

# A Congenital Brucellosis Case of 34-day-old Girl

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## Case Report

**Keywords:** Brucella meliteusis, congenital, next-generation sequencing, meningitis

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# Abstract

**Background:** Brucellosis is the most common zoonotic infection over the world, caused by bacterial genus brucella. The disease is transmitted rarely via human-to-human transmission. Limited data support vertical transmission of human brucellosis. Herein, we reported a case of congenital brucellosis case with solid evidence of pathogen detected in mother's placental specimen.

**Case presentation:** A 34-day-old girl was admitted to department of pulmonology because of fever for eight days. Her mother had fatigue and arthralgia for 2 weeks, fever and membrane rupture 1 day before the baby was born. Three blood samples and one sample of cerebrospinal fluid showed positive with *Brucella meliteusis*. The diagnosis of brucellosis and *Brucella meliteusis* meningitis were established with hyperbilirubinemia and liver dysfunction. Treatment of rifampicin (6 weeks) and meropenem (2 weeks) was applied. However, the disease relapsed 3 weeks. A combination therapy of rifampicin and SMZ/TMP lasted for eight weeks. *Brucella meliteusis* DNA was detected by next-generation sequencing and bacterial identifying under microscope in mother's placental specimen, which also proved chorioamnionitis. The baby was still in following-up.

**Conclusions:** We reported a confirmed case of congenital brucellosis. This disease should be paid enough attention even in non epidemic areas. The treatment of brucellosis in infancy face the challenge of medicine choosing and disease relapse.

## Background

Brucellosis is the most common zoonotic infection over the world, caused by bacterial genus brucella [1]. It causes half a million new cases annually in some countries[2]. Zhejiang is not an endemic province, where no infection occurred during 1983–2003. However, seldom cases occurred after 2003. Symptoms are fever, arthralgia or arthritis, night sweats, asthenia, insomnia, anorexia and headache. On physical examination, findings are hepatomegaly and splenomegaly, lymphadenopathy, osteoarticular manifestations, genitourinary complications, neurological findings, mucocutaneous manifestations, and pulmonary manifestations. The disease is transmitted via consumption of unpasteurized dairy products, direct contact with infected animals, inhalation of contaminated aerosols, and rarely human-to-human transmission [3]. Although intrauterine transmission, transmission during delivery, and transmission through breast milk are indeed among the main routes of transmission in the mammalian reservoirs, limited data support vertical transmission of human brucellosis [4, 5]. In this work, a congenital brucellosis case was reported. This helps to provide a scientific basis for the prevention and control of brucellosis in pregnant women and their newborn babies.

## Case Presentation

A 34-day-old girl was admitted to department of pulmonology because of fever from day 28. The peek body temperature was 37.6 to 37.7°C. She was born to a Chinese 25-year-old G1P0 at 37 weeks 4 days'

gestation (3300 g birth weight without resuscitation). Her mother had visited and stayed for several periods in her own parents' house, where also once kept 20 sheep. Although she had never fed or touched those sheep, the mother had fatigue and arthralgia for 2 weeks, fever and membrane rupture 1 day before the baby was born. Considering the mother might have been experiencing chorioamnionitis, which was later confirmed by pathology, the baby was delivered by Cesarean section. The baby was fed mother's milk only for 4 days until the mother's blood culture revealed a positive result of brucellosis. The mother immediately started 6 weeks' course of rifampicin and doxycycline. A screening of Rose Bengal plate test among her family showed that the mother's father was also positive and symptomatic while other family members were negative. The grandfather had fatigue, arthralgia and low grade fever for 4 months without seeking medical help. He had killed and sold out all the sheep because of his fatigue and arthralgia before the baby was born.

The baby's father took her to the pediatric department at another hospital on the 3rd day of fever, where acute upper respiratory tract infection was diagnosed and she was observed for one night. Blood samples were obtained for blood culture and Rose Bengal plate test. The baby's body temperature turned to normal since the second day. So she was discharged. However, fever came back again after 3 days of normal body temperature. This time, she was agitated and easy to cry. She had a peak body temperature of 37.7°C, once a day. Her father immediately took her to our hospital. She was admitted into department of pulmonology after only a short lingering in outpatient clinic without doing laboratory test or therapy. On physical examination, the girl was febrile (37.6°C), with heart rate 144 beats per minute, respiratory rate 34/min, blood pressure 74/43 mm Hg. She appeared acutely ill but nontoxic. Her oral mucosa was normal. Her lungs were clear in auscultation. Her abdomen was not distended. Liver and spleen was not palpated below the costal margin. Her joints were all normal. Findings of neurologic and dermatologic examinations were normal.

