The Brief Case: A Maggot Mystery—*Ignatzschineria larvae* Sepsis Secondary to an Infested Wound

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**CASE**

A 58-year-old man called 911 because his 54-year-old brother fell in their apartment. When emergency medical services (EMS) arrived at the apartment, they found it to be infested with insects and covered with animal feces. The EMS personnel deemed the apartment unfit for human habitation and were worried about either of the brothers remaining in the apartment. They brought both men to the Emergency Department (ED) for evaluation.

Upon ED presentation, the 58-year-old man who called to report his brother’s fall also appeared unwell in triage and underwent a full medical evaluation. He was known to have a past medical history of hypertension, bipolar disorder, alcoholism, polysubstance abuse with methadone maintenance, treated hepatitis C infection, and chronic venous stasis with ulceration of the lower extremities. He complained of a left ankle wound associated with increasing pain and drainage for the past 4 days. He denied fevers, chills, cough, nausea, chest pain, and headaches but did note increased diaphoresis, attributed to living in a non-air-conditioned apartment during a concomitant heat wave.

On physical exam, he was afebrile and had a stable blood pressure of 150/80 mm Hg. His lung fields were clear to auscultation, and there was no evidence of respiratory or gastrointestinal infection. The exam was notable for tremulousness, uneven smile with sluggish left pupillary reflex, poor dentition, distant heart sounds, and an open wound measuring 3 by 5 cm on the medial malleolus of the left lower leg, with evidence of dermatosclerosis and fluctuance but no visibly exposed bone. The lesion was tender, erythematous, and infested with maggots.

Laboratory results were notable for hyponatremia, hypoglycemia, leukocytosis, acute kidney injury, and elevated blood lactate. He received 1 liter of normal saline and empirical antimicrobial coverage with piperacillin-tazobactam and vancomycin. Several hours later, his blood pressure dropped to 85/56 mm Hg, at which point he was transferred to the intensive care unit (ICU). A wound culture obtained from the ulcer showed pure growth of methicillin-resistant *Staphylococcus aureus* (MRSA).

Admission blood cultures turned positive from the aerobic bottle after approximately 54 h, and the Gram stain was interpreted as positive for Gram-positive rods. After consultation with the Infectious Diseases Department, the differential diagnosis included contamination with nonpathogenic skin flora (e.g., *Corynebacterium*) versus a mixed aerobic/anaerobic soft-tissue infection, and metronidazole was added to improve anaerobic coverage.

After subculture and overnight incubation, abundant growth of small, translucent colonies was observed on Columbia agar with 5% sheep’s blood and chocolate agar (Fig. 1A), with scant growth of non-lactose-fermenting colonies on MacConkey agar. Gram stain from the solid media revealed Gram-negative rods (Fig. 1B), and...
both catalase and oxidase reactions were positive. The Gram stain from the positive blood culture bottle was reviewed and showed a Gram-variable appearance more consistent with underdecolorized Gram-negative rods. Further workup was performed using matrix-assisted laser desorption/ionization time of flight mass spectrometry (MALDI-TOF MS; Bruker Daltonics, Billerica, MA), but the highest matches were all associated with low-confidence scores (<1.30), with the top match being Chryseobacterium gleum (1.26) using the research-use-only (RUO) 7854 MSP Library. As an accurate phenotypic identification could not be made, the full 16S rRNA gene was amplified by PCR, and the amplicon underwent Sanger sequencing (Applied Biosystems 3500; ThermoFisher Scientific, Waltham, MA). The sequence was analyzed using BLAST (https://blast.ncbi.nlm.nih.gov), which yielded 99.5% sequence homology to both Ignatzschineria larvae and Ignatzschineria ureiclastica, with 98% homology to Ignatzschineria indica. As the top two sequence matches were identical, the isolate was reported as “Ignatzschineria spp.” Antimicrobial susceptibility testing was performed using a Microscan GN 42 panel (Beckman-Coulter, Brea, CA) with breakpoints for other non-Enterobacterales applied. Testing showed resistance to tetracycline but susceptibility to all other tested antimicrobials, and the Infectious Diseases team recommended discontinuing vancomycin, piperacillin-tazobactam, and metronidazole and switching the patient to oral levofloxacin.

