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Case Report

A Rare Congenital Brucellosis Re-Emerging in Kuwait: A Case Report

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Abstract

A neonate product of a 29-year-old asymptomatic G2P1, Saudi mother, and Kuwaiti father through spontaneous vaginal delivery admitted to neonatal intensive care unit with respiratory distress, meconium aspiration syndrome, intrauterine growth retardation & poor suckling. Routine blood work showed thrombocytopenia, high C reactive protein positive brucella agglutination test and positive culture for Brucella species. The first Brucella standard agglutination test (SAT) for both mother & neonate and blood cultures of the neonate were positive for brucella species & the child was never breastfed or blood transfused, indicating an intrauterine transmission of brucellosis. The neonate treated with dual antibiotics regimen Rifampicin & Ciprofloxacin for 42 day (6 weeks). Missed follow up then shown at age of 5 months with below 5th percentile weight and skeletal malformation and positive SAT and blood culture for Brucella species. This is the first congenital brucellosis discovered since 1994, although cases of human Brucellosis rising in Kuwait in the last 10 years.

Keywords: Congenital Brucellosis; Brucella Treatment; Manifestations; Malformations; Abortion

Introduction

Brucellosis is one of the world's most widespread bacterial zoonoses [1]. It affects domestic and wild animals and causes significant economic losses in livestock due to miscarriages, reproductive disorders, infertility, decline in milk production and serious public health problems [2,3]. Human can be infected by eating or drinking unpasteurized/raw dairy products causing a common zoonotic disease of great concern to people [1,4,5]. The global prevalence and annual incidence of brucellosis in humans remain elusive [4]. That the World Health Organization (WHO) ranks Brucellosis among the seven most neglected diseases [6,7]. Human-to-human transmission of brucellosis is rare but documented, including blood transfusions [8-12], transplantation [13,14] breastfeeding [8,15,16], sexual contact [17-19] and aerosol or subcutaneous administration common laboratory-associated diseases pathogens [7,20]. Also, classified as a Category (B) pathogen with potential development as a biological weapon [21,22]. Extremely rare congenital brucellosis (CB) due to acquired infection during the perinatal period was also reported [8,23]. CB can be transmitted vertically across the placenta from a mother with bacteraemia [24]. Or through contact with maternal blood, urine, or genital secretions during childbirth [8,25,26]. CB affects approximately 2% of the new-borns exposed to brucellosis in utero [27]. Infected newborns may have low birth weight, failure to thrive, jaundice, hepatomegaly, splenomegaly, difficulty breathing and general symptoms of sepsis (fever, vomiting). Some cases are asymptomatic [26,27]. Despite its endemic nature of brucellosis in Kuwait 3, cases of CB are extremely rare as the only and last confirmed case reported in 1994 [28]. This report describes a premature infant diagnosed with Tran's placental transmitted congenital brucellosis.

