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First Report of *Atopobium vaginae* Bacteremia with Fetal Loss after Chorionic Villus Sampling▽

Marjolein Knoester,[1]* Lisa E. E. L. O. Lashley,[2] Els Wessels,[1] Dick Oepkes,[2] and Ed J. Kuijper[1]

Department of Medical Microbiology[1] and Department of Obstetrics and Gynecology,[2] Leiden University Medical Center, Leiden, Netherlands

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Infectious complications after chorionic villus sampling (CVS) are rare (<0.1%) but can lead to maternal sepsis and spontaneous abortion. We report the first bacteremia with *Atopobium vaginae* and suggest *A. vaginae* to be a pathogenic microorganism that can lead to intrauterine infection and fetal death following CVS.

CASE REPORT

A 40-year-old woman, gravida 7, para 3, underwent transcervical chorionic villus sampling (CVS) in the 12th week of pregnancy for advanced maternal age. Her obstetric history revealed three healthy children, one spontaneous miscarriage, one induced abortion, and an ectopic pregnancy with tubal removal. Her medical history revealed a mild diaphragmatic hernia for which she used acid secretion inhibitors. The CVS was done under ultrasound guidance using a biopsy forceps. In a single attempt, 30 mg of villi were obtained without complications.

In the days following the CVS procedure, the patient developed fever with temperature up to 40°C and vomiting. Seven days after the CVS, she visited the emergency room for ongoing fever and chills; there was no abdominal pain or vaginal blood loss. Laboratory results were as follows: Hb, 10.8 g/dl; white blood count, 2.5×10^9/liter (89.6% neutrophils); C-reactive protein, 222 mg/liter. On X-ray and abdominal ultrasound no signs of pneumonia or abdominal focus were found and a normal fetal heartbeat was observed. The patient was admitted. A blood culture (including two bottles, for aerobic and anaerobic incubation, respectively) and a cervix sample were taken, after which antibiotic treatment was initiated with intravenous cefuroxime (750 mg, three times a day [t.i.d.]). Three days later, the patient developed cramping abdominal pain and had blood-stained vaginal discharge. By ultrasonography, fetal death was observed. The abortion started spontaneously but had to be completed by aspiration curettage. Following the procedure, the temperature normalized and cefuroxime therapy was ended (day 4). The patient was discharged from the hospital at day 5 after admission. At the day of discharge, the anaerobic blood culture bottle became positive with *Atopobium vaginae* (see below), after which amoxicillin (1 g, four times a day [q.i.d.]) was prescribed for 2 weeks.

Microbiological data. No cultures of the cervix or vagina were done before the CVS procedure since the patient had no symptoms of vaginitis or bacterial vaginosis.

At hospital admission, a sample of the cervix and one set of blood cultures were taken before antibiotics were initiated. A urinary culture and three more blood cultures were taken in the next 14 h.

Microscopic examination and culture of the urinary sample were not indicative for an infection. The culture of the cervix smear yielded no *Neisseria gonorrhoeae*, no group B beta-hemolytic streptococci, and no yeasts. However, a culture of small grayish nonhemolytic colonies grew on the blood plate in an anaerobic environment. Gram staining showed Gram-positive rod-shaped organisms which were considered a nonpathogenic component of the vaginal flora. Of the four pairs of blood culture bottles, one bottle of the first set became positive in the automated blood culture system (BACTEC; BD Diagnostics) with Gram-positive streptococci after 4 days of anaerobic incubation. The isolate grew on sheep blood agar as small bright gray colonies, nonhemolytic, after 48 h of anaerobic incubation at 37°C. It was catalase and oxidase negative and could not be identified by the use of RAPID ID 32A (bioMérieux, Sweden). Identification by matrix-assisted laser desorption/ionization–time of flight mass spectrometry (MALDI-TOF MS; 3,476 spectra, updated through 17 February 2010; Microflex; Bruker Daltonics, Germany) resulted in the determination of *Atopobium vaginae* (identification score, >2.0; reliable identification at species level). The result was confirmed by 16S rRNA gene sequencing, which was performed as described in a previous article (16), with some minor changes. The 1,033-bp amplicon was obtained using the P0 (5′-GGC TCA GAT TGA ACG CTG GC −3′) and P4 primer pair. It showed 100% sequence similarity with the 16S rRNA gene sequence of *A. vaginae* (GenBank accession no. AF325325).

Antimicrobial susceptibility was determined by the Etest assay (bioMérieux, Sweden). EUCAST clinical breakpoints for Gram-positive anaerobic bacteria were applied (http://www.eucast.org). The following results were obtained: penicillin MIC, 0.094 μg/ml (clinical breakpoint, 0.025 to 0.5 μg/ml); metronidazole MIC, 24 μg/ml (clinical breakpoint, 4 μg/ml); clindamycin MIC, <0.016 μg/ml (clinical breakpoint, 4 μg/ml); vancomycin MIC, 1.5 μg/ml (clinical breakpoint, 2 μg/ml); and cefuroxime MIC, 0.125 μg/ml (no clinical breakpoint available for anaerobic Gram-positive bacteria).

