

Maternal and Congenital Brucellosis in Texas: Changing Travel Patterns and Laboratory Implications

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Abstract Brucellosis is an uncommon disease in the US, but Texas reports approximately a third of cases. We review the investigation of a pair of mother-infant cases that were unique in the demographics, the nature of travel exposure and the resulting brucellosis exposure in a hospital's delivery suite and laboratory. These cases illustrate the changing nature of travel and the need to obtain a relevant travel history and adequate laboratory procedures. Clinicians and laboratory workers in Texas need to understand that brucellosis remains an endemic disease, but that its epidemiology is changing.

Keywords Brucellosis · Changing patterns of disease · Migrant · Immigrant · Travel patterns · Zoonotic diseases

Background

Brucellosis, a zoonotic disease considered to be a possible cause of bioterrorism [1], is uncommonly reported in the United States. However, many of the approximately 100 US cases reported annually occur in Texas [2]. The state has reported about 30% of all US cases in recent years

[2, 3]. Historically, Texas' geographic location on the Mexican border [4] was considered the major reason that brucellosis cases occurred. The porous border permits the flow of unpasteurized dairy products [5, 6] brought in for personal use or commercial sale. In addition, rare Texas cattle herds have been infected with brucellosis [7]. In some cases, residents have also purchased unpasteurized dairy products on individual farms [5, 7, 8].

Infected persons experience a clinical picture that ranging from vague complaints of headache, back pain, muscle aches and fatigue to rare cases of sepsis and meningitis [1, 7, 8]. The incubation period varies from a short 2–3 weeks to as long as 6 months [1, 7, 8]. The variable incubation period and the nonspecific symptoms mean that many cases go undiagnosed, and experts have estimated that only 10–15% of cases are actually reported [8].

Brucellosis, also known as Malta/Mediterranean/undulant fever, has historic transmission modes of direct contact with infected animals or consumption of contaminated animal products [1, 7], including milk and cheese. Four *Brucella* species cause disease in man, and each species is specific for domesticated animals [8, 9].

The historic decline in brucellosis cases occurred after the implementation of compulsory milk pasteurization, the routine culling of infected animals and the initiation of cattle vaccination programs [8, 9]. However, brucellosis has adapted to the modern world with transmission with outbreaks documented through organ transplantation and blood transfusions [8], and in laboratory settings [9]. Brucellosis transmission in laboratory settings has prompted concern about its use as a potential bioterrorism agent [8, 9]. Even sexual transmission has been reported [10]. Rarely, brucellosis has also been transmitted vertically from mother to child [11, 13–26]. Such a case occurred in Collin County, Texas in 2004.

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Methods

In this report, we present two cases of brucella in a mother and her infant, and document the case investigations and the unexpected exposure of laboratory and healthcare workers to brucellosis. We also review the epidemiology of brucellosis in Texas and how international migration is shaping the disease in Texas.

Results

Mother and Child Cases

On October 23, 2003, a 36-year-old white female delivered a 24-week, 480-g, male infant at Hospital A in Collin County, a suburban county of 500,000 population located in the metropolitan Dallas-Fort Worth area. The woman delivered vaginally and had prenatal care. She had immigrated from Bosnia-Herzegovina 6 years earlier with her husband and settled in Collin County.

The woman had a suspected urinary tract infection, and went into preterm labor in October 2003 and delivered 5 days after her membranes ruptured. The medical staff in the neonatal intensive care unit followed standard protocol, treating the infant for suspected sepsis with a 10-day course of ampicillin and gentamicin.

The infant was septic at birth and additional blood cultures yielded 20 *Candida* isolates, until the 39th day of life (December 2, 2003) when a blood culture yielded a gram variable coccobacillus. The isolate was sent to the hospital's reference lab in a neighboring county before submission for identification to another reference lab in California. The California Department of Health Services immediately notified Texas Department of State Health Services of the brucellosis culture results and had an isolate sent to Texas. Speciation by Texas Department of State Health Services resulted in the identification of *B. melitensis* on Dec. 5. *B. melitensis* was isolated from five additional blood cultures in December. The infant was treated with rifampin and trimethoprim/sulfa for 8 weeks, and repeat cultures were negative.

Serologic testing of all household contacts was performed. The mother, who had remained asymptomatic throughout her pregnancy, had blood drawn in December 2003. The brucella agglutination titer of 1:640 prompted her therapy with rifampin and doxycycline for 6 weeks. The father's brucella agglutination test was non reactive, and he was not treated.

Collin County staff re-interviewed the infant's parents about possible exposures, specifically seeking details about dairy consumption and travel during the pregnancy. The mother denied consumption of unpasteurized dairy

products. The parents were also asked about the details of any travel during her pregnancy. The parents reported visiting several small cities and small, rural villages in Bosnia-Herzegovina and Croatia during a 2-week trip in June and July 2003. The parents did not recall any direct contact with animals or consumption of unpasteurized dairy products during the trip.

At 3 years of age, the infant is surviving with developmental delays.

Investigation of Hospital and Laboratory Exposures

Hospital A notified the Collin County Health Department of the infant's positive culture for brucellosis and the investigation was started within 24 h. The epidemiology staff in Collin County reviewed medical records of both mother and infant to determine how many hospital staff had direct contact with the mother and infant. The staff interviewed the obstetrician and nurses in the labor and delivery suite about their contact with the mother and infant during the delivery.

