Contents lists available at ScienceDirect



Journal of Microbiology, Immunology and Infection

journal homepage: www.e-jmii.com



Culture-negative orthopedic implant-associated infection due to Mycoplasma hominis: A case report

ARTICLE INFO

Keywords: Mycoplasma hominis Orthopedic implant-associated infection Periprosthetic joint infection Osteosynthesis-associated infection

Dear Editor:

Effective treatment of orthopedic implant-associated infections (OIAIs) or periprosthetic joint infections (PJIs), both used interchangeably in this report, is challenging, especially for the cases of unrecognized etiology. *Mycoplasma hominis*, a fastidious bacterium, has been acknowledged as one of the pathogens of urogenital diseases. However, extra-urogenital infections, especially OIAIs caused by *M. hominis* have been reported, although rarely.^{1,2} Here we report a case of OIAI due to *M. hominis*.

A 20-year-old man with a high body mass index (35.9 kg/m²) and without a past history of sexually transmitted disease or recent genitourinary symptoms, had a Garden IV closed fracture of left femoral neck in a traffic accident. He was admitted for orthopedic surgery and underwent urethral insertion of an indwelling Foley catheter at 14 hours before surgery. Turbid urine with sediments was observed after insertion and urinalysis showed neither pyuria nor bacteriuria. There were no symptoms or signs of urinary tract infection. However, transient gross hematuria was ever noted, and the urethral catheter was removed on the second day after surgery. However, no perioperative urine culture to verify the presence of *M. hominis* was obtained. On the sixth day after open reduction and internal fixation as shown in Fig. 1a, he presented with fever as well as erythema and purulent discharge at the surgical site (Fig. 1b). Empirical oral amoxicillin-clavulanic acid was administered, but the signs of incisional surgical site infection (SSI) persisted. Five days later, emergent surgical debridement was performed. Piperacillintazobactam and vancomycin were parenterally administered for severe SSI. Due to persistent fever and pus from the incisional site, surgical debridement extending into left hip joint was performed three days later. The pathological diagnosis of debrided soft tissue was acute suppurative inflammation, which is suggestive of OIAI. However, from two aerobic and anaerobic bacterial cultures of pus and debrided soft tissue, blood cultures, and Gram staining of purulent discharge, no etiological pathogen could be identified. Therefore, oral doxycycline was empirically prescribed for the suspicion of incisional SSI and OIAI due to a fastidious pathogen. Surgical debridement was conducted again one week later, and polymerase chain reaction (PCR) targeting bacterial 16S ribosomal RNA (rRNA) was performed on the debrided tissue (Fig. 1c), in which no bacterial, mycobacterial, or fungal pathogen was isolated. The diagnosis of *M. hominis* infection was supported by the 16S rRNA PCR assay, which demonstrated that the partial sequences of the amplified fragment were 99.61 % (770/773) identical to those of *M. hominis* ATCC 23114 (accession number JN935871) deposited in the GenBank database. Parenteral tigecycline therapy was initiated, defervescence occurred, and serum inflammation markers, including C-reactive protein (CRP), erythrocyte sedimentation rate and leukocyte count, declined gradually. Incisional wound was closed after four weeks of tigecycline therapy, and he was discharged with oral doxycycline, which was prescribed for eight weeks. Doxycycline was replaced by moxifloxacin due to persistent elevated levels of serum CRP, which became normalized after 8 weeks' moxifloxacin therapy (Fig. 1d). He underwent total hip replacement at another hospital by the patient discretion.

M. hominis is an uncommon cause of extra-genital infections, and its infection can be a diagnostic dilemma due to its fastidious nature. In orthopedic surgeries, OIAIs or PJIs are serious types of SSIs, and pathogen-specific antimicrobial therapy is strongly recommended.^{3,4} To our knowledge, OIAIs or PJIs due to *M. hominis* were not reported in Taiwan. In a study of 178 episodes of PJIs after total knee arthroplasty between 2002 and 2014 in Taiwan, *Staphylococcus aureus*, coagulase-negative *Staphylococcus* and *Streptococcus* species were the common pathogens.⁵ However, no pathogen could be identified by conventional cultures in more than a quarter (27.5 %) of these PJI episodes.5 Thus, to maximize the diagnostic yield of OIAIs or PJIs, prolonged incubation of aerobic and anaerobic bacterial, mycobacterial, and fungal cultures, and broad-range 16S rRNA PCR for tissue samples or body fluids, and *Coxiella burnetii* serology may be utilized.

There were some microbiological or clinical hints of *M. hominis* infections warranting physicians' attention, including pinpoint and transparent colonies on conventional agars, the staining failure by Gram stain, culture-negative OIAIs in immunocompromised patients, and recent urinary tract manipulation. The speculative pathogenesis of extra-urogenital infection involves hematogenous seeding of colonized *M. hominis* from urogenital tract to osteoarticular prostheses following urinary manipulation, particularly in the immunocompromised individuals.^{6,7} Thus, differential diagnosis of culture-negative OIAIs

https://doi.org/10.1016/j.jmii.2025.03.007

Received 9 August 2024; Received in revised form 9 March 2025; Accepted 15 March 2025 Available online 17 March 2025

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Fig. 1. Radiological image, wound pictures, and timeline of the case. (1a) A radiographic film shows dynamic hip screw fixation for left femoral neck fracture with good alignment. (1b) Purulent discharge springs up from the surgical site after squeezing. (1c) Infected surgical site was debrided. (1d) Clinical course and serial white blood cell counts and serum levels of C-reactive protein. Note: WBC, white blood count; CRP, C-reactive protein; Lt: left; ORIF, open reduction internal fixation; rRNA, ribosomal RNA; ABX, antibiotic; THR, total hip replacement; AMC, amoxicillin-clavulanate; TZP, piperacillin-tazobactam; VAN, vancomycin; DOX, doxy-cycline; MPM, meropenem; TGC, tigecycline; MOX, moxifloxacin.

should take *M. hominis* into consideration, and 16S rRNA gene sequencing can improve the diagnostic yield for etiological surveys. Clinical awareness of variable etiologies for culture-negative OIAIs is crucial for appropriate management to improve patient and prosthetic outcomes.

Ethics statement

Informed consent of the case report was waived as the patient could not be identified in descriptions or photographs.

Funding statement

This study was supported by the grants from National Science and Technology Council, Taiwan (NSTC 113-2321-B-006-007).

CRediT authorship contribution statement

Tian-Yu You: Writing – original draft, Data curation, Conceptualization. Nan-Yao Lee: Writing – review & editing, Formal analysis. Tai-Hua Yang: Data curation. Po-Lin Chen: Writing – review & editing, Data curation. Ming-Chi Li: Writing – review & editing, Data curation. Shu-Li Su: Data curation. Yu-Wei Hsu: Data curation. Wen-Chien Ko: Writing – review & editing, Conceptualization.

Conflict of interest

There are no conflicts of interest to be declared by the authors.

Acknowledgment

We are grateful to the Diagnostic Microbiology and Antimicrobial Resistance Laboratory, National Cheng Kung University Hospital, for providing technical services in microbiological investigations.

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