Case Report

Molecular evidence for vertical transmission of listeriosis, Taiwan

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The case is presented of a pregnant woman at the 31st week of gestation with *Listeria monocytogenes* bacteraemia and microabscess formation in the endometrium, who delivered an infant with disseminated infection (meningitis and bacteraemia). The two patients were successfully treated with intravenous ampicillin and gentamicin. Molecular typing using random amplified polymorphic DNA (RAPD) analysis disclosed that three isolates from the mother (blood) and infant (blood and cerebrospinal fluid) had identical RAPD profiles.

Introduction

Infections (sepsis or meningitis) due to *Listeria monocytogenes* mainly occur at the extremes of life, and in pregnant women and patients with various underlying medical conditions (AIDS, diabetes mellitus, malignancy, and hepatic and renal failure) (Gellin & Broome, 1989; Southwick & Purich, 1996). In Taiwan, three patients with perinatal listeriosis have been reported, but to the best of our knowledge, fetomaternal infection has not been described (Chen *et al.*, 1998, 2003; Cheng *et al.*, 1990).

Case report

A 38-year-old woman (gravida 1, para 0) was at her 31st week of gestation. She had previously been well, except that she was a hepatitis B virus carrier and was regularly monitored at our clinic. She was admitted to the hospital because of fever (38.2 °C) and chills for 3 days. Her pregnancy course was uneventful until 1 week prior to admission, when she suffered from one episode of chills at home. There was no fever or any symptoms and signs of respiratory, urinary or gastrointestinal tract infection at that time. Chills recurred again accompanied by general malaise 3 days prior to this admission. Decreased fetal movement and fetal tachycardia were also noted.

On admission, leukocytosis [white blood cell (WBC) count 20 220 cells μl^{-1}] and hyponatraemia (129 mmol l^{-1}) were found. Levels of serum creatine and aminotransferase were normal. Ritodrine (67 $\mu\text{g min}^{-1}$) was given for tocolysis and betamethasone (12 mg per day) was given for fetal

pulmonary maturation after admission. Intravenous cefazolin (1 g every 8 h) and gentamicin (80 mg every 12 h) were administered empirically for possible amnionitis. Rupture of membrane with meconium stain was noted 12 h after admission. Fourteen hours after admission, the fetal heart rate suddenly decelerated from ~150 to 90 beats min^{-1} , and this episode lasted for 2 min. Decreased fetal movement was also noted. A male infant was delivered by emergent caesarean section 15 h after admission, giving the impression of fetal distress. The endometrium was noted to be thickened during the Caesarean section, and a sample of endometrium from the uterine portion was sent for histopathological examination. The latter revealed acute chorioamnionitis with microabscess formation without visible micro-organisms (Fig. 1). Intravenous clindamycin (600 mg every 8 h) was added to the patient's treatment on the basis of the diagnosis of acute chorioamnionitis.

The infant was 1558 g in weight and had a head circumference of 29 cm. The Apgar scores were 4 at 1 min and 7 at 5 min after delivery. Generalized bleachable papules and pustules were found over the trunk and extremities. He was transferred to the neonatal intensive care unit (ICU) for possible neonatal sepsis. Seizure developed after admission to the neonatal ICU. Laboratory tests revealed a WBC count of 7990 cells μl^{-1} (84 % normoblast), haemoglobin 13.9 g dl^{-1} and hematocrit 43.1 %. The C-reactive protein level was 12.84 mg dl^{-1} . Cerebrospinal fluid (CSF) was yellow and turbid. The total CSF WBC count was 87 cells μl^{-1} with neutrophil predominance (mononuclear cells, 20 cells μl^{-1} and polymorphonuclear cells, 67 cells μl^{-1}). The CSF protein level was 693 mg dl^{-1} and the glucose level was 3 mg dl^{-1} . Ampicillin (100 mg kg^{-1} per day) and cefotaxime (200 mg kg^{-1} per day) were used initially for treatment

Abbreviations: CSF, cerebrospinal fluid; ICU, intensive care unit; RAPD, random amplified polymorphic DNA; WBC, white blood cell.

Fig. 1. Pathological examination (haematoxylin and eosin stain) of the endometrium revealing microabscess formation and accumulation of pus cells with fibrinoid necrotic substances ($\times 200$). Bar, 100 μm .

of neonatal meningitis. A brain echo of the infant on the second ICU hospitalization day revealed grade II bilateral intra-ventricular haemorrhage, which could have been due to the prematurity of the infant, and suspected ventriculitis and cerebritis.

