Septic Abortion with Intact Fetal Membranes Caused by Campylobacter fetus subsp. fetus

GREGORY E. STEINKRAUS[1] AND BRENT D. WRIGHT[2,3,4]*

Department of Pathology and Laboratory Medicine[1] and Department of Obstetrics and Gynecology,[2]
New Hanover Regional Medical Center, and Department of Obstetrics and Gynecology, Coastal
Area Health Education Center,[3] Wilmington, and Department of Obstetrics and Gynecology,
University of North Carolina at Chapel Hill, Chapel Hill, North Carolina[4]

We report a case of septic abortion with intact fetal membranes caused by Campylobacter fetus subsp. fetus in an 18-year-old woman who was 9 1/2 weeks pregnant.

Septic abortion develops in approximately half of 1% of all pregnant women. The leading cause of septic abortion in which the fetal membranes are intact is reported to be Listeria monocytogenes (9). The association of Campylobacter fetus subsp. fetus with disease in humans has not been frequently documented. The most common type of infection encountered is septicemia in a compromised host (11). In cattle and sheep, C. fetus subsp. fetus possesses a marked tropism for placental tissue and is responsible for abortion (3). Recently it was documented to be the cause of premature labor and neonatal sepsis in humans (2). Prior to the case reported here, reported cases of campylobacteriosis in pregnant women have occurred during the second and third trimesters.

We report here a case of septic abortion with intact fetal membranes caused by C. fetus subsp. fetus in an 18-year-old woman who was 9 1/2 weeks pregnant. She presented to our hospital with a 3-week history of lower abdominal pain with associated fever and chills. Her medical history was unremarkable except for an uncomplicated spontaneous vaginal delivery 3 years earlier.

On admission, her temperature was 102.4°F (39.1°C), her pulse was 106/min, and her respirations were 18/min. The abdomen was tender in the bilateral lower quadrants, with guarding in response to deep palpation. Cervical motion tenderness was present, and the cervix was noted to be dilated to the width of a fingertip. The uterus was enlarged and tender. A pelvic ultrasound demonstrated a crown rump length consistent with a 9 1/2-week intrauterine pregnancy. There was no fetal cardiac or other type of activity noted.

The patient's total leukocyte count was 9,400/mm³, with 77% segmented neutrophils, 4% band neutrophils, 135 lymphocytes, and 6% monocytes. The hemoglobin level was 9.6 mg/dl and the hematocrit concentration was 27.7%. The total platelet count was 333,000/mm³. Blood cultures were reported as negative following 7 days of incubation, while a cervical culture demonstrated a moderate amount of usual vaginal flora. Blood cultures were processed with the BACTEC NR 730 system. All cultures were read both visually and by the instrument twice a day for the first 3 days and daily for the final 4 days. At the end of the 7 days, each culture was subcultured to TSA II sheep blood agar plates and incubated under microaerophilic conditions for 48 h before finalization of cultures.

The patient underwent suction curettage. Prior to surgery, 1 g of cefoxitin and 100 mg of doxycycline were administered. The cervical os easily admitted a no. 33 Pratt dilator. A polyp forceps was used to open the internal os. A long spinal needle was inserted through the intact membranes, and approximately 2 ml of greenish fluid was obtained and immediately sent for culture.

Postoperatively, the patient was treated with cefoxitin and doxycycline for 72 h. Fever subsided on the second postoperative day. The patient was discharged and given oral ampicillin and metronidazole.

A Gram stain of the greenish fluid revealed the presence of curved, spiral-shaped, weakly staining gram-negative rods. On the basis of this microscopic morphology and staining reaction, the specimen was also cultured for Campylobacter species by inoculating the surface of the following agar media: Mueller-Hinton agar with 5% sheep blood (Remel, Lenexa, Kans.), TSA II 5% sheep blood, and chocolate II agar (BBL, Cockeysville, Md.). The inoculated plates were then placed in a GasPak jar (BBL) along with a CAMPYPAK II microaerophilic envelope (BBL), and incubated at 35°C.