Case

A full term at 38 weeks+4 days premature boy born to a 29-year-old asymptomatic G2P1, Saudi mother and Kuwaiti father through spontaneous vaginal delivery. He was low weight for gestational age (2.3 kg), height (47cm) & head circumference (33cm). The baby has was admitted to neonatal intensive care unit (NICU) and intubated as a case of respiratory distress (RD), meconium aspiration syndrome (MAS), intrauterine growth retardation (IUGR) & poor suckling. Routine blood work showed thrombocytopenia (platelets 70), high C reactive protein (CRP) (41, 60) sepsis was suspected, blood cultures were made and the neonate was treated empirically with antibiotics Ampicillin & Gentamycin then changed to Gentamycin & Cefotaxime for 7 days. The mother showed hyperpyrexia (39.40C) few hours after delivery, septic workup showed Brucella standard agglutination test (SAT) positive (1 in 640 dilution). The mother used to drink raw camel & cow milk in the Kingdom of Saudi Arabia (KSA) while visiting her family farm and some of her relatives had history of brucellosis. In addition, she had one abortion. She was treated with Doxycycline and Rifampicin for 6 weeks and advised follow up monthly. Blood culture for the mother was negative after 7 & 14 days but blood culture for the baby showed presumptive brucella species grown. Infectious diseases specialist advised to change antibiotics to Rifampicin & Ciprofloxacin for 42 day (6 weeks). The baby gradually improved and maintained O_2 saturation after weaning to room air with no respiratory distress, started feeding after 9 days with gradual increment of formula milk with improved suckling & swallowing. After one month of treatment, the infant showed significant improvement, culture repeated it was negative but SAT positive (200 IU/ml). The baby discharged from hospital after 2 months with 2.61 kg weight, 47 cm height & 36.5 cm head circumference and was given appointments for follow up in the infectious disease hospital. The parents missed many follow up appointments, until show up at age of 5 months. The baby was alert, conscious, socially active, playful, afebrile, well hydrated, mixed (formula & breast milk) feeder and vaccinated until the 4 months doses according to the national immunization schedule. However, he has failure to thrive: weight 4.3kg (below 5th percentile on growth chart), height 58cm (below 5th percentile on growth chart), and head circumference 41.5cm (normal on growth chart). Also, has abnormal features in the form of deep infraorbital ridges, slopping forehead, rotated ears and microretrognathia. Magnetic resonance imaging (MRI) showed dorsal scoliosis with convexity to the right with multilevel dorsal vertebra deformities with fusion and segmentation anomalis in the form of DV5 & DV9 butterfly vertebrae and supernumerary vertebra with DV12, associated with accessory rib. No remarkable findings of concern Chest, heart, abdominal & neurologic examination, lower neither limb enema nor signs of bone aches or arthritis.

Discussion

The losses due to brucellosis are not only enormous in animal production, but also in human health [4,6]. Congenital brucellosis affects approximately 2- 6% of the new-borns exposed to infection in utero [27,29]. The new born of an infected pregnant lady may not be infected, which is more common, or infected with CB [30]. The infant in our case report was symptomatic with perinatal infection and possible sepsis, presented as a full-term but prematurely showed signs of IUGR, MAS, RD, hypotension elevation CRP and thrombocytopenia similar to previous reports [4,22,23,31,32]. Also, had skeletal malformations in the form of deep infraorbital ridges, slopping forehead, rotated ears and microretrognathia. MRI showed dorsal scoliosis with convexity to the right with multilevel dorsal vertebra deformities with fusion and segmentation anomalis in the form of DV5 & DV9 butterfly vertebrae and supernumerary vertebra with DV12, associated with accessory rib, were noted on follow up such results have been previously reported [29,33]. Although earlier consensus that congenital malformations are not associated with brucellosis in pregnant women [27]. The mother had frequent visits to farms in KSA, which is known endemic area [34], she had history spontaneous abortion of her first pregnancy, and apparently, she had subclinical infection but bacteraemia causing spontaneous abortion. This in consensus to earlier reports in literature that in-utero infection causes up to a 13-40% in spontaneous abortions in early pregnancy, and 2-8% of foetal deaths during later stages of pregnancy [29,35]. The product of the second pregnancy is a full term but premature neonate with CB, most probably due to an intrauterine transmission of infection via the placenta. This is supported by positive results of the first SAT for both mother & neonate and blood culture of the neonate, and strengthened by the fact that the child was not breastfed or blood transfused, thus these routes of transmission were unlikely. In our study the diagnosis of Brucellosis in the mother, based on medical history & serologic, test SAT, although she had negative blood culture for brucella species & antibodies (ELISA) but positive SAT. It is reported that blood culture for brucellosis was only successful in people over 40-70% of cases in the acute phase of the disease. Owing to the slowly growing nature of Brucella that need special CO2-enriched media, blood cultures are frequently ineffective [36]. Moreover, Serologic tests are also important methods for clinical diagnosis even though lacking specificity. However, a negative serologic test should never exclude the diagnosis of brucellosis in neonates [31,32]. Of note, molecular methods such as targeted Polymerase Chain Reaction (PCR) and Next Generation Sequencing (NGS) have also proved to yield a high sensitivity and specificity [36,37]. Variety of pharmaceuticals can be used safely and effectively in treating a premature newborn with brucellosis including Ampicillin [30]. In addition, Gentamicin for 5 days followed by Rifampicin for at least 6 weeks was effective in new-borns [38]. The latest systematic review of the literature

