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Complex trauma sequelae: *Mycobacterium goodii* and *Priestia endophytica* Hardware infection in a patient with Ehlers-Danlos syndrome

Andrea L. Covington[1], Filipe M. Cerqueira[2], Jonathan E. Pavia[1], David Reynoso[1] and Ping Ren[2*]

Abstract

A 26-year-old man with Ehlers-Danlos syndrome, recurrent otitis externa, and chronic otitis media sustained a left lower extremity amputation and open femur fracture with internal hardware fixation after a motor vehicle collision in Arizona. He presented to the emergency department at our institution with severe left leg pain and purulent discharge despite receiving two unidentified antibiotics upon discharge. Evaluations revealed an abscess and malunion of the femur. Initial cultures yielded scant *Priestia endophytica*, leading to daptomycin treatment. His condition worsened until Gram-positive bacilli identified as *Mycobacterium goodii*, a rare nosocomial mycobacterial species, were found. Significant improvement occurred with appropriate antibiotics. This case highlights the challenges in diagnosing and managing *M. goodii* infections in immunocompromised patients with orthopedic complications and notes *P. endophytica* as a previously unreported, possibly opportunistic human pathogen.

Keywords *Mycobacterium goodii*, *Priestia endophytica*, Post-traumatic hardware infections, Ehlers-Danlos Syndrome

Introduction

Ehlers-Danlos Syndrome (EDS) comprises a group of inherited connective tissue disorders characterized by varying degrees of skin hyperextensibility, joint hypermobility, and tissue fragility [1]. These disorders result from defects in the structure, production, or processing of collagen or related proteins, which are essential components of connective tissue [2]. EDS may increase the risk of infections and allergic disorders and is potentially associated with immune deficiencies [3]. The convergence of EDS, innate immunity dysfunction, and the aftermath of a motor vehicle collision leading to below-the-knee amputation (BKA) and hardware fixation presents a distinctive clinical challenge. Here, we present a case that delineates the intricate management complexities inherent in such a multifaceted presentation, specifically focusing on the emergence of *Mycobacterium goodii* and *Priestia endophytica* infections, the latter being an organism not previously identified as a human pathogen.

Case presentation

A 26-year-old man with EDS presented after a motor vehicle collision in Arizona resulting in significant trauma and soil-contaminated wounds to his left lower extremity and underwent BKA and femoral intramedullary nail placement. After a three-week hospitalization, he was discharged with two unspecified antibiotics.

*Correspondence:
Ping Ren
piren@utmb.edu
[1]Department of Internal Medicine, Division of Infectious Diseases, University of Texas Medical Branch, Galveston, TX, USA
[2]Department of Pathology, University of Texas Medical Branch, Galveston, TX, USA

