Chapter

Neonatal Brucellosis

Fatemeh Eghbalian

Abstract

Brucellosis is a zoonotic infectious disease caused by the *Brucella* bacteria. Neonatal brucellosis is very rare and preventable and is an example of intrauterine infection, but clinical manifestations as well as transmission route are not well defined but presumed transplacental transmission. The neonate can be either infected transplacentally, or by ingestion of mother's secretions and blood during delivery, or by ingestion of breast milk. Presentation of the neonatal brucellosis including fever, arthralgia, weakness, malaise, respiratory distress, pneumonia, enlargement of liver and spleen, fever, thrombocytopenia, late neonatal hyperbilirubinemia, and septicoemia. The diagnosis of brucellosis was based on a positive blood culture (isolation *Brucella* of blood culture from both the mother and the neonate or only neonate) and on a high or rising titer of antibodies to the *Brucella* organism (positive serology only in the mother or both). The neonates with negative *Brucella* serology may also have *Brucella* infection. The mortality rate is very high, and infected neonates need early detection and timely treatment. Early detection and treatment reduce the incidence of complications. The treatment of rifampicin and trimethoprim/sulfamethoxazole is useful for neonatal brucellosis. More patients with neonatal brucellosis well respond to antibiotic therapy and must monitor by a *Brucella* titer of <1:40.

Keywords: neonate, brucellosis, congenital

1. Introduction

Brucellosis is one of the most widespread zoonoses world [1, 2]. It is an acute or chronic zoonotic infection usually transmitted to humans through direct contact with infected animals or by eating contaminated food from infected animals (cattle, sheep, goats, pigs, or another animals) or food products such as unpasteurized milk, cheese or inhalation of contaminated air or dust particles and exposure is frequently occupational [1–4]. The prevalence of brucellosis has been increasing due to growing international tourism and migration of peoples [5, 6]. It is an important cause of economic loss and public health problems and is one of the important human infections in many developing countries or parts of the world. Brucellosis affects humans in all age groups and both genders with variable incidence according to the geographic location and the strain [1–43]. Although this disease is now uncommon in the United States and Britain but common in the Latin America, Africa, Mediterranean and Persian Gulf regions and parts of Asia specially in Iran [1–8, 32, 39]. Brucellosis has high morbidity both for animals or humans and one of the causes of abortion in animals but in humans it causes multisystem disease [1–8, 44]. Brucellosis is not uncommon in many parts of the world but human-to-human transmission, for example, through sexual intercourse, mother to newborn is rare,

but possible and has been reported [9–11]. Vertical transmission from mother to fetus during pregnancy (transplacental) or perinatal exposure has been reported [7, 8, 12, 13, 16–18, 25, 44]. Other modes of human-to-human transmission of brucellosis include blood transfusion, bone marrow transplantation and breastfeeding [20–25]. Although few cases of perinatal brucellosis have been reported but the mode of transmission of *Brucella* from the mother to the baby remains uncertain.

2. Neonatal brucellosis

Brucellosis is a primarily zoonotic infection, public health problem and serious threat for people living in endemic areas of world which is caused by Gram-negative, intracellular, non-spore-forming, non-capsulated, aerobic, nonmotile *Coccobacilli* [1, 26–41]. *Brucella melitensis* is the most important species for human brucellosis, but other species, including *B. abortus*, *B. suis*, *B. canis*, and *B. novel* marine have also been associated with human cases [1–3, 26, 29, 32, 43]. Brucellosis can be transmitted to humans from direct contact by infected animals, products of conception, or animal discharge, and by consumption of infected milk, milk products or meat [2, 3, 5, 26, 32, 43]. Human-to-human transmission is rare, but has been reported in association with blood transfusions, bone marrow transplantation, trans placental or perinatal exposure and possibly postnatally by consumption breast feeding [7, 8, 12, 13, 16–18, 20–25, 44].

Neonatal brucellosis is rare and there are only a few reports of congenital brucellosis [7, 8, 12–14, 17, 43, 44]. There are few data supporting transmission from mother to fetus or transmission via breast milk [7, 8, 12, 13, 16–18, 23, 25]. It seems that in most cases *Brucella* passes through the placenta. Transplacental and consumption breast milk are the main routes of *Brucella* transmission in mammalian reservoirs [7, 8, 12, 13, 23–25]. Ingestion of maternal blood, urine or feces during delivery might be another rout of *Brucella* transmission [10, 14, 19].

Although infected pregnant animals transfer *Brucella* to their offspring transplacentally with resultant massive wastage of conception, this mode of transmission and resultant interference with the normal course of pregnancy has been disputed in humans [2, 32, 43].

Neonatal brucellosis is a very rare cause of early onset neonatal sepsis but should be considered in neonates born from mothers at risk for brucellosis [7–10]. Physicians dealing with mothers who lived in endemic areas during pregnancy should maintain a large index of suspicion when these mothers present with unexplained symptoms, especially for those with social and occupational risk for brucellosis because as soon as diagnosis and therapy can lead to good and better outcome. Education for pregnant women living in endemic areas for avoidance of exposure to sheep, goat, camels and do not consumption of unpasteurized products is most important and highly recommended. Family history of brucellosis or exposure must be obtained during prenatal care in endemic areas [1, 38, 39]. Sometimes maternal brucellosis lead to preterm delivery and with adverse long-term outcomes [16]. Transplacental transmissions from an infected mother, exposure to maternal blood, urine, or genital secretions during delivery are the main routes of transmission of neonatal brucellosis [10, 14, 19].