demonstrated that effective treatment regimen depends on age group. For children under 8 years old, oral Trimethoprim TMP (6-8 mg/kg/day), Sulphamethoxazole SMX (30-40 mg/kg/day), and Rifampicin (20 mg/kg/day) are typically prescribed for 6-8 weeks to prevent Complications and relapse [39]. However, in our case report; the infant received Ampicillin empirically for sepsis for 2 days then changed to Cefotaxime, Gentamycin & Rifampicin for 1 week then the infections changed it to Ciprofloxacin and Rifampicin for 6 weeks, since treatment with gentamicin for 5 days followed by Rifampicin is effective in new-borns [38]. This infant not given any Aminoglycoside derivatives for treatment, as the parents gave history of four deaf aunts (father's sisters) nor sulphonamides derivatives fearing from allergy. It is reported that the criteria to indicate a cure of brucellosis is not definite, since negative blood cultures do not exclude the presence of the disease [40]. The disease has the ability to relapse, 5-15% of cases, even with treatment. Host characteristics like advanced age, immunity status, severity of infection, and treatment delays are potential risk factors of relapse [41]. The baby in our case report improved and discharged after completion of the dual antibiotic regimen and negative blood culture. However, presented after 5 months with positive SAT and blood culture indicating a possible re-infection via breastfeeding from the mother that caused him a neonatal brucellosis 27 or a relapse [41]. In summary, congenital brucellosis is a rare disease associated with morbidity and mortality. It should be suspected in critically ill new-borns if other bacterial infections ruled out, especially if the maternal history is compatible with Brucellosis. Healthcare workers should remain vigilant in patients living in endemic areas [42]. Thus, getting detailed medical history from parents is important pillar for diagnose and in-time treatment for a favourable outcome. There is no satisfactory vaccine against brucellosis in humans available for prevention of brucellosis in humans. Once controlling the occurrence of brucellosis in animals' reservoirs, there is a corresponding significant decrease in morbidity in humans [1].

Ethical consideration: This study was conducted in accordance with the declaration of Helsinki. The Ethics Committee for Medical Research at the Ministry of Health State of Kuwait research provided approval for the study (ID #: MOH/2226/2023) on January 12, 2023. The confidentiality of participants was secured by de-identifying all data included in the analysis. Data were kept in an encrypted file and saved on a computer, which was accessible to the principal investigator only.

Disclosure of relationships and activities (conflict of interests): The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest. All authors work in the public health field in Kuwait; they share the same career activities in vaccination field and control of communicable diseases.

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Highlights

- The First Congenital Brucellosis Discovered Since 1994, Although Cases Of Human Brucellosis Rising In Kuwait In The Last 10 Years.
- A Neonate Product Of A 29-Year-Old Asymptomatic G2P1, Saudi Mother, Kuwaiti Father Through Spontaneous Vaginal Delivery Admitted To Neonatal Intensive Care Unit With Respiratory Distress, Meconium Aspiration Syndrome, Intrauterine Growth Retardation & Poor Suckling. Routine Blood Work Showed Thrombocytopenia, High C Reactive Protein, Positive Brucella Standard Agglutination Test (SAT) And Positive Culture For Brucella Species.
- The Mother Showed Hyperpyrexia (39.40C) Few Hours After Delivery, SAT Positive (1 In 640 Dilution). The Mother Used To Drink Raw Camel & Cow Milk.
- The First SAT For Both Mother & Neonate And Blood Cultures Of The Neonate Were Positive For Brucella Species & The Child Was Never Breastfed Or Blood Transfused, Indicating An Intrauterine Transmission Of Brucellosis
- The Neonate Treated With Dual Antibiotics Regimen Rifampicin & Ciprofloxacin For 42 Day (6 Weeks). After One-Month Culture Repeated It Was Negative But SAT Positive (200 IU/Ml).
- Missed Follow Up Then Shown At Age Of 5 Months With Below 5th Percentile Weight And Height, Skeletal Malformation And Positive SAT And Culture For Brucella Species. Treated Again With Rifampicin & Ciprofloxacin For Another 6 Weeks.

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