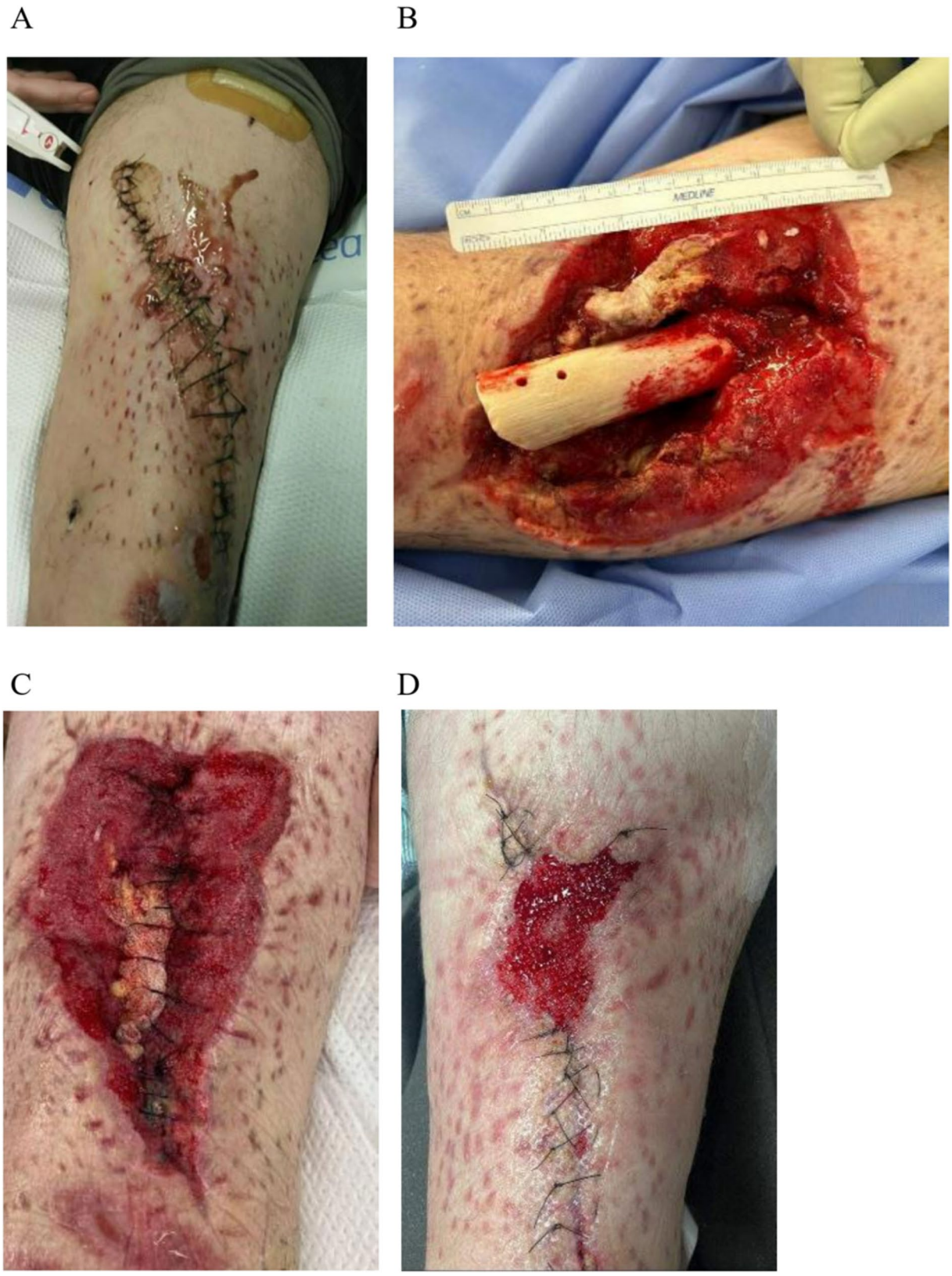

Fig. 1 (**A**) Wound at the admission. (**B**) 5th debridement. (**C**) Pos-operative wound dehiscence. (**D**) Two weeks after wound dehiscence and antibiotic switch

Table 1 Blood test results at the time of admission

Parameter	Result	Reference range
White blood cell	8.84×10^3/μL	$4.20–10.70 \times 10^3$/μL
Lymphocyte count	1.73×10^3/μL	$1.90–3.23 \times 10^3$/μL
Neutrophil count	5.81×10^3/μL	$1.99–6.95 \times 10^3$/μL
Hemoglobin	10.1 g/dL	12.2–16.4 g/dL
Platelet	467×10^3/uL	$150–328 \times 10^3$/uL
C-reactive protein	2.0 mg/dL	< 0.8 mg/dL
Sedimentation Rate	55 mm/HR	2–30 mm/HR

Approximately one week after discharge, the patient presented to the emergency department at our institution with severe left leg pain and purulent drainage from an anterior thigh surgical incision (Fig. 1A; Table 1). He was hospitalized and underwent surgical debridement after a two-week delay due to unexpected circumstances. The area of debridement measured approximately 44 cm × 15 cm × 2 cm with extensive purulence. Notably, antibiotics were not administered prior to this surgical intervention.

