

CASE REPORT

A confusing case – *Weissella confusa* prosthetic joint infection: A case report and review of the literature

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The authors describe the first case of *Weissella confusa* infection of a prosthetic joint. Identification of the pathogen required 16S ribosomal RNA sequencing of isolates obtained on two separate occasions during the assessment of an elderly woman with a painful, swollen knee following total knee arthroplasty. A review of reported human infections due to *W confusa* are summarized, and risk factors and pitfalls in the application of empirical antimicrobial therapy pending definitive microbiological identification are discussed.

Key Words: Prosthetic joint infection; Vancomycin resistance; *Weissella confusa*

CASE PRESENTATION

A 94-year-old woman was referred to the general internal medicine service for functional decline secondary to longstanding knee pain. Her medical history included osteoarthritis and her surgical history was significant for a right total knee arthroplasty in 1996. On examination, her vital signs were normal; she was afebrile, but her right knee was red, warm and swollen. A joint effusion was believed to be present. Orthopedic surgery was consulted to help determine whether a prosthetic joint infection was present. Her initial blood work showed an erythrocyte sedimentation rate of 54 mm/h (normal 0 mm/h to 27 mm/h), a C-reactive protein level 52.6 mg/L (normal 0 mg/L to 1 mg/L) and a white blood cell count of $6.2 \times 10^9/L$ (normal $4.0 \times 10^9/L$ to $10.5 \times 10^9/L$). A plain radiograph of the knee demonstrated loosening of the tibial component, with a large joint effusion believed to show metallosis – a deposition of metallic debris in the periprosthetic soft tissues from abrasion of metallic components (1). An aspirate of the knee revealed calcium pyrophosphate crystals, with a total nucleated cell count of $11.3 \times 10^9/L$ and differential of 97% neutrophils. She was subsequently discharged to a nursing home with a tentative diagnosis of pseudogout. Later, an enrichment broth subculture of the aspirate demonstrated growth of a Gram-positive bacillus, which was identified as a *Lactobacillus* species based on the following results: unidentifiable profile on RapID™ ANA II panel (Oxoid Canada), catalase-negative, PYR-negative, LAP-negative and vancomycin resistance.

She presented six weeks later with *Escherichia coli* bacteremia arising from an acute urinary tract infection. A reassessment of the right knee showed a marked increase in swelling with persistent pain and tenderness. Orthopedics was once again consulted to evaluate the knee. Infectious diseases was subsequently consulted to comment on the significance of the *Lactobacillus* species that had grown on culture from the previous admission. A second aspirate was requested and grew the same organism, which was identified as a *Lactobacillus* species. Of note, there were no calcium pyrophosphate crystals apparent in this aspirate and the total nucleated cell count and differential were

L'infection d'une prothèse articulaire par le *Weissella confusa* : rapport de cas et analyse bibliographique

Les auteurs décrivent le premier cas d'infection d'une prothèse articulaire par le *Weissella confusa*. Il a fallu séquencer l'ARN ribosomique 16S des isolats à deux moments distincts de l'évaluation d'une femme âgée dont le genou était enflé et douloureux après une arthroplastie totale du genou. Les auteurs résument l'analyse des infections causées par le *W confusa* chez les humains et traitent des facteurs de risque et des écueils dans l'instauration d'une thérapie antimicrobienne empirique en attendant de confirmer l'agent microbiologique en cause.

TABLE 1
Antimicrobial susceptibilities of two *Weissella confusa* isolates according to the agar dilution method

Antibiotic	Minimum inhibitory concentration, mg/mL	
	Isolate 1	Isolate 2
Ampicillin	0.5	0.5
Chloramphenicol	8	4
Ciprofloxacin	≤1	2
Clindamycin	≤0.5	≤0.5
Daptomycin	≤0.5	≤0.5
Erythromycin	≤0.25	≤0.25
Gentamicin	≤2	≤2
Levofloxacin	2	2
Vancomycin	Resistant	Resistant
Linezolid	4	2
Moxifloxacin	0.5	0.5
Penicillin	0.5	0.5
Tetracycline	8	4
Trimethoprim/sulfamethoxazole	>4	>4

$3.1 \times 10^9/L$ and 96% neutrophils, respectively. The isolate was sent to the Ontario Public Health Laboratory (Toronto, Ontario) for identification using 16S ribosomal RNA sequencing (2).

DIAGNOSIS

16S ribosomal RNA sequencing revealed that the organisms from both knee aspirate cultures were identical and were subsequently identified as *Weissella confusa*. Susceptibility testing of the organism from both isolates was performed using the agar dilution method and minimum inhibitory concentrations for various antibiotics are summarized in Table 1.

