

Congenital brucellosis in a Chinese preterm neonate: A case report

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Abstract

Although extremely rare, congenital brucellosis can occur via perinatal transmission. We report a case of an infant born prematurely at 34–36 weeks' gestation who had pyrexia, shortness of breath, hepatosplenomegaly and thrombocytopenia. Blood cultures were positive for Gram-negative coccobacilli and *Brucella* infection was suspected. While, serological tests were negative for *Brucella* antibodies, *B. melitensis* infection was confirmed by polymerase chain reaction (PCR). Serology of the parents' blood confirmed the presence of *Brucella*. The family did not live in an endemic area but had ridden a camel 12 months before the pregnancy. The bacteria may have been sexually transmitted from father to mother and then to foetus via an intrauterine infection. In endemic areas or where the family has been in close contact with infected animals, brucellosis should be suspected in a severely ill neonate with an unknown infection. Thorough medical histories from the family are essential as early diagnosis and prompt therapy will almost certainly improve neonatal outcome.

Keywords

Congenital brucellosis, *Brucella*, neonate, perinatal transmission

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Introduction

Over recent years, the incidence of human brucellosis in China has increased significantly and has become a major public health issue.¹ Studies from China have shown that most cases of the disease have

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been reported in pastoral farming areas of northwest, northeast, Qinghai-Tibet Plateau and Inner Mongolia.¹ A zoonotic infection, transmission of brucellosis to humans occurs primarily through direct contact with infected animals or consumption of infected animal products.¹ Brucellosis is caused by gram-negative, intracellular coccobacilli and the major reservoirs of the disease are goats, camel, sheep (*Brucella melitensis*), swine (*B. suis*), cattle (*B. abortus*) and dogs (*B. canis*).² Human-to-human transmission is rare but has been reported in association with sexual intercourse,³ blood transfusion, and organ transplantation.^{4,5} In addition, transmission through breastmilk has also been reported in neonates.^{6,7} Although extremely rare, congenital brucellosis acquired through perinatal foetal infection has also been reported.² We report here on a case of congenital brucellosis in a Chinese preterm neonate contracted through an intrauterine infection.

Case report

This study was approved by the Ethics Committee of Hunan Provincial People's Hospital (201707116) and informed consent was obtained from the parents of the participant.

The infant

A 26-year-old woman was admitted to a local hospital one month before delivery of her baby because of weakness in her lower extremities and hip joint pain. Serological tests for TORCH infections (i.e., Toxoplasmosis, Other (syphilis, varicella-zoster, parvovirus B19), Rubella, Cytomegalovirus, and Herpes infections) were negative. She delivered a preterm male infant at 34–36 weeks' gestation without complication. Amniotic fluid detection and placental examination showed no irregularities. At birth, the amniotic fluid was

clear and five minutes after birth the baby boy had an Apgar score of 9. However, his birth weight was 2.0 kg, he had shortness of breath, poor response to stimuli and was foaming at the mouth and moaning. Six hours after birth the neonate received oxygen therapy via a nasal cannula and was transferred from the local hospital to the Children's Medical Centre at Changsha. Examination on admission showed: temperature, 36.7°C; pulse rate, 130/min; blood pressure, 60/31 mmHg; weight, 2.0 kg; head circumference, 32 cm. The boy had poor response to stimuli and was moaning and crying weakly. Abdominal distension was noted (Figure 1a). His liver was hard and palpable 4.5 cm under the costal margin and his spleen was 3.5 cm below the costal margin. No other abnormalities were detected by physical examination. Chest X-ray showed bilateral decreased translucency and the bronchus was visible, suggesting neonatal respiratory distress syndrome (Figure 2a). Routine blood work showed: white blood cell (WBC) count, $35.9 \times 10^9/l$; red blood cell (RBC) count, $4.14 \times 10^{12}/l$; neutrophils 67.4%; haemoglobin, 156 g/l; platelets, $48 \times 10^9/l$. Blood gas analysis suggested respiratory acidosis. His procalcitonin level was 2.8 ng/ml and C reactive protein (CRP) was 45.7 mg/l. Because severe sepsis was suspected, blood cultures were made and the neonate was treated empirically with antibiotics (i.e., trimethoprim/sulfamethoxazole [TMP-SMX]) 25 mg/kg bid oral, rifampicin 10 mg/kg bid oral,^{2,8} and meropenem 20 mg/kg intravenously (IV) tid. On the third day, small 0.5 mm, Gram-negative coccobacilli were detected (Figure 2b). Further detection of urease positive strains suggested the presence of a *Brucella* species and so a sample was sent to CDC at Hunan Province for identification. Although, serological testing (i.e., rose bengal plate test [RBPT] and standard tube agglutination test [STAT]) were negative for *Brucella*



Figure 1. (a) Photograph of the neonate at the time of admission showing enlarged liver. (b) Photograph of the neonate just before discharge showing the liver has reduced to a normal size.