Intraoperative tissue cultures collected during surgical debridement yielded grey-white, gamma-hemolytic colonies with a ground glass appearance, accompanied by long Gram-positive bacilli on Gram stain (Fig. 1). Initially, *Bacillus anthracis* was considered and was excluded by molecular testing conducted by the Houston Health Department. Thereafter, our laboratory performed further analysis using Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry (MALDI-TOF MS) (Bruker, Billerica MA) and sequencing of the 16S rDNA gene on both isolates from two tissue cultures collected from the first debridement and before initiation of antibiotics, which identified the organism as *Priestia endophytica* (NCBI GenBank accession # PP533212, 1459 base pairs, 100% query coverage, and 100% identity with OP437686), previously known as *Bacillus endophyticus* [4].

Post-operatively, the patient received vancomycin and later daptomycin due to suboptimal vancomycin levels. As *P. endophytica* was the only organism isolated from tissue samples from his first debridement, daptomycin was continued and later transitioned to doxycycline based on susceptibility testing (Table 2) and extrapolation of the efficacy of doxycycline from *Bacillus* species. Subsequent surgical interventions involved incision and drainage procedures every 2–4 days for approximately 3 weeks, culminating in a bone graft placement and permanent intramedullary nail placement (Fig. 1B). The postoperative course was complicated by wound dehiscence (Fig. 1C).

During hospitalization, aerobic, anaerobic, fungal, and acid-fast bacilli (AFB) cultures were collected as a standard-of-care protocol on the first, fourth, and eleventh debridement. Including the first debridement, all AFB cultures eventually were identified as *Mycobacterium goodii. P. endophytica* was not isolated again after initial debridement and targeted antibiotic therapy.

Empiric trimethoprim/sulfamethoxazole (TMP/SMX) was initiated for the treatment of *M. goodii*, as it is typically susceptible to SMX. Doxycycline was continued for

Table 2 Antimicrobial susceptibility for *Priestia Endophytica* and *Mycobacterium goodii*

Antibiotics	MIC[1] (μg/mL)	Interpretation	MIC (μg/mL)	Interpretation
	Priestia endophytica		*Mycobacterium goodii*	
Amikacin	–[2]	–	≤ 1	Susceptible
Cefoxitin	–	–	≥ 256	Resistant
Ceftriaxone	≥ 4	No Interpretation	–	–
Ciprofloxacin	–	–	1	Susceptible
Clarithromycin	–	–	≥ 32	Resistant
Clindamycin	0.5	Susceptible	–	–
Doxycycline	≤ 0.25	No Interpretation	≤ 0.12	Susceptible
Erythromycin	2	Intermediate	–	–
Gentamicin	≤ 2	Susceptible	–	–
Imipenem	–	–	8	Intermediate
Levofloxacin	≤ 0.25	Susceptible	–	–
Linezolid	0.5	No Interpretation	2	Susceptible
Meropenem	0.12	Susceptible	–	–
Moxifloxacin	–	–	0.12	Susceptible
Penicillin	1	Resistant	–	–
Tigecycline	–	–	≤ 0.03	No interpretation
Trimethoprim/Sulfamethoxazole	≤ 0.06/1.2	Susceptible	≤ 0.25/4.8	Susceptible

[1]MIC: minimal inhibitory concentration. Performed by ARUP Laboratories (Salt Lake City, UT)

[2]–: Not done/not applicable

P. endophytica, and as a second agent for empiric treatment of *M. goodii*. Remarkably, the patient's wound began to heal promptly upon initiating combination antimicrobial therapy (Fig. 1D). The susceptibility profile obtained from ARUP Laboratories (Salt Lake City, UT) (Table 2) confirmed that this isolate of *M. goodii* was susceptible to both TMP/SMX and doxycycline. Therefore, this targeted antibiotic regimen was continued throughout the rest of his hospitalization and on discharge. The patient recovered well without any complications at the 3-month follow-up, with a plan to continue treatment for 6–12 months depending on clinical progress. As there are no clinical practice guidelines to direct the specific treatment of *M. goodii* infections, we chose a prolonged duration based on clinical experience, extrapolating evidence from recommendations for tissue and skeletal infections caused by related nontuberculous mycobacteria (NTM) [5].

