FATAL INTRAUTERINE INFECTION ASSOCIATED WITH PENICILLIN-RESISTANT STREPTOCOCCUS PNEUMONIAE

Streptococcus pneumoniae is a major respiratory pathogen and it is rarely found in the female genital tract. Pelvic infection may occur, especially in puerperal women and in nonpregnant women using intrauterine contraceptive devices. Pneumococcal early onset septicemia with a high mortality rate has been described in neonates. We report an intrauterine infection with S. pneumoniae in the third trimester of pregnancy resulting in stillbirth.

Case report. A 27-year-old woman, gravida 2, para 0, had Crohn's disease that was quiescent while receiving mesalazine 500 mg daily. Her first pregnancy 2 years earlier ended in a spontaneous abortion at 6 weeks of gestation. Her prenental course was uneventful and the gestational age was confirmed by an early ultrasound examination. At 26 weeks of gestation she developed a cough for a few days but had had no fever. At 27 weeks of gestation she was admitted to our hospital with a 3-day history of ruptured membranes. There were some uterine contractions, the oral temperature was 37.3°C and the fern test was positive, indicating the presence of amniotic fluid in the vagina. On examination the cervix was closed and no vaginal discharge was seen. At this time routine surveillance cultures of the cervix were obtained. Fetal heart rate was about 150 beats/min without abnormalities. Almost no amniotic fluid was seen on ultrasound.

The laboratory data included a white blood cell count of 8400 cells/mm³. In the absence of signs and symptoms of intrauterine infection, it was decided to use ritodrine therapy intravenously, resulting in cessation of contractions. Betamethasone was given to promote lung maturation. Twenty-four hours after admission the contractions returned and the dose of ritodrine was increased. Twelve hours later the temperature rose to 38.1°C and the white blood cell count increased to 25 100 cells/mm³. The nonstress test (cardiotocogram) was normal. The cervical culture obtained on admission grew a pure culture of S. pneumoniae serotype 14. Because intrauterine infection was suspected, penicillin therapy, 2 million units every 4 h intravenously, was started. The next day, after the mother had received 6 doses of penicillin and 60 h after admission, fetal heart activity was absent and intrauterine death was confirmed by ultrasound examination. Ritodrine was stopped and 6 h later a 940-g lifeless female was born vaginally. The temperature returned to normal within a few hours. Susceptibility testing showed that the isolate had a penicillin MIC of 1 µg/ml (E-test AB Biodisk®, PCH Diagnostica, Haarlem, the Netherlands). Two days after delivery the patient was discharged in good clinical condition to receive oral amoxicillin for 1 week. Blood and urine cultures remained negative.

Postmortem examination of the fetus showed aspiration of purulent amniotic fluid and the Gram-stained smear of lung tissue showed sporadic Gram-positive diplococci but all cultures of internal organs were sterile. Histopathologic examination of the placenta showed a severe purulent chorioamnionitis and umbilical panvasculitis. Cultures taken from the interior of the placenta after surface sterilization yielded S. pneumoniae serotype 14. All surface cultures of the fetus (ears, nose, throat) grew S. pneumoniae serotype 14. Six weeks postpartum smears were taken from the cervix, throat and rectum of the patient and from the throat of her husband to detect possible carriage of pneumococci. All cultures were negative. Adequate concentrations (19 unit/ml; negative <5 units/ml) of serum antibody to serotype 14 capsular polysaccharide were detected in the mother at that time. No acute serum was available for testing.

Discussion. To the best of our knowledge, this is the first case of an intrauterine fetal death in the second half of pregnancy associated with S. pneumoniae. Bruno et al. presented a case of fetal death caused by the pneumococcus at 16 weeks of gestation. The remaining literature reports cases of neonatal mortality related to early onset pneumococcal sepsis which mimics early onset neonatal sepsis caused by group B streptococci. S. pneumoniae is rarely isolated from the female genital tract, but infection does occur. In 1990 Westh et al. reviewed the literature on this topic and summarized the results of 36 cases of pneumococcal infection of the female genital tract and 23 cases of neonatal pneumococcal disease associated with maternal infection. Predisposing conditions for genital tract infection were use of an intrauterine contraceptive device, recent birth and gynecologic surgery. Five of 36 reported women died, all in the preantibiotic era. In contrast
the prognosis of neonates has not improved during past decades, and 11 of 23 reported neonates died.\(^1\)

The findings in this case make it likely that the death of the fetus was caused by pneumococcal intrauterine infection. It is possible that the clinical course would have been different if the patient had not been treated with ritodrine and betamethasone. The latter drug might have facilitated the infection, and if no ritodrine had been given the patient might have delivered before fetal death occurred. However, because there were no signs of intrauterine infection and because the gestational age was only 27 weeks, we decided to delay delivery.

