Sexually Transmitted Brucellosis in Humans

Eyal Meltzer,1,2 Yechezkel Sidi,1,2 Gili Smolen,2 Menachem Banai,4 Svetlana Bardenstein,4 and Eli Schwartz1,3

1Center for Geographic Medicine and Department of Medicine C and 2Microbiology Laboratory, The Chaim Sheba Medical Center, Tel Hashomer, 3Sackler School of Medicine, Tel Aviv University, Tel Aviv, and 4Department of Bacteriology, Kimron Veterinary Institute Bet Dagan, Israel

Sexual transmission of brucellosis has rarely been reported in humans. We describe 2 cases of probable sexual transmission of Brucella from husband to wife. In 1 case, orchidoepididimitis existed, whereas in the other case, the presence of Brucella in the semen in the absence of genital symptoms was demonstrated by polymerase chain reaction.

Brucellosis is a zoonosis caused by Brucella species. The main sources of infection are food-borne, usually through the consumption of contaminated dairy products, and occupational exposure, as seen in veterinarians or abattoir workers. Case clusters of brucellosis often represent common source outbreaks, whereas human-to-human transmission has rarely been described.

In livestock, sexual transmission of brucellosis is well documented, with Brucella being present in both semen and vaginal secretions. In humans, sexual transmission has rarely been reported. Here, we describe 2 couples in which food-borne Brucella infection in the husband was followed several weeks later by brucellosis in the wife and in which the sexual route was the only possible mode of transmission.

Couple 1. A 55-year-old previously healthy man was evaluated for a 6-week history of fever and recurrent rigors. A year before his present illness, he traveled to Ethiopia. During his trip, he adhered to recommended dietary precautions and avoided dairy products. Two weeks prior to his fever, he recalled consuming unpasteurized goat’s milk, purchased from an Arabic village in Israel, to treat oral aphthous ulcers (a form of traditional therapy sometimes practiced in Israel). The findings of a physical examination were unremarkable. Thick and thin blood smears ruled out late vivax malaria. However, repeated blood cultures grew Brucella melitensis biovar 1. Abdominal sonography, echocardiography, and Tc99 bone scan findings were normal. The patient was treated initially with doxycycline and rifampin (which was subsequently changed to a quinolone and rifampin because of gastrointestinal intolerance), and he experienced an uneventful recovery. The patient’s wife had not traveled with him to Ethiopia and denied any consumption of goat’s milk or any other unpasteurized dairy products. A month after her husband received a diagnosis and started treatment, she developed fever and myalgia. The findings of a physical examination were normal. The results of routine laboratory tests were unrevealing, but blood cultures were positive for B. melitensis biovar 1. Doxycycline and rifampin therapy was initiated and led to the resolution of all symptoms. Culture of a semen sample taken from the husband after the wife’s diagnosis (near the end of his therapeutic course) did not grow Brucella species; however, a polymerase chain reaction (PCR) test for Brucella species (using DNA extracted from urine and semen samples at the Brucellosis national reference center [1] was positive (Figure 1A). Two weeks after completing the initial course of therapy, the wife again became febrile and was again bacteremic with B. melitensis. Findings of a thorough examination for localized disease with a bone scan, thoraco-abdominal computed tomography, and transesophageal echocardiography were all unremarkable; a semen sample was again obtained from the husband and was negative on culture but remained positive by PCR (Figure 1B). On repeated questioning, it appeared that the patient took only one-half of the daily doxycycline dose. A repeat course of the same therapy led to a complete cure.

Couple 2. A 65-year-old man was evaluated for a 4-week history of fever and rigors. In addition, increasing pain with neck movement and testicular pain were also present.

Physical examination revealed pain in the cervical spine on rotation, mild hepato-splenomegaly, and left testicular tenderness. Magnetic resonance of the cervical spine revealed discitis and osteomyelitis in C4; sonography revealed bilateral orchidoepididimitis. Several blood cultures grew B. melitensis. On repeated questioning, the patient recalled exposure to unpasteurized cheese, bought in a remote village. The patient was initially treated with doxycycline and gentamycin for 2 weeks, completed 6 weeks of therapy with oral doxycycline and rifampin, and recovered uneventfully.