Following 48 h of incubation, all plates displayed a moderate amount of single colony morphology. Colonies were 1 to 2 mm in diameter and were smooth, convex, translucent, and nonhemolytic. A Gram stain of the growth revealed curved, spiral-shaped, weakly staining gram-negative rods. The isolate was catalase and oxidase positive. A characteristic darting motility was demonstrated following suspension of the isolate in brucella broth and examination by phase-contrast microscopy. A test for nitrate reduction was positive, and there was growth in 1% glycine. A test for hippurate hydrolysis was negative, and there was no production of hydrogen sulfide in triple-sugar-iron agar. The isolate's identity was confirmed by the Laboratory Section of the North Carolina Department of Human Resources. In vitro susceptibility testing was performed by agar dilution with Wilkins-Chalgren medium. The isolate was susceptible to ampicillin (0.5 µg/ml), amoxicillin-clavulanic acid (0.125 µg/ml), cefotaxime (0.125 µg/ml), cefoxitin (4.00 µg/ml), ceftazidime (1.00 µg/ml), cephalothin (4.00 µg/ml), ciprofloxacin (0.125 µg/ml), doxycycline (0.25 µg/ml), erythromycin (0.5 µg/ml), gentamicin (0.25 µg/ml), imipenem (0.12 µg/ml), mezlocillin (0.5 µg/ml), tobramycin (0.25 µg/ml), and trimethoprim-sulfamethoxazole (1.0 µg/ml).

Serological testing for antibodies to C. fetus was performed by complement fixation. Single convalescent-phase specimens from both the patient and her sexual partner were tested. The normal reference range was less than 1:8; the patient had a C.

* Corresponding author. Mailing address: Department of Obstetrics and Gynecology, Coastal Area Health Education Center, 2131 S. 17th St., P.O. Box 9025, Wilmington, NC 28402-9025. Phone: 910-343-0161. Fax: 910-762-9203.

fetus titer of 1:8, while her sexual partner had a titer of less than 1:8. Testing was performed by Specialty Laboratories, Inc., Santa Monica, Calif.

The association of *Campylobacter* species with disease in animals has been known for approximately 80 years. Early findings showed that *C. fetus* subsp. *fetus*, then called *Vibrio fetus*, caused diarrhea in cattle and septic abortion in sheep and cattle (6, 8, 10). Approximately 99% of all human *Campylobacter* isolates reported to the Centers for Disease Control from 1982 to 1986 were *Campylobacter jejuni*, while less than 1% were *C. fetus* subsp. *fetus* (12). Infection with *C. fetus* subsp. *fetus* has been suggested to be more common than is generally assumed (1). Among the cases in which a clinical source was reported, approximately 78% of *C. jejuni* isolates were recovered from stool matter, whereas for *C. fetus* subsp. *fetus* isolates, 54% were recovered from blood (12).

C. fetus subsp. *fetus* is a recognized cause of bacteremia and sepsis in immunocompromised human hosts (11). The organism is also a leading cause of sporadic and epidemic abortions in cattle and sheep (3). In 1960, it was reported to be the etiologic agent in a case of human abortion (5), and recently it was implicated in premature labor and neonatal sepsis in a 26-week human pregnancy (2).

Septic abortion with intact fetal membranes is an infrequent event, reportedly occurring in approximately 0.5% of all pregnant women. The intact placental membranes, cervical mucus, and bacterial inhibitory nature of amniotic fluid are effective barriers and are principally responsible for maintaining sterility in the amniotic cavity. A number of bacteria and viruses are capable of causing septic abortion in the presence of intact membranes, including *L. monocytogenes, Streptococcus agalactiae, Proteus mirabilis, Staphylococcus aureus, Escherichia coli, Enterococcus faecalis, Klebsiella pneumoniae*, coagulase-negative staphylococci, *Pseudomonas aeruginosa, Fusobacterium nucleatum*, and *Bacteroides bivius* (7).

The most likely mechanism of infection in our patient appears to be vascular or lymphatic spread from the gastrointestinal tract. This is the mechanism of infection most commonly seen in cattle and sheep. It is not uncommon to recover *C. fetus* subsp. *fetus* from the intestinal tracts of asymptomatic cattle and sheep. Stool matter was not collected for culture, as our patient displayed no gastrointestinal symptoms. Additionally, the prevailing view is that this organism does not cause diarrhea or gastroenteritis. This perception may not be correct and may be a function of the incubation temperature and selective media employed by laboratories to recover *C. jejuni* and other enteric campylobacters from stool matter.

Ginsberg et al. (4) reported the presence of *C. fetus* subsp. *fetus* sepsis in cancer patients receiving "nutritional therapy" requiring the consumption of raw beef liver. Although our patient denied ingestion of any food or drink possibly linked to *Campylobacter* species, it is our feeling that the gastrointestinal route represents the most likely portal of entry for the organism.

Additional evidence supporting a gastrointestinal source with vascular spread comes from serological data. The patient's serological response to the organism was measured at 1 year following infection. A complement fixation titer of 1:8 was recorded at this time, which suggests previous exposure. The patient's sexual partner was also tested, and his titer was less than 1:8. We were unable to obtain serologic titers prior to this time. These data indicate that the patient's disease was, in all probability, not sexually transmitted and supports the mechanism of hematogenous spread.

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