Throughout his hospitalization, the patient's known history of EDS, poorly healing wounds, and frequent need for debridement of infected tissues prompted the investigation into possible immune dysfunction. Laboratory findings (Table 3) were remarkable for diminished percent and absolute natural killer (NK) cells (CD16+and CD56+), suggestive of innate cell-mediated immune system dysfunction. Further immunologic investigations are ongoing to determine the significance of this lymphocytopenia and its potential contribution to the infection.

Discussion

P. endophytica was recovered from the hardware infection, along with *M. goodii* in this patient. *P. endophytica*, a Gram-positive, rod-shaped, spore-forming bacterium in the family *Bacillaceae* [4], was previously known as *Bacillus endophyticus* (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?mode=Info&id=135735). Originally isolated from plant tissue, particularly cotton, *P. endophytica* has been explored for its potential role in enhancing crop productivity [6, 7]. It is characterized as an endophytic bacterium that colonizes the internal tissues of plants without causing disease [8]. The identification of *P. endophytica* as a pathogen in human infections is unprecedented [9].

Table 3 T and B natural killer cells panel results

Component	Result	Reference Range and Units
CD3%	**85%**	55–84%
CD4 ABS#[1]	1,412 Cells/ µL	690–2,540 Cells/ µL
CD4%	50%	31–60%
CD4 ABS#	867 Cells/ µL	410–1,590 Cells/ µL
CD8%	33%	13–41%
CD8 ABS#	559 Cells/ µL	190–1,140 Cells/µL
CD16 + 56%	**4%**	5–27%
CD16 + 56 ABS#	**56 Cells/ µL**	90–590 Cells/ µL
CD4/CD8 Ratio	1.5	0.8–4.2 Ratio
CD19%	10%	6–25%
CD19 ABS#	165 Cells/ µL	90–600 Cells/ µL

[1]ABS#: absolute count

Macroscopically and microscopically, *P. endophytica* closely resembles *Bacillus anthracis*, the causative agent of anthrax, posing challenges in differentiation. On Sheep Blood agar (SBA), *P. endophytica* colonies exhibited a white or grey-white, non-hemolytic appearance with irregular edges and a ground-glass appearance. Additionally, comma-shaped projections from the colony edge produced "Medusa-head" colonies (Fig. 2A). Gram staining (Fig. 2B) revealed endospore-forming, box-shaped rods of *P. endophytica* arranged in short to long chains. Lekota et al. [10], through whole-genome shotgun sequencing, demonstrated the absence of *B. anthracis*-related plasmids or virulence genes in *P. endophytica* genomes. Due to the similarity between *P. endophytica* and *B. anthracis* and the latter's classification as a biosafety level 3 (BSL-3) agent, molecular methods are typically utilized to rule out *B. anthracis* before further identification using MALDI-TOF MS or other manipulations in a clinical sentinel laboratory.

In our case, while the possibility of environmental contamination cannot be completely ruled out, the isolation of *P. endophytica* from intraoperative cultures, particularly in two out of three initial surgical tissue samples collected before antibiotic administration, along with the clinical presentation strongly suggests its involvement in the infection. However, it is also possible that an additional pathogen, undetected by culture, contributed to the infection and responded to the antibiotics administered. Ideally, 16S rRNA amplification and sequencing should have been performed on the original samples to confirm the absence of other contributing pathogens, which is a limitation of this study. Despite this, our report represents the first documented instance of *P. endophytica* potentially causing infection in humans.

