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Case Report

Periprosthetic joint infection associated with *Mycoplasma hominis* after transurethral instrumentation in an immunocompetent patient. Unusual or underestimated? A case report and review of the literature

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ABSTRACT

Judging by the small number of published cases, periprosthetic joint infections (PJI) caused by *Mycoplasma species* are regarded as unusual. This is not surprising as special growth conditions are necessary for diagnosis and therefore the laboratory must be informed of any clinical suspicion. However, surgeons are generally not aware of the risk factors associated with certain microorganisms causing an infection. Our laboratory therefore decided to adopt a new strategy: first, to address specific questions concerning the medical history of the patient and second, to make diagnosis of rare and fastidious microorganisms part of routine investigation, even if detailed information is not available.

Introduction

Judging by the small number of published cases, periprosthetic joint infections (PJI) caused by *Mycoplasma species* are rather unusual. They are regarded as microorganisms with fastidious growth requirements for detection under culture conditions. Owing to their small cell size, they usually do not even produce turbidity in broth cultures. Consequently, routine conditions may fail to isolate them. We have introduced a method for diagnosis of PJI that covers the identification of fastidious microorganisms, including *Mycoplasma hominis,* under routine conditions.

Case report

A 68-year-old man with a history of osteoarthritis underwent total knee arthroplasty in 2005. In 2018 he was diagnosed with prostatic hypertrophy. Because of restricted miction he received an indwelling catheter for several weeks before being admitted to hospital for a transurethral biopsy. Ten days later, the patient experienced increasing pain at the site of his knee prosthesis. Effusion and fever occurred, and he was hospitalized in the orthopaedic department of the Johanniter Hospital in Rheinhausen. Radiological assessment showed no signs of fractures or prosthesis loosening. C-reactive protein was elevated at 279 mg/L, and aspirated joint fluid revealed a white blood cell (WBC) count of 223,688/μL with 82% polymorphonuclear neutrophils. The alpha-defensin test was positive. The aspirated fluid was sent for analysis in a blood culture bottle and reported negative after 14 days.

Three days after admission, irrigation and debridement were performed and several days later the modular components were exchanged. Five biopsies were sent for microbiological investigation. Empirical therapy was initiated with IV cefazolin 2 g/8 h in combination with rifampicin 600 mg/24 h for ten days. In addition, ciprofloxacin 500 mg/12 h was administered for ten days because of catheter-related genitourinary infection with *Pseudomonas aeruginosa.* Histological examination of periprosthetic tissue revealed inflammatory infiltrates of neutrophil granulocytes.

Aerobe and anaerobe culture on diverse agar plates remained sterile after 14 days of incubation. We have published detailed information about culture conditions for PJI elsewhere (Rieber et al., 2018). All specimens were cultured in the routinely used modified semifluid thioglycollate broth (LT) containing ox liver digest supplemented with horse serum and hemin (SIFIN, Berlin, Germany), and after seven days of incubation they all showed

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unevenly distributed turbidity due to agar content. Gram staining revealed no visible microorganisms.

Mass spectrometry (MALDI-TOF, BrukerDaltonics, Bremen, Germany) failed to identify any organisms to the species level. Molecular 16S rRNA partial gene sequence analysis was performed from LT broths showing a similarity of 99.80% (507/508 nucleotides) compared to the reference sequence of the type strain *Mycoplasma hominis* (GenBank accession no. AF443616). For antimicrobial susceptibility testing the strain was subsequently sub-cultured using the commercial selective kit Mycoplasma IST 2 (bioMerieux, Marcy l'Etoile, France).

The strain revealed low minimum inhibitory concentration (MIC) for doxycycline, tetracycline, ciprofloxacin and ofloxacin. Elevated MICs were found against macrolides, underlining the intrinsic resistance of *M. hominis*. Furthermore, the strain was tested using the agar gradient diffusion technique for tetracycline and levofloxacin, evaluated by Waites et al., yielding results comparable to broth microdilution (Waites et al., 1999; Waites et al., 1997). The MICs were interpreted according to the guidelines of the Clinical and Laboratory Standards Institute (CLSI) (CLSI, 2011). For quality control the type strain *M. hominis ATCC* 23114 was used.

