuan ZC. Current knowledge and perspectives of *Paenibacillus*: a review. *Microb Cell Fact* 2016;15:203.
2. Ebeling J, Knispel H, Hertlein G, Funfhaus A, Genersch E. Biology of *Paenibacillus* larvae, a deadly pathogen of honey bee larvae. *Appl Microbiol Biotechnol* 2016;100:7387–7395.
3. Vreeland RH, Rosenzweig WD, Powers DW. Isolation of a 250 million-year-old halotolerant bacterium from a primary salt crystal. *Nature* 2000;407:897–900.
4. Wang Y, Jenkins SA, Gu C, Shree A, Martinez-Moczygemba M, Herold J, et al. Bacillus anthracis spore surface protein BclA mediates complement factor H binding to spores and promotes spore persistence. *PLoS Pathog* 2016;12:e1005678.
5. Choo MK, Sano Y, Kim C, Yasuda K, Li XD, Lin X, et al. TLR sensing of bacterial spore-associated RNA triggers host immune responses with detrimental effects. *J Exp Med* 2017;214:1297–1311.