Pregnancy caused to impaired immunological status, and infection with *Brucella* can deformation obstetric outcomes, including congenital infection [44, 45]. At one point it was believed that adverse pregnancy outcomes associated with human brucellosis should be uncommon due to the absence of erythritol in the human placenta [46, 47]. Another theory was that amniotic fluid contains anti-*Brucella* activity [48]. However, many reports describe apparent increased rates of

spontaneous abortion, intrauterine fetal death, and preterm birth in mothers with brucellosis during pregnancy [49]. Recognition and suitable treatment of infection in early course of pregnancy lead to decrease of incidence of spontaneous abortion, intrauterine fetal death, and congenital infection [44, 46–49]. The clinical manifestations of brucellosis in pregnancy are similar to other infected people and include arthralgia, arthritis, fever, chills, sweating, headache, malaise, nausea, vomiting, lymphadenopathy, hepatosplenomegaly, anorexia and weight loss [1–3, 45–47]. Positive blood or bone marrow culture are definite diagnosis but serologic tests (Wright and 2-mercapto ethanol, 2ME) are the commonest diagnostic methods [1, 3, 45–47].

The choice treatment for brucellosis in infected mother during pregnancy is a combination of rifampin and trimethoprim-sulfamethoxazole but trimethoprim-sulfamethoxazole is contraindicated in first trimester and the last 2–4 weeks of pregnancy. During the third generation and first trimester of pregnancy, cephalosporins have been used and in the last month of pregnancy, combination of aminoglycosides (gentamycin) with rifampin is an alternative regimen [33, 39, 45–49].

3. Clinical manifestations

Newborns with symptom onset in the first week of life have presumably congenital brucellosis, although the incubation period of *Brucella* in newborn period can vary from less 1 week to 1 months (typically 2–4 weeks) [50]. Delayed diagnosis of congenital brucellosis in preterm infants can overlap with other diseases of prematurity. Term infants with onset of symptoms beyond 1 week of age may have acquired *Brucella* through breastfeeding or ingestion of nonhuman milk but congenital infection can also have a delayed presentation [9]. The neonatal immune system is immature, the response to well-characterized infective processes varies from that described in older children and hence clinical manifestations may differ. Differential diagnosis between other bacterial infections in the newborn and brucellosis is difficult and presentations of brucellosis in the neonate are nonspecific and it is very difficult to distinguish brucellosis clinically from other bacterial infections. Fever, arthralgia, night sweating, anemia, bone marrow failure, jaundice, respiratory distress, vomiting, irritability, seizure, hepatosplenomegaly, dearie, skin rash, nausea, vomiting, malaise, poor feeding, failure to thrive (FTT) and distended abdomen are probable signs and symptoms in neonatal brucellosis [48]. The role of *Brucella* in myocarditis and hydrocephalus is difficult to determine both reported from neonates who acquired *Brucella* from breast milk [51, 52]. In summary, brucellosis should be considered as a possible cause of early or late onset sepsis in newborns presenting with fever, respiratory distress and hepatosplenomegaly in endemic regions [53].

4. Diagnosis

Hematological and biochemical tests used in neonatal sepsis are of limited value for the diagnosis of brucellosis [17, 18]. In brucellosis, the white blood cell count is often normal or low. In neonates suspect to brucellosis, the diagnosis was made by the unexpected isolation of *Brucella* from blood culture obtained from a sick neonate with suspected sepsis. Serologic tests are also important methods for clinical diagnosis but should be interpreted judiciously because of transplacental passage of maternal IgG antibodies [54]. A negative serologic test should never exclude the diagnosis, particularly in preterm neonates who may not have mounted their own

antibody response nor received transplacental antibodies. For further evaluation, blood should be sent for nested PCR and DNA sequencing. Definite diagnosis in neonates could be verified based on separating etiologic agent since maternal IgG exists in infant serum till 6 months after delivery [7–9, 17, 18, 54].

5. Treatment

Tetracycline or doxycycline with streptomycin or gentamicin are recommended therapies in older children or adults [39, 55]. Quinolones and doxycycline are sometimes used for treatment of brucellosis in adolescents but their safety in infants and newborns has not been established [32, 33]. Because of the side effects of tetracycline and doxycycline in children younger than 10 years of age, a variety of drugs can be used safely, for example a combination of rifampin and trimethoprim-sulfamethoxazole [32, 33, 43, 55].

The combination of intravenous aminoglycosides for 5–7 days plus with rifampicin and trimethoprim-sulfamethoxazole orally 6–8 weeks is a commonly regimen and has been suggested as the treatment of choice for neonatal brucellosis [7, 8, 12, 13, 56].

Author details

Fatemeh Eghbalian
Department of Pediatrics, Hamadan University of Medical Sciences, Hamedan, Iran

*Address all correspondence to: eghbalian_fa@yahoo.com

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