Finally, the patient was treated orally with levofloxacin 500 mg/12 h and doxycycline 100 mg/12 h according to testing results for four weeks.

Three weeks after revision the patient was discharged from hospital without impairment of wound healing. Two months later, he underwent a transurethral prostatectomy with complication and died unexpectedly.

Discussion

The genus *mycoplasma* is included in the class known as *Mollicutes. Mycoplasma species* are smaller than most bacteria and are distinguished by the lack of a cell wall. Fourteen species of human origin are described within this genus (Jorgensen et al., 2015). Among other species, *M. hominis* can exist as commensals primarily associated with mucosa in the urogenital tract of healthy humans. For an overview of related systemic infections see Manual of Clinical Microbiology (Jorgensen et al., 2015).

Focusing on joint-related infection, *M. hominis* has been found to cause septic arthritis in rare cases, especially if associated with immunosuppression (Garcia-Porrua et al., 1997; MacKenzie et al., 2010). However, only six articles have linked *M. hominis* to PJI; interestingly, with a long interval between the reports: three in the mid-1980s and three within the last decade.

All cases from the last decade were associated with postoperative wound infection after joint replacement surgery (Lee et al., 2009; Smith et al., 2016; Qiu et al., 2017). On the other hand, two articles from the mid-1980s reported two cases of PJI with *M. hominis* as the sole causative agent (Sneller et al., 1986; Nylander et al., 1989). Finally, a review article introduced 11 cases investigated by the authors with *M. hominis* infection occurring outside the genitourinary tract in adults, and 14 cases from the literature. In each group the authors presented only one case associated with PJI (Madoff and Hooper, 1988).

Overall, little attention has been paid to the method of antimicrobial susceptibility testing. It is worth mentioning that the agar disk diffusion test is no longer useful because there have been no correlations between inhibitory zones and MICs. However, reliable information about MICs is an important prerequisite to prevent treatment failure because of antimicrobial resistance. Furthermore, there are no studies investigating whether the strategy used for urogenital infections can be applied to PJI. This is important as the common factor in most of the reported cases was a severe course of long-lasting and difficult-to-treat infection.

Waites et al. demonstrated that the ingredients of commercial blood culture media are not suitable for multiplying *M. hominis,* confirming our negative results from incubated joint fluid (Waites and Canupp, 2001). We therefore investigated the amount of *Mycoplasma hominis* in LT broth, a nutritionally high-complex medium that we had evaluated for better and faster growth of anaerobes (Rieber et al., 2018). Using quantitative real-time PCR, a high bacterial concentration was detected (Table 1). To our surprise, this offers an opportunity for cultivation of *Mycoplasma* and *Ureaplasma species* in a non-selective medium, making diagnosis easier under routine conditions. Further investigations are needed to confirm this observation.

As a short-cut, next-generation sequencing is a powerful method in microbiology, harbouring simultaneous information about the identity, drug sensitivity and if necessary, tracing sources of outbreaks. At present, we prefer the more cost-effective eubacterial PCR, if culture generates negative results even though infection is suspected or one of the following factors has been reported in the patient's medical record: immunosuppression, rheumatoid arthritis and related genitourinary infection or manipulation. Thanks to this concept, we can now report a further unpublished case with PJI of the hip in an immunocompromised patient where we detected *Ureaplasma urealyticum* as the causative agent.

PJI caused by *Mycoplasma* and *Ureaplasma species* must certainly be regarded as rare, but it is not as exceptional as the few isolated cases reported in the literature might make us believe. Due to its affinity to human mucosa, there must be a great reservoir of carriers. Disruption of the mucosal barrier might easily promote bacterial dissemination and cause joint and implant-associated infections.

In our case, despite the tragic outcome, PJI was well managed and the prosthesis was retained. The result may have been positively influenced by the early administration of ciprofloxacin against the catheter-related infection with *P. aeruginosa,* as this antibiotic was probably effective against *M. hominis* even before its detection, and the absence of severe risk factors like immunosuppression. This case certainly shows that being immunocompetent does not rule out PJI *with M. hominis*. Accurate diagnosis of

Table 1
Molecular investigation from blood culture bottle and Liver-Thioglycollate broth (LT).