The patient improved symptomatically and was discharged 3 days later to a subacute rehabilitation facility on oral levofloxacin and doxycycline. After completion of a 7-day course, the medical team at the nursing home noted a resolution of the patient’s cellulitis with a healed 5-cm eschar over the left medial malleolus. No further antimicrobial treatment was given, and the patient was advised to follow up in the clinic if needed.

Whole-genome sequencing (WGS) was subsequently performed on the isolate for species-level resolution for research purposes. DNA extracted from the isolate (DNeasy blood and tissue kit; Qiagen, Germantown, MD) was used to prepare libraries (Nextera Flex library preparation kit; Illumina, San Diego, CA), which were sequenced on an Illumina MiSeq using 2×300-bp paired-end reads. Illumina reads were then mapped to an I. ureiclastica reference genome (NCBI accession no. GCF_003121845) using snippy (https://github.com/tseemann/snippy) to identify single-nucleotide polymorphisms (SNPs) in the core chromosome, along with publicly available reads from NCBI for Ignatzschineria sp. strain F8392, Ignatzschineria cameli (strains UAEHKU57 to UAEHKU61), Ignatzschineria indica KCTC22643, and I. larvae DSM13226. Concatenated core genome SNPs totaling 1,302 bp were used to generate a maximum-likelihood phylogenetic tree with 100 bootstrap replicates using RaxML (1). Phylogenetic analysis showed separate clustering of Ignatzschineria sp. and I. indica (121-SNP pairwise distance) and I. larvae and I. ureiclastica (258-SNP pairwise distance), with 948- to 985-SNP distance across these two groups (Fig. 2). I. cameli isolates also formed a distinct
phylogenetic clade 369 to 1,000 SNPs apart from the other *Ignatzschineria* strains. The study isolate showed pairwise distances of 159 SNPs to *I. larvae* and 280 SNPs to *I. ureiclastica*, demonstrating that the patient isolate was most closely related to *I. larvae*.

**DISCUSSION**

*Ignatzschineria* is a genus of aerobic, Gram-negative rods first described in 2001 by Tóth et al. (2). It was isolated from the first and second larval stages of flies of the *Sarcophagidae* family and identified on the basis of 16S rRNA sequencing. The genus was named to honor Ignaz Rudolph Schiner, an Austrian entomologist who first described *Wohlfahrtia magnifica*, also known as the spotted flesh fly, in 1862. Tóth and her colleagues originally termed this new genus *Schineria* but in 2007 proposed a name change to *Ignatzschineria*, as a phylogenetically distinct genus of bacteria had already been given the name *Schineria*. They named the type species *Ignatzschineria larvae* (3).

Members of the *Ignatzschineria* genus are nonmotile, non-spore-forming, Gram-negative rods that grow on blood and MacConkey agars and form colonies that are small, convex, nonpigmented, and translucent. They are catalase and oxidase positive. Automated biochemical instruments may produce an incorrect identification or no identification at all (4). *Ignatzschineria* species have been described in human infections in several case reports, most of which involve wound infestation with *Wohlfahrtia larvae* and identification of *Ignatzschineria* species in blood and/or wound cultures. Of note, a large proportion of these case reports involve patients with peripheral neuropathy secondary to alcohol use disorder. Due to the association of *Ignatzschineria* infection with maggot-infested wounds, the isolation of *Ignatzschineria* species in clinical cultures should prompt a search for evidence of maggot infestation, and laboratories

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**FIG 2** Maximum-likelihood phylogenetic tree of the patient isolate (NK0278) and other members of the *Ignatzschineria* genus. Publicly available *Ignatzschineria* genomes and NK0278 Illumina reads were mapped against the *Ignatzschineria ureiclastica* KCTC 22644 genome (NCBI accession no. GCF_003121845) using Snippy. Core genome concatenated single-nucleotide polymorphisms (SNPs) were used to construct the maximum-likelihood phylogeny using RAxML with 100 bootstrap replicates. The sizes of the circles at each node are scaled to indicate bootstrap support.
should report any *Ignatzschineria* growth in culture, even if identified as a minor component of a polymicrobial infection.