Chorionic villus sampling (CVS) is considered a relatively

* Corresponding author. Mailing address: Department of Medical Microbiology, Leiden University Medical Center, Postbus 9600, 2300 RC Leiden, The Netherlands. Phone: 31 71 526 5781. Fax: 31 71 526 6981. E-mail: m.knoester@lumc.nl.

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safe, though invasive, procedure for prenatal diagnosis if early diagnosis is required. CVS can be performed either transcervically or via the abdomen. The choice between transcervical and transabdominal CVS is made on the basis of the location of the placenta and the expertise of the operator.

Intrauterine infection is a rare complication of CVS but can lead to maternal sepsis with serious and lethal impacts (2, 18). Interestingly, in early studies the rate of fetal loss was not associated with microbial colonization of the instruments used (4, 24, 26). However, the incidence of intrauterine infection after CVS declined to <0.1% since the use of a single catheter was abandoned when multiple insertions to obtain placental tissue are required (14). Still, Silverman et al. reported a transient bacteremia in 1.8% of women undergoing CVS, finding no significant difference between the transcervical and transabdominal approaches (25).

The current procedure for the prevention of infections due to transcervical CVS consists of antiseptic cleansing of the genital tract with iodine on cotton wool. An active vaginal infection is a contraindication for an invasive transcervical procedure (14), though the need for routine cultures before CVS has so far been declined by the studies of Kagie et al. (15) and Wilson et al. (30).

In literature, few examples of proven septic abortions following CVS, due to *Candida albicans* (21) or group B beta-hemolytic streptococci (9, 20), have been depicted. *A. vaginae* bacteremia after CVS, however, has never been described.

***Atopobium vaginae*.** The genus *Atopobium* belongs to the class *Actinobacteria*, order *Coriobacteriales*, and family *Coriobacteriaceae*. In 1992 the genus was proposed (6) to accommodate the species *Atopobium rimae* (formerly known as *Lactobacillus rimae*), *Atopobium parvulum* (formerly *Streptococcus parvulus*), and *Atopobium minutum* (formerly *Lactobacillus minutum*). In 1999 a facultative anaerobic Gram-positive bacterium that was isolated from the vaginal flora of a healthy woman was phylogenetically and phenotypically designated *A. vaginae* (22). Microscopically, it appeared as small elongated Gram-positive cocci, which occurred singly, in pairs, or in chains (22). The new species was assumed to be as nonpathogenic as *Lactobacillus* species, but from 2004 on it has been suggested to play a role in bacterial vaginosis (3, 5, 10–12, 29), which in turn is associated with premature birth (8, 17, 19). *A. vaginae* has also been found to have caused a tuboovarian abscess following transvaginal oocyte recovery (13). Recently, a case of uterine endometritis caused by *A. vaginae* has been reported (31).

No previous cases of *A. vaginae* bacteremia have been described in the literature, but two reports are available on sepsis with other species from the genus *Atopobium*: a 38-year-old man suffering from an *Atopobium detroiti* sepsis that probably originated from a necrotic decubitus ulcer of the hip or from poor oral hygiene and an *Atopobium rimae* sepsis in a 77-year-old women with pneumonia (1, 23).

The *A. vaginae* isolate described in this case report was identified by MALDI-TOF MS as described by van Veen et al. (28) and confirmed by 16S rRNA gene analysis. The MALDI-TOF MS reference database by Bruker (updated through 17 February 2010) contained one strain of *A. vaginae*.

Susceptibility testing of the first few *A. vaginae* strains suggested intrinsic metronidazole resistance (10, 13) and susceptibility to clindamycin (10), which is in line with our results. However, De Backer et al. showed that *A. vaginae* is not intrinsically resistant to metronidazole, since they found a variable susceptibility ranging from 2 to more than 256 μg/ml (7).

We suggest that in the present case *A. vaginae* was transported from the woman's cervix into the uterus during the chorionic villus sampling, where it caused an intrauterine infection that led to fetal death and bacteremia of the mother. The small grayish colonies that grew in the culture of the cervix sample may have represented *A. vaginae*, but as it was not possible to reexamine the culture, we cannot provide evidence for this. A second hypothesis, given that the literature shows that transient bacteremia occurs in nearly 2% of women undergoing CVS (25), is that the mother may have had a CVS-induced bacteremia and the fetus was subsequently infected. In both scenarios it is remarkable that only one out of four sets of blood cultures became positive. This may be due to the initiation of antimicrobial therapy with cefuroxime after obtaining the first set. Additionally, the bottles were incubated for only 7 days and *Atopobium* species tend to grow slowly. It has been described that anaerobic streptococci are less easily detected by automated blood culture systems (27). This may contribute to an underestimation of the role of *A. vaginae* in clinical syndromes.

In conclusion, we suggest *A. vaginae* to be a pathogenic microorganism that can lead to maternal bacteremia and fetal death following CVS. The association between cervical colonization and septic abortion after CVS should be reassessed using the advanced techniques of bacterial identification now available.

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