M. goodii was the second uncommon organism isolated from our patient, contributing to the complexity of the infection. *M. goodii* is characterized as a rapid grower, acid-fast mycobacterium, forming smooth to mucoid, off-white to cream-colored colonies. These colonies may be nonpigmented or late pigmented [11]. It is quite ubiquitous in the environment and can be found in soil, dust, and drinking water [5, 12]. As a pathogen, *M. goodii* has been primarily associated with posttraumatic wound infections, particularly those following open fractures and associated osteomyelitis [11, 13]. Additionally, reports indicate its involvement in infections associated with surgical implants over the past two decades [14–16]. Our case adds to this body of evidence, representing another instance of *M. goodii* infection following traumatic injury with wound contamination, and

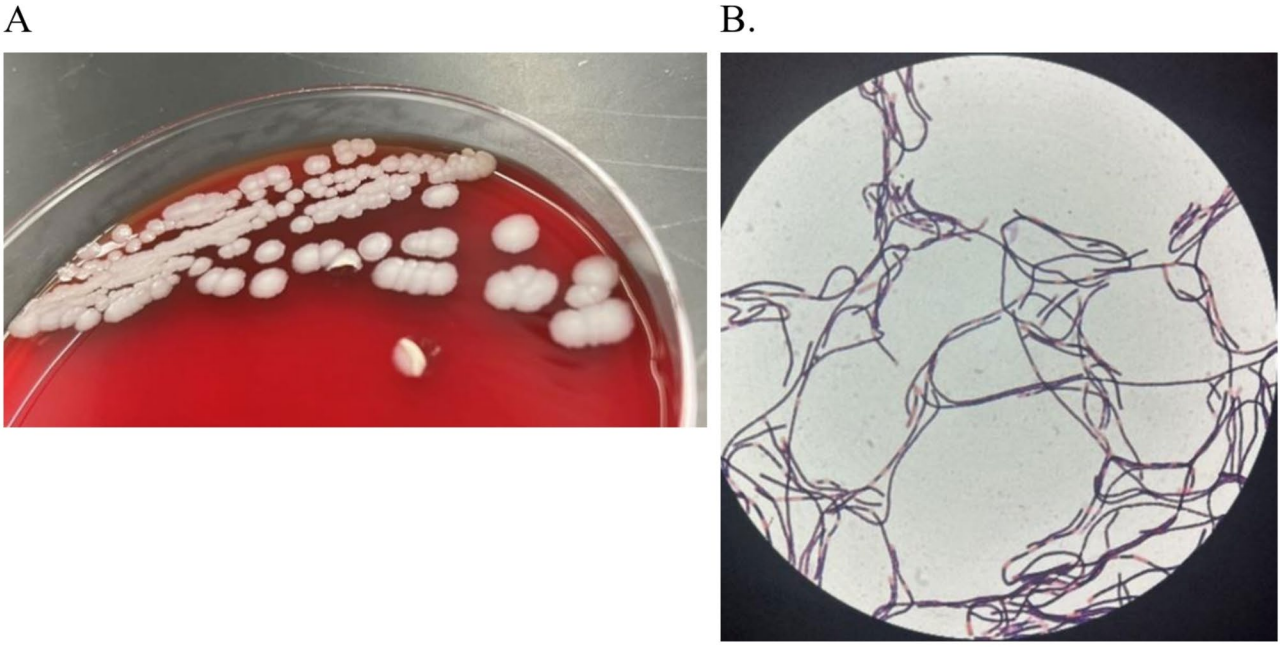

Fig. 2 (**A**) Isolate of *Priestia endophytica* on Sheep Blood agar. (**B**) Gram-stain of *Priestia endophytica* (1000×)

subsequent implantation of a foreign body. *M. goodii* typically displays susceptibility to amikacin, ethambutol, and sulfamethoxazole [11]. It exhibits intermediate susceptibility to ciprofloxacin, doxycycline, and tobramycin, with variable susceptibility to cefmetazole, cefoxitin, and clarithromycin. However, it is resistant to isoniazid and rifampin [11]. This susceptibility profile is not consistent with empiric therapy with clarithromycin and rifampin, commonly used for other rapidly growing NTM. Given the potential for treatment failure associated with monotherapy regimens utilizing TMP/SMX or doxycycline [15], a combination of TMP/SMX and doxycycline was administered to our patient to minimize the risk of recurrence or development of resistance.

