Case Report

Chorioamnionitis associated with Crohn’s disease and azathioprine treatment: a case report

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This paper reports a case of S. constellatus chorioamnionitis in a pregnant Crohn’s disease patient who was taking azathioprine. Chorioamnionitis is a major cause of perinatal morbidity. Azathioprine, an immunosuppressive antimetabolite, is widely used to treat inflammatory bowel disease. Streptococcus constellatus is a Gram-positive bacterium that has not previously been associated with chorioamnionitis. A high index of suspicion for chorioamnionitis and unusual pathogens should be maintained in the management of obstetric patients on immunosuppressive agents.

Case report

The patient, a 27-year-old, gravida I, para 0, at 29 weeks and 4 days of gestation was hospitalized due to fever, abdominal pain and contractions of 2 days’ duration. She had a 5-year history of Crohn’s disease, for which she took azathioprine, 50 mg three times daily, and mesalamine, 1 g three times daily.

On admission, the patient’s blood pressure was 125/75 mmHg and body temperature was 38.5°C. Foetal heart rate was 170 beats min⁻¹ with good variability and short variable decelerations. Mild uterine contractions were noted every 3–6 min. Pelvic examination was significant for a dilatation of 1 cm, 0% effacement and cephalic presentation. The patient denied rupture of membranes. Ultrasonography revealed a single intrauterine foetus, cephalic presentation, posterior placenta and a biophysical profile score of 8/8 with an amniotic fluid index of 12. Significant laboratory values included negative urinalysis and a white blood cell count of 3400 mm⁻³ (90% neutrophils). The patient’s chest X-ray was normal.

The patient was given intravenous antibiotics: loading dose of 5 000 000 IU penicillin G sodium followed by 2 500 000 IU six times daily, and 240 mg gentamicin once daily. Penicillin was given according to the department’s protocol for pre-term delivery, and gentamicin was added for suspected infection based on maternal fever at presentation. The origin of the presumed infectious process was unidentified at this point.

Spontaneous rupture of membranes accompanied by a foul odour occurred 2 h later. Chorioamnionitis was diagnosed and an emergency caesarean section was performed when a non-stress test (NST) revealed deep and prolonged decelerations. A 1286 g female infant, with Apgar scores of 5 and 7 at 1 min and 5 min, respectively, was delivered. Streptococcus constellatus sensitive to penicillin was later cultured from the amniotic fluid and the placenta.

Anaerobic cultures of the endometrium side of the placenta and neonatal blood cultures were negative. Placental pathological features were described as ‘placenta showing acute changes of chorioamnionitis’.

The neonate was transferred to the neonatal intensive care unit with normal vital signs and spontaneous respiration. She needed no respiratory support throughout her course and remained haemodynamically stable. An echocardiogram was performed due to a systolic murmur on auscultation and revealed normal ventricular function, a patent foramen ovale and a small muscular ventricular septal defect. Gastrointestinal and metabolic functions were normal and she was neurologically intact.

Given the presumptive diagnosis of chorioamnionitis, blood cultures were taken after delivery and antibiotic treatment with penicillin and gentamicin was continued. When streptococci were cultured from the amniotic fluid and placenta, this treatment was continued for 7 days postpartum and until final culture results were obtained. The patient’s fever resolved 48 h after treatment initiation.

Neonatal blood cultures were all negative. The remainder of the infant’s hospital stay was uneventful, and she was discharged on postpartum day 49 weighing 2260 g. The mother’s hospital stay was also uneventful, and she was discharged on postpartum day 9.

Discussion

Chorioamnionitis is considered a common cause of pre-term birth, which accounts for 70% of perinatal mortality and 50% of long-term neurological morbidity (Goldenberg et al.,...
2000) and, in term infants, constitutes an important risk factor for neurological morbidity (Grether & Nelson, 1997). An increasing body of evidence has recently suggested that not only is clinical infection responsible for pre-term birth but also for many serious neonatal sequelae, including periventricular leukomalacia, cerebral palsy, respiratory distress and even bronchopulmonary dysplasia and necrotizing enterocolitis (Bracci & Buonocore, 2003).

Intrauterine infection induces an intra-amniotic inflammatory response involving the activation of a number of cytokines and chemokines, which, in turn, may trigger pre-term contractions, cervical ripening, rupture of the membranes and the neonatal sequelae mentioned above (Hagberg et al., 2005).

The predictors of chorioamnionitis include pre-term labour or rupture of membranes, abnormal vaginal flora [e.g. *Streptococcus agalactiae* (GBS)], sexually transmitted disease, bacterial vaginosis, obstetric manipulations (e.g. vaginal examinations, internal foetal monitoring) in the presence of ruptured membranes, and diminished host response (due to smoking, drug abuse, obesity, immunodeficiency states, etc.). Group B streptococci and *Enterobacteriaceae* are the most important organisms associated with polymicrobial infection (Gibbs et al., 2004; Newton, 1993). Chorioamnionitis is associated with intubation in the delivery room, pneumonia and sepsis (Alexander et al., 1999; Petrova et al., 2001). These outcomes are kept to a minimum if maternal antibiotic chemotherapy is initiated intrapartum with agents that are safe for the foetus and effectively cross the placenta (Mercer et al., 1997). Antipyretics, such as acetaminophen, will reduce the hyperthermic stress on the foetus, while persistent foetal tachycardia after antipyretics may indicate foetal infection. Continuous electronic foetal monitoring is appropriate in cases of chorioamnionitis, and providers should be prepared for neonatal resuscitation, early neonatal intravenous antibiotics and respiratory support at delivery (Newton, 1993).

Crohn’s disease commonly affects women of childbearing age. Women with Crohn’s disease can expect to conceive successfully, carry to term and deliver a healthy baby. Control of disease activity before conception and during pregnancy is critical in order to optimize both maternal and foetal health. Most drugs, including sulfasalazine, mesalazine, corticosteroids and immunosuppressors, such as azathioprine and 6-mercaptopurine, are considered safe, whereas methotrexate is contraindicated (Mottet et al., 2005).

Azathioprine is the most commonly used immunomodulatory drug for treating inflammatory bowel disease. Its mode of action is thought to be multifactorial, and it is also known to alter lymphocyte function and affect natural killer cell function (Nielsen et al., 2001). It is used in pregnant patients with Crohn’s disease to reduce disease activity, maintain remission and prevent relapse. We found no prior report on chorioamnionitis associated with azathioprine treatment. *S. constellatus* is a species of Gram-positive bacteria in the ‘*Streptococcus milleri*’ group, whose members are variably haemolytic and microaerophilic and tend to produce serious invasive infections or localized abscesses in almost any part of the body (Bert et al., 1998). Although placental pathological features suggested chorioamnionitis and *S. constellatus* was isolated from our patient’s amniotic fluid, there was no evidence of foetal infection. Moreover, the route or source of infection was not identified: the medical centre’s epidemiology unit reported no similar concurrent infections in other hospital wards.

The decision to deliver was based on the presumed diagnosis of intra-amniotic infection, as indicated by maternal fever (38-5 °C) and persistent uterine contractions; the decision to deliver by emergency caesarean section was motivated by the non-reassuring foetal heart rate. The maternal and foetal courses were uncomplicated, with each receiving postpartum penicillin treatment.

A high index of suspicion for chorioamnionitis and unusual pathogens should be maintained in the management of obstetric patients on immunosuppressive agents in order to ensure appropriate and timely intervention and increase the chances of a benign clinical course.

**References**