The clinical presentation of our patient suggests an ascending infection which is in agreement with data from the literature.\(^1\) Pneumococci do not survive well in the vagina because of the low pH but may grow when alkaline pH changes have occurred.\(^7\) Rupture of the membranes, as in our patient, may cause such alkaline changes and therefore support growth of pneumococci. Because our patient had been coughing before admission, a hematogenous route of transmission during a respiratory pneumococcal infection cannot be excluded, although the absence of fever does not support this possibility. Because \textit{S. pneumoniae} is a commensal of the upper respiratory tract, it has been suggested that pneumococcal infection of the female genital tract may be caused by oral-genital contact.\(^2\) Our patient did not participate in oral-vaginal sex and cultures of the throat of her husband were negative for pneumococci. In addition only 1 of the 36 women reported in the review of Westh et al.\(^1\) had oral-vaginal contact 6 weeks before the infection. An alternative route of infection might be via the gastrointestinal tract, although no data can be found in the literature to support this suggestion. Moreover, culture of the rectum of our patient did not show \textit{S. pneumoniae} carriage.

It is uncertain whether the fatal course of the present case was a result of penicillin resistance of the infecting strain. It is generally accepted that penicillin resistance is only of clinical significance in pneumococcal meningitis because of the unreliable concentrations of antibiotics in cerebrospinal fluid. The same might hold true for intrauterine infections. Furthermore our case is of importance because of the rare incidence of penicillin resistance in the Netherlands (less than 1%).\(^8\) A low concentration of pneumococcal IgG antibodies might be an immunologic risk factor for recurrent disease. Wright et al.\(^5\) described a woman who delivered premature infants affected by early onset pneumococcal sepsis in two successive pregnancies. This woman had low pneumococcal antibody titers and vaccination with 23-valent pneumococcal vaccine produced a rise in antibodies. Our patient appeared to have an adequate titer of anti-serotype 14 antibody 6 weeks after the infection, and her following pregnancy was uneventful.

In conclusion \textit{S. pneumoniae} is rarely found in the female genital tract but may cause intrauterine infection and fetal demise. Because resistance to penicillin does occur, higher doses of penicillin or a cephalosporin should be considered for optimal treatment of pneumococcal intrauterine infection.

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\section*{GROUP B STREPTOCOCCAL SEPSIS AND MENINGITIS
COMPLICATED WITH SEVERE SENSORINEURAL HEARING LOSS IN A FOURTEEN-YEAR-OLD BOY}

Group B \textit{Streptococcus} (GBS) is a common bacterial pathogen causing infections in neonates and very young infants. The clinical spectrum of GBS disease includes septicemia, meningitis, pneumonia, arthritis, osteomyelitis, urinary tract infection, sinusitis and skin and soft tissue infections.\(^1-3\)

Recently increasing incidence of invasive GBS disease in nonpregnant adults has been reported. There is little information available on GBS infection in pediatric patients beyond early infancy. We report a case of GBS sepsis and meningitis in a previously well 14-year-old boy.

\textbf{Case report.} A 14-year-old Thai boy was admitted to a municipal hospital with a 2-h history of severe headache and vomiting. Physical examination revealed a stiff neck. Cerebrospinal fluid (CSF) examination showed a white blood cell count of 150/mm\(^3\), protein 114 mg/dl, glucose 0 mg/dl and blood glucose 125 mg/dl. Gram-stained smear of CSF revealed Gram-positive cocci. A diagnosis of acute bacterial meningitis was made. Antibiotic therapy with intravenous penicillin and chloramphenicol was initiated. He received three doses of antibiotics before he was transferred to Chulalongkorn Hospital on request of the parents.

On arrival he was oriented. His temperature was 37.5°C with a pulse of 100/min, respirations of 24/min and blood pressure of 110/70 mm Hg. Physical examination revealed a stiff neck. The remainder of the examination was unremarkable except for a healed wound on right index finger. The same antibiotics were continued.

Admission laboratory studies included a white blood cell count of 20 500/mm\(^3\) with 2% band forms, 90% polymorphonuclear leukocytes and 8% lymphocytes; platelets were 203 000/mm\(^3\). Repeat lumbar puncture revealed cloudy CSF.