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CASE REPORT

Actinomyces urogenitalis Bacteremia and Tubo-Ovarian Abscess after an *In Vitro* Fertilization (IVF) Procedure

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We describe the first case of bacteremia due to *Actinomyces urogenitalis*. Bacteremia was secondary to a tubo-ovarian abscess following transvaginal oocyte retrieval. Identification was established by matrix-assisted desorption ionization–time of flight mass spectrometry (MALDI-TOF MS) and confirmed by 16S rRNA gene sequencing. *A. urogenitalis* should be considered as a potential causative agent of infection after gynecological procedures.

CASE REPORT

We report a case of a 40-year-old, nulliparous woman presenting to the emergency department with high fever (40.7°C), shivering, and vomiting. These symptoms began immediately after coitus. Anamnesis revealed a 2-week history of intermittent fever, low abdominal pain, headache, and anorexia following a transvaginal oocyte retrieval (TVOR) and embryo transfer in the context of *in vitro* fertilization (IVF). Moreover, the patient suffers from Crohn's disease, which had resulted in a right hemicolectomy in the past. She had not received any treatment for Crohn's disease in the last 2 years. She had no history of intrauterine contraceptive device (IUCD) use. Clinical examination showed blood pressure of 110/60 mm Hg, a heart rate of 74 beats per min, and saturation of 98%. Auscultation of the lungs, heart, and abdomen gave normal results. The abdomen was soft, nontender, and nondistended. There was no cervical discharge. Laboratory analysis demonstrated a normal white blood cell (WBC) count (4×10^9/liter) and moderately elevated C-reactive protein (CRP) (26.8 mg/liter). The serum beta-human chorionic gonadotropin (beta-HCG) level was undetectable (<0.1 U/liter). No WBCs were detected in the urine. Both abdominal and vaginal ultrasounds were performed, with no abnormalities visualized except for a swollen right adnexa uteri. The patient was at that point discharged from the hospital with the presumptive diagnosis of pelvic inflammatory disease (PID). In attendance of results of cultures of vagina, urine, and blood, empirical antibiotic therapy was started: amoxicillin-clavulanic acid (two doses, 2 g each) and doxycycline (two doses, 100 mg each). Furthermore, a vaginal specimen for *Chlamydia trachomatis* detection and bacterial culture was taken. Only 2 days later, the patient presented again to the emergency department with persistent lower abdominal pain. A computed tomography (CT) scan of the abdomen showed a large right adnexal multilocular collection. The WBC count was increased to 19.6×10^9/liter, and CRP was increased to 261.7 mg/liter. By then, the original blood cultures had become positive, showing straight to slightly curved Gram-positive rods with rudimentary branching. The original urine culture was negative, and the vaginal culture showed a normal presence of *Lactobacillus* spp. in the absence of WBCs. Neither *C. trachomatis* nor *Neisseria gonorrhoeae* was detected. A diagnosis of PID with abscess formation and bacteremia was made. Antibiotics (amoxicillin-clavulanic acid, four doses, 1 g each) were given intravenously, and laparoscopic exploration was performed. Because of many adhesions due to a previous hemicolectomy for Crohn's disease, switching to a laparotomy was mandatory. The right adnexal abscess was drained, and a microbiological culture was taken. Gram staining of the drained fluid showed Gram-positive rods, similar to those in the blood culture, in the presence of abundant polymorphonuclear leukocytes. Both blood culture and drained fluid culture revealed anaerobic growth of smooth colonies which were catalase-negative, nonsporulating, nonmotile, nonhemolytic, and aerotolerant Gram-positive rods. Both isolates were identified as *Actinomyces urogenitalis* by matrix-assisted laser desorption ionization–time of flight mass spectrometry (MALDI-TOF MS) (score > 2.0) using a Bruker Biotyper (Bruker Daltronics, Inc., Leipzig, Germany). The phenotypic characteristics, as determined using API 20 strep (bioMérieux, Marcy l'Etoile, France), resulting in profile 5356450, were similar to those described by Nikolaitchouk (1). Identification was further confirmed by partial sequencing of the 16S rRNA gene, according to interpretative criteria as defined by the Clinical and Laboratory Standards Institute (CLSI) (2). Our strain exhibited 99.8% similarity (508 bp) with the type strain CCUG 38702 (AJ243791) of *A. urogenitalis*, using the GenBank database and the BLAST algorithm for sequence alignment. Furthermore, our strain differed from other species in 16S rRNA gene sequence by more than 1%. The most closely related species was an *Actinomyces bovis* strain with 97% identity. Susceptibility testing was performed using Etest strips (bioMérieux) according to the method of Smith et al. (3). MICs were interpreted following the guidelines of the European Committee on Antimicrobial Susceptibility Testing (EUCAST), indicating susceptibility to ampicillin, piperacillin-tazobactam, ceftriaxone, meropenem, clindamycin, linezolid, and vancomycin. MICs of penicillin, ciprofloxacin, moxifloxacin, and metronidazole showed resistance (Table 1). Postoperatively, the patient

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TABLE 1 Susceptibility results

Antimicrobial agent	MIC (mg/liter)	Interpretation[a]
Penicillin	1	R
Ampicillin	0.5	S
Ceftriaxone	0.25	S
Piperacillin-tazobactam	0.5	S
Meropenem	0.008	S
Ciprofloxacin	>32	R
Moxifloxacin	1.5	R
Metronidazole	>256	R
Erythromycin	0.5	
Clindamycin	2	S
Cotrimoxazole	0.5	
Tetracycline	0.125	
Linezolid	0.25	S
Vancomycin	0.25	S

[a] Interpretation following EUCAST clinical breakpoints, v. 3.0. R, resistant; S, susceptible.

recovered well. Inflammatory parameters decreased to normal values. Eight days after surgery, the patient was discharged from the hospital. However, antibiotic therapy was continued for 5 more days *per os*.