Clinical Infectious Diseases 2010;51(2):e12–e15
© 2010 by the Infectious Diseases Society of America. All rights reserved.
1058-4838/2010/5102-0023$15.00
DOI: 10.1086/653608

Received 21 January 2010; accepted 4 March 2010; electronically published 15 June 2010.
Reprints or correspondence: Dr Eli Schwartz, The Center for Geographic Medicine and Dept of Medicine C, The Chaim Sheba Medical Center, Tel Hashomer, 52621 Israel (elischwa@post.tau.ac.il).
Figure 1. Amplification of a partial sequence of the *Brucella omp2* gene [1]. A, DNA size markers, DNA from the urine of the infected man, duplicate DNA, DNA from the sperm of the infected man, DNA from *Brucella melitensis* strain 16M, and DNA from *Brucella abortus* strain 2308 are shown from left to right. B, DNA size markers, DNA from the sperm of the husband (second ejaculate), duplicate DNA, DNA from the sperm of a healthy person, duplicate DNA, and DNA from *B. melitensis* strain 16M are shown from left to right.

Four weeks after the completion of therapy, the patient’s wife developed fever and chills. Blood cultures grew *B. melitensis*. A thorough history revealed no potential source of infection. She had not consumed any unpasteurized dairy products and had not traveled. She also recovered uneventfully with oral antimicrobial therapy.

**Discussion.** Brucellosis remains a common disease in many developing countries [2]. The main modes of *Brucella* transmission are considered to be dietary, from the consumption of contaminated dairy products, and occupational, from exposure to infected livestock. Brucellosis causes a high incidence of clinically evident orchido-epididimitis in humans. In large series from Saudi Arabia, Kuwait, and Turkey, incidence rates of 1%–22% have been reported [3]. However, although the presence of *Brucella* in both vaginal secretions [4] and semen [5] has been described, sexual transmission of *Brucella* species has rarely been reported in humans (Table 1). Moreover, in all previous case reports, definite proof for the existence of *Brucella* species in the semen has been lacking.

The dearth of reports on sexual transmission in human brucellosis, despite the high incidence of genital involvement in the infection, raises the question of whether this mode of transmission is in fact underreported. In areas of high endemicity, case clusters in families are common, and rates of secondary cases among family members of index patients may reach 50% [6]. However, because of continuous exposure to infected food and the highly variable incubation period of brucellosis, it is impossible to distinguish sexual transmission in areas of endemicity.

All of the case reports cited above were reported in areas of low endemicity (Table 1). In such cases, in which only 1 spouse was exposed, either through travel [7–9] or occupationally [10–13], sexual transmission to the other spouse is probable. In Israel, brucellosis can still be acquired through exposure to small ruminant products from certain remote villages but is otherwise rarely encountered. In the cases of the 2 Israeli couples reported here, the epidemiological scenario makes sexual transmission of *Brucella* species more than likely. It is interesting to note that, although concern about the possible transmission of brucellosis from female to male was raised by the original Mediterranean fever commission in the beginning of the 20th century (when the presence of *Brucella* species in vaginal secretions of Maltese prostitutes was demonstrated) [4], in all of the cases presented in Table 1, the sequence of infection was from the male to the female individual. Whether this implies that the risk for acquiring sexually transmitted brucellosis is higher for females than for males (a feature common to many sexually transmitted infections) cannot yet be established.

In the first couple described above, *B. melitensis* biovar 1 was isolated from both the husband and the wife. Semen culture was negative for *Brucella* species, as was also seen in previous reports, because attempts to culture usually come after the initiation of therapy, at the time of the diagnosis of the spouse’s illness [11, 13]. Furthermore, semen cultures are read after 48 h and are often contaminated with skin and urogenital flora; therefore, one may miss slow growing organisms. In the case of extended incubation, the normal flora of the area would mask their growth. In our case, however, a semen PCR assay had results that were positive for *Brucella* species.