On the second day, the girl still had fever. The highest body temperature was 38.2°C. Moreover, she seemed lethargy. Bacterial meningitis was suspected and lumbar puncture was done. The cerebrospinal fluid (CSF) contained 85 leukocytes per microliter (86% mononuclear cells), with a protein level of 102.6 milligram per deciliter and a glucose level of 40 milligram per deciliter. The local hospital reported us positive blood culture with *Brucella meliteusis* and positive Rose Bengal plate test. Culture of two samples of blood and one sample of CSF also showed positive with *Brucella meliteusis*. The diagnosis of brucellosis and *Brucella meliteusis* meningitis were established with hyperbilirubinemia and liver dysfunction. For sulfamethoxazole/trimethiprim (SMZ/TMP) is forbidden to used in children < 2 months, we started treatment of rifampicin (6 weeks) and meropenem (2 weeks). Her body temperature turned to normal within two days of treatment but reoccurred 3 weeks after discontinuing rifampicin. Laboratory test including positive blood culture with *Brucella meliteusis*, positive Rose Bengal plate test, and > 1:400 in serum agglutination test (SAT) of brucellosis all suggested relapse of brucellosis. This time, her liver function was also affected. A combination therapy of rifampicin and SMZ/TMP was started immediately. Body temperature turned to normal on the third day. This time the therapy lasted for eight weeks. She was normal after one month of weaning the therapy. The baby was still in following-up. Later *Brucella*

*meliteusis* DNA detected by next-generation sequencing and bacterial identifying under microscope (Fig. 1) in mother's placental wax specimen suggested this is a congenital brucellosis case.

## Discussion And Conclusions

Congenital brucellosis is systematically review by Alsaif et al [6], who reported 44 cases dating back to 1941. In these 44 cases, only one infant had a cord blood bacteremia which was clearly congenital. Other cases were diagnosed mainly based on positive blood culture from 1 day to 3.5 months, in which 7 cases had mothers infected with brucellosis during pregnancy. We describe a case of congenital brucellosis with solid evidence of intrauterine transmission. In our case, positive blood culture in mother suggested mother's infection. Positive blood and CSF culture, and serologic results suggested baby's infection. Finally, chorioamnionitis and bacterial identifying pathologically and *Brucella meliteusis* DNA detected in mother's placental specimen established the diagnosis of congenital brucellosis although the baby was breastfed for 4 days right after birth. The incubation period of brucellosis is usually between 1–3 weeks. In our case, the baby had symptom onset from 28 days.

WHO had not updated its recommended treatment regimens for brucellosis in more than 30 years [7]. Ministry of Health of the People's Republic of China released a 2012 version of 'Guidelines for diagnosis and treatment of brucellosis (Trial)' in Chinese [8]. The clinical management of brucellosis is of particular concern because of high initial treatment failure and relapse rates [2]. The treatment failure and relapse rates were ranging from 4.6–24% for the oral regimen and 5–8% for the oral/ parenteral regimen [2]. The independent predictors of relapse were temperatures of 38.3°C or higher, positive blood cultures at baseline, and a duration of symptoms before treatments of less than 10 days [9]. In this case, we had even difficult in the challenge of antibiotic choosing because of her age. According to our Chinese version of guidelines [8], the medicine for children are rifampicin plus sulfamethoxazole/ trimethoprim (SMZ/TMP) for children aged 6 weeks and older. Moreover, SMZ/TMP is forbidden to use in children < 2 months. The baby was only 34 days. So in the first course, we chose rifampicin (6 weeks) and meropenem (2 weeks). In children, rifampicin monotherapy, which can be used but not recommended, because it is associated with a high relapse rate [10]. The disease relapsed only 3 weeks after discontinuing rifampicin. She was 3-month-old then. Extending the antibiotic treatment also appears to have a positive effect on relapse [2]. So we applied rifampicin and SMZ/TMP for 8 weeks this time.

In conclusion, we reported a confirmed case of congenital brucellosis. This disease should be paid enough attention even in non epidemic areas. The treatment of brucellosis in infancy face the challenge of prevention from infected mother and medicine choosing.

## Abbreviations

CSF: Cerebrospinal fluid; SMZ/TMP: Sulfamethoxazole/trimethoprim

## Declarations

## Acknowledgement

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## Ethics approval and consent to participate

This research was carried out according to the principles of the Declaration of Helsinki and was approved by the Ethics Committee of Children's Hospital, Zhejiang University School of Medicine (2020-IRB-152). No animal work was carried out as part of this study.

## Consent for publication

Consent for publication have been obtained from patient's parent.