Specimen	Eubacterial PCR from blood culture bottle after 14 days of cultivation	Real-time PCR from LT broth after 7 days of cultivation	Copies/ml from LT broth
Joint fluid	*M. hominis*[a]		
Biopsy/patellar		*M. hominis*	8×10^7
Biopsy/patellar		*M. hominis*	5×10^8
Biopsy/medial		*M. hominis*	2.4×10^8
Biopsy/lateral		*M. hominis*	2.7×10^8
Biopsy/dorsal		*M. hominis*	5×10^8

[a] Flagged negative by the instrument.

infections such as these present a great challenge to microbiologists.

Conflict of interest statement

None of the authors has a conflict of interest.

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Ethical approval was not required.

References

CLSI. Methods for antimicrobial susceptibility testing for human mycoplasmas; approved guideline CLSI document M43-A. Wayne, PA: Clinical and Laboratory Standards Institute; 2011.

Garcia-Porrua C, Blanco FJ, Hernandez A, Atanes A, Galdo F. Septic arthritis by *Mycoplasma hominis*: a case report and review of the medical literature. Ann Rheum Dis 1997;56:699–700.

Jorgensen JH, Pfaller MA, Carroll KC, Funke G, Landry ML, Richter SS, 11th ed. Manual of clinical microbiology, vol. 1. American Society of Microbiology; 2015.

Lee JH, Lee JH, Lee NY, Ha CW, Chung DR, Peck KR. Two cases of septic arthritis by *Mycoplasma hominis* after total knee replacement arthroplasty. Korean J Lab Med 2009;29(2):135–9.

MacKenzie CR, Nischik N, Kram R, Krauspe R, Jäger M, Henrich B. Fatal outcome of a disseminated dual infection with drug-resistant *Mycoplasma hominis* and *Ureaplasma parvum* originating from a septic arthritis in an immunocompromised patient. Int J Infect Dis 2010;14(Suppl. 3):e307–9.

Madoff S, Hooper DC. Nongenitourinary infections caused by *Mycoplasma hominis* in adults. Rev Infect Dis 1988;10:602–13.

Nylander N, Tan M, Newcombe DS. Successful management of *Mycoplasma hominis* septic arthritis involving a cementless prosthesis. Am J Med 1989;87:348–52.

Qiu H-J, Lu W-P, Li M, Wang Z-M, Du Q-Y, Wang A-M, et al. The infection of *Mycoplasma hominis* after total knee replacement: case report and literature review. Chin J Trauma 2017;20:243–5.

Rieber H, Frontzek A, Jerosch J, Alefeld M, Strohecker T, Ulatowski M, et al. Periprosthetic joint infection caused by anaerobes. Retrospective analysis reveals no need for prolonged cultivation time if sensitive supplemented growth media are used. Anaerobe 2018;50:12–8.

Smith BJ, Crowe A, Comahig J, Sheorey H, Stanley P. A 27-year-old woman with an Unusual cause of periprosthetic joint infection. Clin Infect Dis 2016;62(11):1463.

Sneller M, Wellborne F, Barile MF, Plotz P. Prosthetic joint infection with *Mycoplasma hominis*. J Infect Dis 1986;153:174–5.

Waites KB, Canupp KC. Evaluation of BacT/ALERT system for detection of *Mycoplasma hominis* in simulated blood cultures. J Clin Microbiol 2001;39:4328–31.

Waites KB, Canupp KC, Kenny GE. In Vitro susceptibilities of *Mycoplasma hominis* to Six Fluoroquinolones as determined by Etest. Antimicrob Agents Chemother 1999;43:2571–3.

Waites KB, Crabb DM, Duffy LB, Cassell GH. Evaluation of the Etest for detection of tetracycline resistance in *Mycoplasma hominis*. Diagn Microbiol Infect Dis 1997;27:117–22.