PCR assay for *Brucella* species in peripheral blood specimens has been shown to be a highly effective diagnostic tool, with both specificity and sensitivity approaching 100%, even in culture-negative cases [14]. In animals, semen PCR has been shown to be highly sensitive and specific. The use of semen
Table 1. Reports on Sexually Transmitted Brucellosis in Humans

<table>
<thead>
<tr>
<th>Reference</th>
<th>Country of primary case acquisition</th>
<th>Country of diagnosis</th>
<th>Mode of primary infection</th>
<th>Sequence of infection</th>
<th>Interval between spouse illness</th>
<th>Epididymo-orchitis</th>
<th>Semen culture (PCR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kato et al [7]</td>
<td>Iraq</td>
<td>Japan</td>
<td>Travel, ingestion of dairy products</td>
<td>M to F</td>
<td>1 Week</td>
<td>No</td>
<td>ND</td>
</tr>
<tr>
<td>Thalhammer et al [8]</td>
<td>Syria</td>
<td>Austria</td>
<td>Travel, ingestion of dairy products</td>
<td>M to F</td>
<td>2 Months</td>
<td>No</td>
<td>ND</td>
</tr>
<tr>
<td>Lindberg et al [9]</td>
<td>Spain</td>
<td>Sweden</td>
<td>Travel, ingestion of dairy products</td>
<td>M to F</td>
<td>5.5 Months</td>
<td>Yes</td>
<td>ND</td>
</tr>
<tr>
<td>Mantur et al [10]</td>
<td>India</td>
<td>India</td>
<td>Occupational exposure</td>
<td>M to F</td>
<td>2 Months</td>
<td>No</td>
<td>Positive during therapy</td>
</tr>
<tr>
<td>Goossens et al [11]</td>
<td>Belgium</td>
<td>Belgium</td>
<td>Laboratory exposure</td>
<td>M to F</td>
<td>2 Months</td>
<td>No</td>
<td>Negative after therapy</td>
</tr>
<tr>
<td>Stantić-Pavlinić et al [12]</td>
<td>Slovenia</td>
<td>Slovenia</td>
<td>Laboratory exposure</td>
<td>M to F</td>
<td>2.5 Months</td>
<td>No</td>
<td>ND</td>
</tr>
<tr>
<td>Ruben et al [13]</td>
<td>United States</td>
<td>United States</td>
<td>Laboratory exposure</td>
<td>M to F</td>
<td>6 Months</td>
<td>No</td>
<td>Negative after therapy</td>
</tr>
<tr>
<td>Present study</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case 1</td>
<td>Israel</td>
<td>Israel</td>
<td>Ingestion of dairy products</td>
<td>M to F</td>
<td>2.5 Months</td>
<td>No</td>
<td>Negative after therapy (PCR positive)</td>
</tr>
<tr>
<td>Case 2</td>
<td>Israel</td>
<td>Israel</td>
<td>Ingestion of dairy products</td>
<td>M to F</td>
<td>3.5 Months</td>
<td>Yes</td>
<td>ND</td>
</tr>
</tbody>
</table>

**NOTE.** ND, not done; PCR, polymerase chain reaction.
PCR, which we report here for the first time, to our knowledge, in humans, enabled us to prove sexual transmission in the first couple. Recently, the persistence of blood PCR positivity in individuals whose brucellosis cases were apparently cured has been reported [15]. The fact that semen PCR results were again positive on repeated testing despite apparent cure (Figure 1B) suggests that the role of PCR in long-term follow up and family counseling regarding the safety of sexual intercourse may be limited.

In conclusion, sexual transmission of *B. melitensis* was the only likely route of transmission in 2 cases according to the case history. In one case, clinical signs of orchido-epididimitis were present, and in the other case, even in the absence of clinical signs of orchitis, semen PCR results were positive. Although rarely described in humans, sexual transmission is frequent in livestock and may be underappreciated in humans, because it can only be demonstrated in regions of low endemicity. Prospective follow-up of male patients with semen cultures and PCR (regardless of symptoms) may help in assessing the true potential of sexual transmission in future cases. On a practical level, abstaining from intercourse or using relevant prophylactic measures during the course of illness should be recommended.

**Acknowledgments**

*Potential conflicts of interest.* All authors: no conflicts.

**References**