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TABLE 2
Summary of previously documented *Weissella confusa* infections

Author (reference), year	Clinical infection (n)	Predisposing factors (n)	Outcome (n)
Salimnia et al (12), 2011	Bacteremia (2)	ALL/ASCT (1); severe burns (1); central catheter (1)	Survived (2)
Harlan et al (8), 2011	Bacteremia (1)	HCC/liver transplant (1)	Survived (1)
Lee et al (10), 2011	Bacteremia (10)	Malignancy (4);CT (3); chronic steroid use (3); abdominal surgery (4); concomitant polymicrobial infection (5); central catheter (6)	Survived (4); death (6)
Kumar et al (9), 2011	Bacteremia (1)	Gastroesophageal adenocarcinoma (1), CT (1), endoscopy (1)	Survived (1)
Kulwichit et al (13)	Osteomyelitis (1)	Unknown	Survived (1)
Shin et al (5), 2007	Endocarditis (1)	None	Survived (1)
Flaherty et al (7), 2003	Endocarditis (1)	Chronic alcoholism (1), previous steroid use (1)	Death (1)
Olano et al (11), 2001	Bacteremia (1)	Abdominal surgery (1), polymicrobial infection (1)	Survived (1)
Bantar et al (6), 1991	Thumb abscess (1)	None	Survived (1)

ALL Acute lymphocytic leukemia; ASCT Autologous stem cell transplant; CT Chemotherapy; HCC Hepatocellular carcinoma

DISCUSSION

Weissella was first described as a new genus in 1993 and was named after Norbert Weiss, a German microbiologist known for his contributions to lactic acid bacteriology. It is identified using 16S ribosomal RNA sequencing to differentiate it from other organisms such as *Lactobacilli* and other members of the family *Leuconostocaceae* (3,4). Usual phenotypic identification methods have been shown to be ineffective and often lead to misidentified organisms (4). Fourteen species in total have been identified, of which two – *W. confusa* and *Weissella cibaria* – are clinically important because of their ability to infect human hosts and intrinsic resistance to vancomycin. *Weissella* species are alpha-hemolytic, Gram-positive coccobacilli that typically grow in chains and are catalase negative and bile esculin positive. What differentiates *W. confusa* and *W. cibaria* are the acidification of different sugars (5). It was named ‘confusa’ because it was often mistaken for members of the *Leuconostoc*, *Pediococcus* and *Lactobacillus* genera (3).

W. confusa has a widespread environmental distribution and has been found in a variety of foods including sugar cane, carrot juice, milk, fermented meats, garlic mix and banana leaves. Congruently, it can be part of the normal microflora of the human intestine and can be found in human stool (4). Conversely, invasive infection with *W. confusa* is rare. A PubMed search was conducted using the search terms “*Weissella confusa*”, “infection” and “immunocompromised”, revealing a total of 19 cases in the English literature: 15 with bacteremia, two with endocarditis, one with osteomyelitis and one with a thumb abscess (Table 2) (4-12). To our knowledge, we present the first case of a prosthetic joint infection caused by *W. confusa*.

In the largest case series, Lee et al (10) reported 10 patients with bacteremia in a tertiary care centre in Taiwan. Risk factors for invasive infection in this series included an immunocompromised host, central line catheter insertion and concurrent polymicrobial bacteremia. Recent chemotherapy and malignancy appeared to be common factors among immune-deficient patients. These findings were similar to case reports by Harlan et al (8) and Salimnia et al (12), who identified bacteremia in patients with hepatocellular carcinoma post-liver transplant and acute lymphocytic leukemia undergoing autologous stem cell transplantation, respectively. Other case reports have included risk factors for immunocompromised states, which consisted of chronic alcoholism, previous long-term steroid use and severe burn patients (7,12). Similarly, gastrointestinal manipulation via endoscopy or surgery may be one of the routes of translocation into the bloodstream because six of the reported 19 cases had documented medical procedures within three months of infection (8-11).

W. confusa is intrinsically resistant to vancomycin and exhibits high minimum inhibitory concentrations (4-12). This is important to recognize because clinicians often use vancomycin empirically as a treatment option in the immunocompromised patient when cultures initially reveal a Gram-positive organism in the blood. This can be

fatal in cases in which recognition of the organism is not identified in a timely fashion. The antimicrobial susceptibilities for *W. confusa* are quite variable and not fully elucidated. Studies have reported high levels of resistance to trimethoprim/sulfamethoxazole, metronidazole, teicoplanin, ceftazidime and ceftriaxone. Varying degrees of in vitro susceptibility have been documented for linezolid and meropenem. In general, penicillin, clindamycin, erythromycin, daptomycin and the fluoroquinolones are effective agents for treating *W. confusa* infections (10).

What was unique to our case was the lack of predisposing factors in our patient. While the patient did have evidence of a concomitant *E. coli* bacteremia at her second presentation, she had already grown *W. confusa* from the first aspirate of her knee six weeks previously. She received a one-week course of levofloxacin for her *E. coli* bacteremia, which unfortunately, provided minimal clinical benefit to her prosthetic knee infection. She was discharged from hospital and returned to her long-term care facility in stable condition. Given her pre-morbid state and non-ambulatory status, it was decided in discussion with the patient and her family to not pursue further medical or surgical therapy for her prosthetic joint infection.

CONCLUSION

W. confusa is a rare, but well documented, cause of invasive infection in humans. Microbiological identification of *W. confusa* is best made using 16S ribosomal RNA sequencing. *W. confusa* infection can be treated with a variety of antimicrobials such as penicillins and fluoroquinolones; however, it exhibits intrinsic resistance to vancomycin.

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