In 2011, two additional species within the *Ignatzschineria* genus were identified by Gupta et al., *I. indica* and *I. ureiclastica* (5). Gupta’s team performed sequence analysis of the 16S rRNA, 23S rRNA, and gyrB genes from two purportedly novel isolates and compared them to gene sequences obtained from Tóth’s original isolate (*I. larvae* L1/68T) and an isolate of a closely related bacteria, *Wohlfahrtiimonas chitiniclastica*, that Tóth et al. first described in 2008 (6), which is also carried by *W. magnifica* larvae. Additional criteria that Gupta et al. used in establishing these two novel species included differential analysis of biochemical reaction patterns and DNA-DNA hybridization studies as well as identification of the predominant respiratory quinones, fatty acids, and cell membrane components in each of the isolates (5).

*I. indica* has been implicated in human infection in a number of case reports, including maggot infestation of the urinary tract (4), breast abscess (7), and several cases of bacteremia following maggot colonization of open wounds (8, 9). Of note, Le Brun et al. described a case of *Ignatzschineria*-associated septicemia arising in a clinical scenario very similar to our case, with the isolate identified only to the genus level, as 16S rRNA sequencing showed homology identical to that of both *I. larvae* (99%) and *I. ureiclastica* (99%) (10). There has been one reported case of sepsis due to *I. ureiclastica* in which a 99.7% 16S rRNA sequence homology was observed to the original *I. ureiclastica* (FFA37) GenBank isolate reported by Gupta et al. (11). To our knowledge, there are no definitive prior case reports of *I. larvae* infection in humans, although there are several reports in which species-level identification could not be reliably performed. Therefore, this case represents the first conclusive documented human infection with *I. larvae* confirmed by whole-genome sequencing.

Interestingly, the WGS data show a very high degree of sequence homology between *I. ureiclastica* and *I. larvae*, which are both substantially different from *I. indica*. Although the original description of *I. ureiclastica* included an extensive phenotypic analysis and 16S rRNA sequencing, WGS was not performed. Our WGS analysis suggests that *I. ureiclastica* and *I. larvae* instead are the same species or two highly related subspecies of *Ignatzschineria* that are genetically distinct from *I. indica*. This similarity may also partially explain the relative abundance of case reports of *I. indica* infection in humans, if clinical laboratories are unable to differentiate between the latter two species based on 16S rRNA sequencing alone, the result is likely to be reported to the genus level only. In addition, some case reports of *I. larvae* infection prior to the 2011 discovery of *I. indica* may actually represent cases of *I. indica*.

Currently, genus-level identification alone is sufficient for appropriate clinical management of patients with *Ignatzschineria* infections. However, in Gupta et al.’s 2011 report, the three purported species exhibited different antibiotic resistance profiles. Therefore, it is possible that species-level identification will be helpful in clinical management if the replicability of these resistance patterns can be demonstrated. Nevertheless, data from the limited number of case reports in the literature support that *Ignatzschineria* infections are typically susceptible to beta-lactams, and antimicrobial susceptibility testing on a clinical isolate, as was performed in this case, is a better tool for guiding therapy. Further studies into the virulence or pathogenicity among different *Ignatzschineria* species may also yield important clues about their relative propensity to cause invasive disseminated infections, as seen in this case.

**SELF ASSESSMENT QUESTIONS**

1. *Ignatzschineria* sepsis has been most frequently associated with which of the following preexisting conditions?
   a. Diabetes mellitus
   b. Hypertension
   c. Bipolar disorder
   d. Alcohol use disorder
2. Which of the following methods can be used to accurately differentiate Ignatzschineria species from one another? 
   a. Oxidase and catalase reactions 
   b. MALDI-TOF mass spectrometry 
   c. 16S rRNA sequencing 
   d. Whole-genome sequencing 

3. The principle arthropod vector of Ignatzschineria is also the major vector of which of the following bacterial species? 
   a. Aeromonas hydrophila 
   b. Wohlfahrtiimonas chitiniclastica 
   c. Wohlfahrtia magnifica 
   d. Chryseobacterium gleum 

REFERENCES