Actinomyces spp. are classically defined as a heterogenous group of anaerobic, nonsporulating, non-acid-fast, Gram-positive rods which are associated with actinomycosis, a rare, chronic granulomatous disease. Since the introduction of 16S rRNA gene sequencing, several new *Actinomyces* spp. have been described. Little is known of their natural habitat or clinical significance, however. *Actinomyces urogenitalis* was described as a novel species in 2000 based upon the characterization of three isolates recovered from the human urogenital tract (1). Since then, it has become clear that *A. urogenitalis* is part of the normal flora of the human vagina. Colonization with high concentrations of *A. urogenitalis* can occur in cases of bacterial vaginosis, but its role in the pathogenesis is unclear (4). Only one case of *A. urogenitalis* infection has been described so far (5). The bacterium was isolated from the IUCD of a patient suffering from fever and cervical discharge. Pelvic actinomycosis is a well-established complication of IUCD use, and several *Actinomyces* spp. have been implicated in this disease (6). We report the first case of *A. urogenitalis* bacteremia secondary to tubo-ovarian abscess. In contrast to findings in previous publications, the infection was not associated with IUCD use but was a complication of ultrasound-guided, transvaginal oocyte retrieval (TVOR). The importance of *Actinomyces* spp. in gynecological surgical-site infections is further supported by two other recent reports of pelvic abscesses, one after TVOR (*Actinomyces israelii*) and another after total abdominal hysterectomy and salpingectomy (*Actinomyces hongkongensis*) (7, 8).

Accurate identification of *Actinomyces* spp. has always been difficult. The many taxonomic changes have made identification by phenotypic tests almost impossible (9, 10, 11). Molecular techniques using 16S rRNA gene sequencing are an effective means for the identification of *Actinomyces* spp. (12, 13, 14). Partial 16S rRNA gene sequencing of our isolate demonstrated more than 99% identity with the *A. urogenitalis* type strain CCUG 38702 (GenBank accession no. AJ243791). Recently, the introduction of MALDI-TOF MS has revolutionized microbial identification in clinical microbiology. Several recent publications demonstrate the ability of MALDI-TOF MS to correctly and rapidly identify *Actinomyces* spp. (15, 16, 17, 18). MALDI-TOF MS may be considered an alternative method for routine identification, provided the database is up to date. The Bruker MALDI Biotyper (Bruker Daltronics) correctly identified our isolate, while Vitek MS (bioMérieux) could not identify the strain, since *A. urogenitalis* is not present in the database.

Data regarding the antimicrobial susceptibility of *A. urogenitalis* are very scarce. The susceptibility profiles of only two *A. urogenitalis* strains have been described previously (5, 19). These strains demonstrated susceptibilities to penicillin, ampicillin, piperacillin-tazobactam, ceftriaxone, and clindamycin but resistance to metronidazole and fluoroquinolones. Our strain showed a similar profile, with the exception of penicillin. There are currently no CLSI or EUCAST standards for testing and reporting of antibiotic susceptibility results for *Actinomyces* spp. In most publications, data were generated by Etest methodology. In general, *Actinomyces* spp. showed susceptibility to a wide range of beta-lactam antibiotics and resistance to fluoroquinolones and metronidazole. Species differences in antimicrobial susceptibility have been described, however, necessitating the need for reliable identification (3, 19, 20).

TVOR is a procedure known to be possibly complicated by infection and pelvic abscess formation. However, the incidence is generally low and varies between 0.03% and 1.3% (7, 21–27). Transvaginal inoculation of bacteria into the peritoneal cavity or ovary by the collecting needle is the most apparent source of these infections (23, 28, 29). Furthermore, reactivation of a latent PID or direct colonic injury is also a possible, but less likely, mechanism of a post-TVOR pelvic infection (28, 30). It is plausible that in our case the organism was inoculated from the vagina into the ovary by the transvaginal procedure. The presence of pelvic adhesions, which were abundant in our case, is a known risk factor for post-TVOR infection (26). It is uncertain to what extent this has contributed to the development of an abscess in our case. As the clinical history of lower abdominal pain and intermittent fever shows, the abscess formation most likely started immediately after the TVOR, while the bacteremia with symptoms of sepsis was most likely mechanically induced by coitus.

The possibility of preventing such infections using preoperative vaginal disinfection or prophylactic antibiotics has been investigated (31). Our patient received neither of the two. Preoperative disinfection of the vagina with topical antiseptics, such as povidone iodine, has been questioned because of potential embryotoxic effects of disinfectants, resulting in a lower pregnancy rate (29, 32, 33). However, this has recently been contradicted (34). The efficacy of the procedure in preventing infection has been evaluated, resulting in opposite conclusions and recommendations (24, 34). The use of prophylactic antibiotics for TVOR is widespread, although the antibiotic used differs greatly: cefoxitin, ceftazidime, cefazolin, and the combination of cefazolin and metronidazole have been proposed (21, 22, 26, 28). The usefulness remains controversial, however, because of the low incidence of post-TVOR pelvic infection whether antibiotics are used or not (23, 26, 35). There is currently no standard of care in terms of antibiotic prophylaxis before TVOR, resulting in a great diversity of approaches between institutes (36).

This is the first case of *A. urogenitalis* bacteremia. Bacteremia

was secondary to tubo-ovarian abscess, complicating TVOR. This report confirms the pathogenic potential of this bacterium to cause human disease. While IUCD use is an established risk factor for pelvic actinomycosis, recent publications, including ours, suggest a broader role of *Actinomyces* spp. in gynecological surgical-site infections. Future publications are needed to further elucidate the clinical significance of these bacteria.

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