Notably, our patient has EDS, a group of inherited disorders that affect the connective tissues in the body, primarily the skin, joints, and blood vessel walls (https://rarediseases.org/rare-diseases/ehlers-danlos-syndrome/). EDS encompasses several subtypes, each linked to mutations in different genes involved in collagen or other connective tissue component production [17]. However, the specific gene mutation underlying our patient's condition is unknown. Nevertheless, individuals with EDS may present compromised immune function as demonstrated in our patient on his lower natural killer cell count or other underlying health conditions that could predispose them to infections [18]. Therefore, it was not unexpected to encounter uncommon pathogens like *M. goodii* as the causative agent of severe necrosis and purulence at the surgical site. Additionally, it is plausible for a bacterium typically associated with plants to play a role in this patient's infection. It is also worth mentioning that the Food and Drug Administration (FDA) recommends avoiding fluoroquinolone antibiotics if a patient has EDS because of an association of this class of medication with the occurrence of aneurysm. This individualized approach emphasizes the importance of considering the specific characteristics of *M. goodii* infections, the patient's underlying conditions, and adapting treatment strategies accordingly.

Given the patient's immunodeficiency, careful consideration was given to its potential impact on treatment response and the risk of recurrent infections. Recognizing the influence of underlying health conditions, such as EDS, is essential in devising appropriate treatment strategies and managing complications effectively. Further investigation into the genetic basis of the patient's EDS subtype may provide valuable insights into their susceptibility to infections and guide future treatment approaches if necessary.

Conclusion

This case report underscores the identification of two infrequently encountered microbes, *P. endophytica* and *M. goodii*, as the potential culprits behind post-trauma hardware infection and abscess in a patient with EDS. Infections caused by *M. goodii*, although rare, can complicate traumatic orthopedic injuries, especially in patients with EDS and immune dysfunction. Successful management in this case required timely diagnosis, susceptibility-guided antibiotic therapy, and surgical intervention. The case emphasizes the importance of considering

atypical pathogens in complex clinical scenarios and tailoring therapeutic strategies accordingly. Furthermore, the use of modern diagnostic tools facilitates the recognition of previously unrecognized pathogens, highlighting the potential emergence of new infectious organisms. This report contributes to our understanding of managing challenging infections and emphasizes the need for continued vigilance and research in infectious diseases.

Abbreviations

EDS	Ehlers-Danlos Syndrome
BKA	Below-the-knee amputation
MALDI-TOF MS	Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry
AFB	Acid-fast bacilli
TMP/SMX	Trimethoprim/sulfamethoxazole
NK	Natural killer
SBA	Sheep Blood agar
BSL-3	Biosafety level 3
NTM	Nontuberculous mycobacteria
FDA	Food and Drug Administration

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Author contributions
A.L.C, F.M.C, J.E.P, and P.R. wrote the main manuscript text, A.L.C prepared Fig. 1 and Table 1, F.M.C prepared Fig. 2, J.E.P. prepared Tables 2 and 3. D.R. and P.R edited the manuscript. All authors reviewed the manuscript.

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Data availability
Sequence data that support the findings of this study have been deposited in NCBI GeneBank with accession # PP533212. Other data is provided within the manuscript.

Declarations

Ethical approval and consent to participate
As a case report, our study was exempt from our institutional clinical ethics committee.

Consent for publication
Written informed consent was obtained from the patient for the publication of this case report and any accompanying data and images.

Competing interests
The authors declare no competing interests.

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