The blood cultures of the mother (isolate A) and her infant (isolate B) both yielded *L. monocytogenes*. The CSF culture of the infant also yielded the same organism (isolate C). Culture of the amniotic fluid was negative. The mother's fever subsided after delivery. The skin rash of the infant disappeared 2 days after the start of antimicrobial treatment. After the notification of positive cultures for *L. monocytogenes*, antibiotic regimens including ampicillin and gentamicin were administered to the infant (for 21 days) as well as his mother (for 14 days). The progress of the infant remained uneventful and he started on oral feeding on the eighth day of his ICU stay.

The three isolates of *L. monocytogenes* were haemolytic on sheep blood agar plates and exhibited a positive Christie–Atkins–Munch–Petersen (CAMP) reaction with *Staphylococcus aureus* (Bille *et al.*, 2003). These organisms were further identified to species level using standard biochemical methods as well as the API Coryne system (bioMérieux). Molecular typing of the three isolates and six other isolates (control strains) was performed by random amplified polymorphic DNA (RAPD), using a method described elsewhere (Boerlin *et al.*, 1995). Three primers, M13, OPA-2 and ERIC2, were used. The three isolates from the infant and his mother had identical RAPD profiles, which were different from those of the six control strains.

The mother reported here had *L. monocytogenes* bacteraemia and had evidence of endometrial infection, and delivered an infant with disseminated infection (meningitis and bacteraemia) caused by the same species of bacterium with a RAPD

profile identical to that of his mother. The incidence of listeriosis among pregnant women is 17-fold higher than that among the general population (Mylonakis *et al.*, 2002). The common presentations of maternal listeriosis are usually non-specific and benign, with fever and flu-like symptoms (Benshushan *et al.*, 2002; Evans *et al.*, 1985; McLauchin, 1990; Silver, 1998; Sirry *et al.*, 1994). Involvement of the central nervous system in pregnant women is rare (Sirry *et al.*, 1994). The micro-organism has been reported to be present in blood (43%), cervical or vaginal swabs (34%), placenta (12%), amniotic fluid (8%), lochia (8%) and urine (2%) (McLauchin, 1990). Maternal listeriosis may result in stillbirth or spontaneous abortion (20%), and the rate of vertical transmission with subsequent fetal infection is high (68–77%) (McLauchin, 1990; Sirry *et al.* 1994). Examination of the placenta usually reveals chorioamnionitis and microabscess formation (Benshushan *et al.*, 2002; Evans *et al.*, 1985; McLauchin, 1990; Silver, 1998; Sirry *et al.*, 1994).

Clinical presentations of infants with listeriosis include respiratory distress, meconium staining at birth, fever, lethargy, jaundice and skin rashes (McLauchin, 1990). The skin rashes are usually distributed on the trunk and extremities, and are maculopapular or papulovesicular lesions. The overall case fatality rate is high (24.5 to ~46.5%). Disseminated neonatal infection (granulomatosis infantisepticum) due to *L. monocytogenes* presents with widespread abscess formation, involving the liver, placenta and skin, and involvement of the brain, spleen, kidney, lungs, adrenal glands and gastrointestinal tract can result in a high mortality (McLauchin, 1990).

Antepartum treatment of listeriosis has been found to have a better outcome for neonates, and ineffective initial treatment might result in a poor outcome in pregnant women (Gellin & Broome, 1989; McLauchin, 1990; Posfay-Barbe & Wald, 2004). High-dose ampicillin and gentamicin

remain the drugs of choice for listeriosis. Trimethoprim-sulfamethoxazole is used for those with penicillin allergy, but is not suitable for pregnant women. Cephalosporins and clindamycin, which are usually recommended for treating chorioamnionitis and septic abortion, are ineffective against *L. monocytogenes*. Our patients responded well to the conventional therapy with ampicillin and gentamicin.

RAPD analysis has been extensively evaluated by Boerlin *et al.* (1995) for typing *L. monocytogenes* isolates alongside other typing methods. They conclude that RAPD analysis is a highly discriminating, timesaving and relatively simple technique for the epidemiological typing of *L. monocytogenes*. Using three primers in this study, the three isolates recovered from our patients were successfully demonstrated to belong to the same strain.

Our observations demonstrated that maternal and perinatal listeriosis responded well to conventional antimicrobial therapy, and provided molecular evidence of vertical transmission of listeriosis.

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