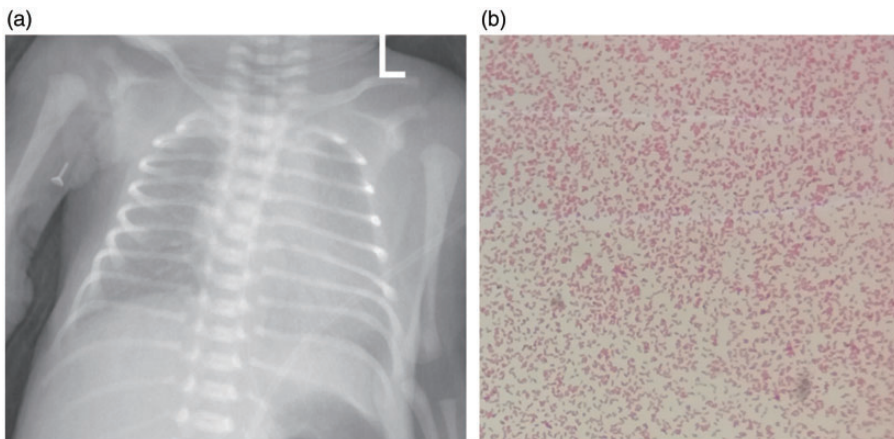


Figure 2. (a) Chest X-ray showing bilateral decreased translucency and a visible bronchus which suggests neonatal respiratory distress syndrome. (b) Bacterial culture indicated that the baby was positive for *Brucella* species. Three days after seeding Gram-negative coccobacilli were detected.

antibodies,⁹ *B. melitensis* infection was confirmed by polymerase chain reaction (PCR).¹⁰ Samples of cerebrospinal fluid taken 15 days after birth showed a WBC count of $30.0 \times 10^6/l$ and meropenem was

replaced by ceftriaxone sodium 80 mg/kg IV qid.

After 28 days of treatment, the infant showed significant improvement (Figure 1b). Blood culture had been

repeated twice after treatment and results were negative for *Brucella* sp. The boy was discharged from hospital and the family were instructed to continue with TMP-SMX 25 mg/kg, bid oral, and rifampicin 10 mg/kg bid oral. The baby was evaluated two months after discharge and his liver and spleen had returned to normal size and his serum antibodies levels were 1:200 against *Brucella*. Therefore, his antibiotic treatment was stopped.

The family

Following positive identification of *Brucella* in blood specimen from the infant, blood specimens were collected from the parents and sent to CDC at Hunan Province. Both blood culture and serology specimens from the parents were positive for *Brucella* and *B. melitensis* was identified by PCR.

The parents were hospitalized and treated with TMP-SMX 25 mg/kg bid oral and rifampicin 10 mg/kg bid oral for 6 weeks after which time they improved and were discharged. They disclosed that they had ridden a camel 12 months before the pregnancy and soon after that the father had experienced orchitis and fever, symptoms suggestive of human brucellosis.

Discussion

Brucellosis continues to be a major public health concern worldwide, especially in the Mediterranean region, Asia, the Middle East, Sub-Saharan Africa, Latin America and the Balkan Peninsula.¹¹ The disease has a wide spectrum of clinical manifestations including flu-like symptoms, osteoarthritis and more serious conditions in different organ systems.¹² In addition, it commonly affects the reproductive system and has been reported to cause up to a 40% increase in spontaneous abortions in early pregnancy and up to 2% of foetal deaths during later stages of pregnancy.¹¹

According to a report from Peru, during 1970 to 2012 of the 101 cases of brucellosis infection during pregnancy, 28% women had threatened miscarriage/preterm labour, 13% had spontaneous abortion, 14% had pre-term delivery, 8% had foetal death and 1% had congenital malformations.¹³ The rate of congenital brucellosis was 6%.¹³ However, two literature reviews on the topic have estimated that since the first published report in 1988, there have only been approximately 20 cases of congenital brucellosis reported worldwide.^{14,15}

The clinical manifestations and outcome of congenital brucellosis are not well delineated.⁷ Therefore, in heavily infected areas, it is important to consider congenital brucellosis if other bacterial infections have been excluded in a severely ill neonate.¹⁶ Early diagnosis and prompt therapy will certainly improve neonatal outcome.^{13,17} The infant in this present case report exhibited clinical characteristics of a perinatal infection and possible sepsis. The symptoms included: premature birth; respiratory distress; pyrexia; hepatosplenomegaly; hard liver and spleen; thrombocytopenia; increased CRP. In addition, although the chest radiograph suggested respiratory distress syndrome, the scan had a speckled and reticular pigmentation. The presence of *B. melitensis* was detected by PCR analysis of the infant's blood. While serology of the mother's blood confirmed the presence of *Brucella*, serological testing of the infant's blood was negative for *Brucella* antibodies. A possible reason for this may have been the infant's premature birth which may have restricted placental transfer of maternal IgG antibodies to the foetus. However, following two months of treatment with antibiotics, the infant was positive for antibodies against *Brucella*.

Interestingly, the family did not raise livestock, nor did they reside in a brucellosis endemic area. However, the parents disclosed that they had ridden a camel a year

before the pregnancy, which was probably the cause of their *Brucella* infection.² The bacteria may have been sexually transmitted from the father to the mother who subsequently passed the infection to the foetus via an intrauterine infection^{2,3} During her pregnancy, the mother had exhibited asthenia in both lower extremities and had pyrexia, but her physician had overlooked the possibility of brucellosis. Consequently, she was not treated during pregnancy which resulted in severe clinical manifestations of the infection in the neonate.

In conclusion, although congenital brucellosis is a rare disease, it should be suspected in a neonate when other bacterial infections have been excluded particularly if there has been close contact with infected animals. Neonates with congenital brucellosis can be effectively treated with rifampicin and TMP-SMX, orally.² However, infected infants require early detection of the pathogen and timely treatment to reduce the incidence of complications. Thorough medical histories from the family are essential in early diagnosis of the disease as prompt therapy will almost certainly improve the neonatal outcome.

Declaration of conflicting interest

The authors declare that there are no conflicts of interest.

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