## Availability of data and materials

The datasets used or analyzed during the current study are available from the corresponding author on reasonable request.

## Competing interests

The authors declare that they have no competing interests.

## Funding

Not applicable.

## Authors' contributions

D Xu designed the work and drafted the manuscript. X Li, B Cheng, Y Zhou, M Zhou and W Gu collected the clinical data and participated in data analysis. Y Wang and Z Chen coordinated all work relate to the study and revised the manuscript. All of the authors read and approved the final manuscript.

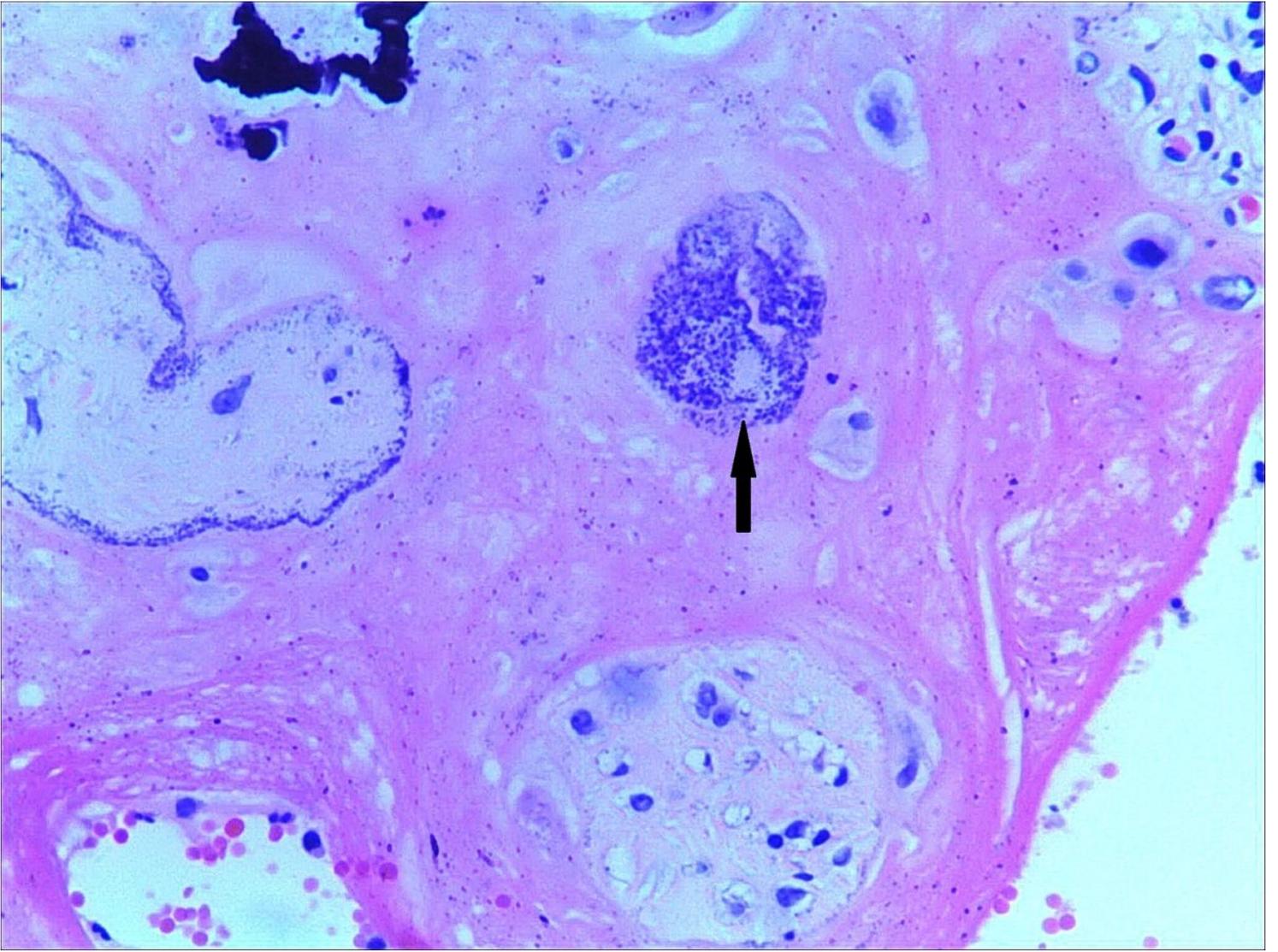
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## Figures



**Figure 1**

HE staining ( $\times 400$ ), coccobacilli in lumps in the connective tissue of chorioamnion (arrow).