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CONCISE ARTICLE

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Severe *Mycoplasma hominis* Infections in Two Renal Transplant Patients

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Abstract Systemic infections due to *Mycoplasma hominis* are rare and occur mainly in immunocompromised patients. Reported here are the cases of two renal transplant patients with peritonitis who did not respond to empirical antimicrobial treatment. Effective treatment with doxycycline was administered only after definitive identification of *Mycoplasma hominis* was achieved. For this identification, the new genetic amplification-sequencing method was invaluable.

Introduction

Mycoplasma hominis is known to colonize the urogenital tract and may cause localized infections, but it rarely causes severe infections [1, 2, 3]. Among the few cases of systemic infection that have been reported previously, the affected patients were mostly immunocompromised and had undergone renal transplantation [2, 4, 5]. Reported here are two additional cases of systemic *Mycoplasma hominis* infections that occurred following renal transplantation.

Case Reports

Case 1 involved a 33-year-old female who had been diagnosed with diabetes mellitus type I in 1975 and had severe hypertension with cardiac complications. Since 1999 she had been receiving hemodialysis treatment for terminal renal insufficiency, and in 2001 she underwent renal and pancreatic allograft transplantation. On day 10 after surgery, the patient presented with fever, diarrhea and abdominal fluid collection in the pouch of Douglas. Drainage was performed, and *Enterococcus faecium* was isolated from a hematoma. Empiric antimicrobial therapy was begun with amoxicillin and gentamicin, but this was replaced by vancomycin and gentamicin when susceptibility testing of the isolate revealed amoxicillin resistance. On postoperative day 27, the nephrotoxic vancomycin and gentamicin combination was replaced by linezolid.

On day 36 a computed tomography-guided aspirate was collected. Although no microorganisms could be visualized microscopically on Gram stain, many leukocytes were present and, after 2 days of incubation on Columbia blood agar, hemolytic, translucent colonies grew abundantly (i.e., on all streaked quadrants). Gram stain of these colonies was also negative, whereupon mycoplasma infection was suspected. Amplification and sequencing of the 16S ribosomal RNA gene from these colonies definitively identified *Mycoplasma hominis* [6]. Based on this result, antimicrobial treatment was changed to doxycycline. In parallel, a urinary tract infection due to *Escherichia coli* and *Klebsiella oxytoca* was diagnosed, and ciprofloxacin was added with a favorable outcome.

Case 2 involved a 56-year-old diabetic female with a history of end-stage renal failure who had received a renal graft in 1986 as well as pancreatic cell injection in 1997. Unfortunately, both organs were non-functional. In 2002 she was readmitted for double transplantation of the kidney and pancreatic islets. The patient's clinical evolution was favorable from the aspect of transplantation, but she experienced several subfebrile peaks (38 to 38.5°C) and a urinary tract infection was suspected to be the cause.

Microbial urine cultures yielded mixed gram-positive flora (10^4 cfu/ml). Antibiotic therapy with ceftriaxone was initiated, but the patient's abdominal status did not improve. An abdominal computed tomography scan was subsequently performed, revealing an infrarenal fluid collection of about 5 cm in diameter; a sample was collected by aspiration on postoperative day 18 and submitted for microbiological analysis. Antibiotic therapy was then switched to imipenem, since a mixed infection with anaerobic bacteria was suspected. As in the preceding case, no microorganisms could be visualized microscopically, but abundant leukocytes and many hemolytic translucent colonies appeared on blood agar plates after 2 days of incubation. Again, infection with a *Mycoplasma* sp. was suspected and subsequently confirmed when *Mycoplasma hominis* was identified by amplification and sequencing. Accordingly, antimicrobial treatment was changed to doxycycline on day 23, and the patient improved remarkably; in fact, she was able to leave the hospital 30 days after surgery.

Discussion

Mycoplasma spp. are small bacteria (0.2–0.3 μm in diameter) that lack a typical bacterial peptidoglycan cell wall; therefore, they cannot be visualized on Gram stain.

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For the same reason, they present a pleomorphic morphology (round to filamentous) and are not susceptible to antibiotics that inhibit peptidoglycan synthesis, like penicillins, cephalosporins, carbapenems, or glycopeptides [1]. Furthermore, mycoplasmas are difficult to detect by culture due to their fastidious growth requirements, which are associated with their extremely small genomes and their limited biosynthetic capabilities.

The origin of *Mycoplasma hominis* infections in transplant patients may be the colonized urogenital tract of either the recipient or the donor of the graft. Renal transplant patients are therefore particularly at risk after surgical interventions of the urogenital tract and due to their immunosuppression. However, extragenital *Mycoplasma hominis* infections have also been reported in heart, heart and lung, or liver transplant patients [2] who have not undergone surgical manipulation of the urogenital tract. In these patients, immunosuppression is certainly the main risk factor.

Although *Mycoplasma hominis* is an organism of low pathogenicity, it can lead to a fatal outcome if adequate treatment is not administered [2]. For this reason, it is important to detect these infections reliably and rapidly. Many cases may not be diagnosed owing to the difficulty of staining, growing and identifying this organism using traditional microbiological techniques. Microbiologists should be aware that *Mycoplasma hominis* grows on common media such as blood agar-based media, on which colonies can often be recognized by their hemolysis [3]. Gram stain of these colonies reveals no common bacteria, subcultures rarely grow, and conventional microbiological procedures can only identify the microorganism with the help of unusual and complicated techniques [4]. Thus, a much more reliable and rapid identification method is the now more commonly applied genetic amplification of the eubacterial 16S ribosomal RNA gene by PCR, using broad-range primers [6]. The subsequent sequencing of the PCR product allows a definitive identification, not only of mycoplasmas but of many other bacteria as well [6, 7]. Nevertheless, the diagnosis may be complicated when mixed infections with other more common bacteria occur, as illustrated in case 1 reported above.

Treatment of *Mycoplasma hominis* infections with certain widely used antimicrobial agents is ineffective, owing to the inherent resistance of *Mycoplasma* spp. to agents acting on peptidoglycan synthesis (e.g., beta-lactam antibiotics, glycopeptides). Susceptibility tests may be performed with commercial kits, such as Mycoplasma IST (bioMérieux, Lyon, France), however it is difficult to achieve standardized inocula and consistent result interpretation [1]. Empirically, tetracyclines and quinolones are the drugs of choice for treating these infections [2, 4, 5].

The two cases reported here emphasize the importance of rapid, definitive diagnosis in order to achieve optimal patient outcome. However, since many cases may remain undiagnosed, the real incidence and outcome of these infections without specific treatment remains unknown. In the cases reported here, the new and more readily available molecular biological methods proved invaluable in achieving an accurate diagnosis.

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