Interviews were also conducted with laboratory staff and work procedures in the laboratory were reviewed to determine how many lab workers had worked with specimens from the mother and child. Laboratory procedures were also reviewed to ascertain if the cultures were handled according to standard CLIA guidelines. The hospital laboratory is a Bio-safety level 2 laboratory and as such no specific ventilation equipment is required. Isolates were handled on an open bench. In an effort to identify the isolate, several staff members had preformed the "sniff test," briefly smelling the isolate.

Four laboratory workers and the delivering physician were considered potentially exposed to brucellosis in the lab or during delivery. All had blood drawn; serum from each was tested using an agglutination reaction in January and again in July 2004. The second testing round was done because the brucellosis incubation period may range up to 6 months [25]. Titers for all five persons were less than 1:40 for both tests and none were considered infected. None of five exposed workers took the recommended prophylaxis of doxycycline and rifampin for 6 weeks.

Discussion

Brucellosis cases are expected to occur in Texas, but these two cases from Collin County are unusual in that the persons infected were an infant-mother pair, non-Hispanic residents, involved new travel patterns and were potential sources of exposure for laboratory workers.

Infant cases are uncommonly reported, especially in the United States [2, 3]. In the last 20 years (1988–2007), only

15 infant cases from 9 different countries (2 in the USA) have been reported in the literature (Table 1) [11, 13–26]. Most of those infants were preterm [11, 13–26] and other reports suggest that the association between brucellosis and abortion in animals may occur in humans as well [27, 28]. In another Texas case, a woman with brucellosis during pregnancy delivered a term, uninfected infant [29].

The mother-infant cases also illustrate that clinicians and public health practitioners need to understand that travel is often more than an overseas vacation. Health care providers in Texas often inquire solely about travel to Mexico, but don't consider the possibility of other destinations in a diverse population. Similar scenarios have been reported in European cases where brucellosis was not initially suspected and a good travel history was not obtained [30].

Today the Dallas-Ft. Worth area is home to immigrants and refugees from at least 50 foreign countries [31, 32]. This mother had traveled back to a former home in Bosnia-Herzegovina 6 years after resettling in the United States. For that reason, she may not have been asked a detailed travel history that likely would have been elicited from a newly arrived refugee. However, the re-interview produced details of a relevant exposure that took place during the parents' visit to two locales in the new countries of Bosnia-Herzegovina and Croatia.

The mother was among the refugees from the former Yugoslavia, who first arrived in Dallas in 1993 [31, 32]. By 2005, the population of refugees from the former Yugoslavia who had relocated to North Texas was estimated at 15,000. At the same time those immigrants and refugees

were relocating, brucellosis had re-emerged as a serious public health threat in the territory of the former Yugoslavia.

In 2000 the US Department of Agriculture and CDC did 3-week survey of animals in Bosnia-Herzegovina evaluating the extent of brucellosis and re-establishing testing protocols for brucellosis in both humans and animals [33, 34]. Documented brucellosis cases have been reported from the teaching hospitals in Sarajevo and in sero-surveys [35–40]. Notably those cases have occurred in the geographic area where the Collin County mother visited while pregnant.

The mother-infant cases illustrate that travel has changed and travel histories taken by clinicians need to reflect that change. The categories of travelers these days include immigrants who are returning home to their country of origin for extended visits, foreign students, families of international adoptees and active duty military personnel on overseas duty for extended periods. Perhaps the most important distinction is in those travelers who return to former homes to visit friends and relative for extended periods of time and venture away from established tourism sites and have an exposure to disease that is very different than that of vacationing tourists [41]. Both clinicians and public health providers need to understand travel patterns and trends.

However the missed travel history does not explain the lapse in adherence to laboratory safety procedures in this hospital (and many others) to appropriately handle culture plates that produce growth of a gram-negative/variable coccobacillus. Such a culture should prompt suspicion of brucellosis. In this case, the hospital failed to work with the culture appropriately, sniffing the culture and not manipulating it under a safety hood. That description—of working on an open bench and sniffing [41–43]—appears again and again in the literature. In fact, brucellosis is the most commonly acquired laboratory infection; hospitals clearly need to improve their ability to recognize and handle this organism appropriately [44]. At least one nosocomial outbreak linked to congenital brucellosis has been reported in Israel [13].

In a world where new foci of brucellosis have appeared [45], clinicians need to improve their questioning about travel history and biosafety issues in labs handling brucellosis cultures must be addressed [45, 46]. Since Texas has both a diverse population and reports 30% of US brucellosis cases, both should be a public health priority.

Table 1 Published cases of congenital brucellosis, 1988–2007

Year	Country	# of infants	Reference
2007	Israel	1	[13]
2007	Greece	1	[13]
2006	Greece	1	[13]
2006	Turkey	1	[14]
2005	Iran	1	[15]
2001	Saudi Arabia	1	[16]
1999	Jordan	1	[17]
1997	USA, Massachusetts	1	[18]
1997	USA, Texas	1	[19]
1992	Spain	1	[20]
1992	Saudi Arabia	3	[21]
1992	Saudi Arabia	1	[22]
1991	Israel	1	[23]
1988	Kuwait	1	[24]
1988	Kuwait	3	[13]
Total	Countries-9	Infants-17	

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