REVIEW

BRUCELLA PERITONITIS IN PERITONEAL DIALYSIS: A CASE REPORT AND REVIEW OF THE LITERATURE

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Brucellosis is a zoonotic infection that humans contract usually by ingestion of unpasteurized milk and milk products or by direct contact with raw infected animal products. Infection is endemic in many countries, including Turkey. Being a systemic disease, brucellosis may affect almost any part of the body. The peritoneum is a site rarely involved in brucellosis. Most peritonitis episodes involving *Brucella* species have been spontaneous cases reported in cirrhotic patients with ascites. To our knowledge, the literature contains only 5 cases of *Brucella* peritonitis related to continuous ambulatory peritoneal dialysis. Here, we report *Brucella* peritonitis in a continuous ambulatory peritoneal dialysis patient, and we discuss the relevant literature.

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Brucellosis is a zoonotic infection that humans contract usually by direct contact with raw infected animal products and materials, by ingestion of unpasteurized milk and milk products, or by inhalation of aerosols (1). This systemic infection can involve every organ system, including epididymis, testes, liver, bones, spleen, meninges, endocardium, and so on. Peritonitis from *Brucella* species has rarely been reported in the

literature; most cases involve spontaneous bacterial peritonitis in cirrhotic patients (2–6). In the setting of continuous ambulatory peritoneal dialysis (CAPD), *Brucella* peritonitis is exceedingly rare. To the best of our knowledge, only 5 cases of *Brucella* peritonitis in CAPD have been reported to date (7–10). Here, we report a case of *Brucella* peritonitis without systemic symptoms that was managed without removal of the peritoneal dialysis catheter. We also discuss important aspects of presentation and management in previously reported cases.

CASE REPORT

A 48-year-old man who had been undergoing CAPD for 3 years presented with complaints of abdominal pain, abdominal bloating, and constipation of 2 weeks' duration. With a preliminary diagnosis of CAPD-related peritonitis, the patient was given two 1-g doses of vancomycin on an outpatient basis. After an increase in the severity of abdominal pain, he was admitted to our nephrology clinic.

On physical examination, no fever or hypotension was evident. The abdomen was mildly tender to palpation. Other aspects of the physical examination were unremarkable, and the peritoneal effluent was not cloudy. The patient's white blood cell (WBC) count was $820/\text{mm}^3$ ($0.82 \times 10^9/\text{L}$; normal value: $<0.03 \times 10^9/\text{L}$), with 1% neutrophils, 48% lymphocytes, and 36% monocytes. Gram stain showed numerous leucocytes, but no micro-organisms. Laboratory findings included a blood urea nitrogen level of 84 mg/dL; creatinine, 5.2 mg/dL;

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WBCs, $7.16 \times 10^3/\text{mm}^3$ ($7.16 \times 10^9/\text{L}$); hemoglobin, 13 g/dL; platelet count, $373 \times 10^3/\text{mm}^3$; C-reactive protein, 54 mg/L; procalcitonin, 0.17 ng/mL; and erythrocyte sedimentation rate, 69 mm/h. Liver function tests were normal. Abdominal ultrasonography and upright abdominal radiography revealed no abnormal findings. The exit site of the Tenckhoff catheter was clean. An investigation of the peritoneal effluent for the presence of acidoresistant bacilli was negative.

Pending culture results, antibiotic treatment comprising intravenous ceftriaxone 1 g twice daily and intravenous vancomycin 1 g every 96 hours was commenced. On the 12th day, the WBC count in peritoneal fluid declined to $150/\text{mm}^3$ ($0.15 \times 10^9/\text{L}$). Culture of the peritoneal fluid yielded *Brucella* spp. sensitive to ceftriaxone, rifampicin, and gentamicin.

When we further explored the patient's history, he acknowledged contact with sheep and cattle in the village in which he lived. Cultures of peripheral blood and bone marrow yielded no bacterial growth. A *Brucella* immunocapture–agglutination test was positive at a titer of 1/5120. An ELISA for *Brucella* immunoglobulin M (IgM) and G (IgG) antibodies was also positive.

Upon the final diagnosis of *Brucella* peritonitis, we administered treatment with oral rifampicin (300 mg twice daily) and oral doxycycline (100 mg twice daily). The patient could not tolerate the doxycycline treatment, and so the doxycycline was switched to intravenous ceftriaxone 1 g twice daily. The rifampicin and ceftriaxone treatment was administered for 45 days. On the 20th day of this regimen, the WBC count in peritoneal fluid was found to be zero.

DISCUSSION

Brucellosis is a worldwide zoonotic infectious disease caused by gram-negative bacteria from the genus *Brucella*. The clinical presentations of brucellosis are myriad; in humans, they include fever and septicemia, and even multiple organ involvement. Because brucellosis is one of the great imitators in the world of infectious diseases, it can mimic various multisystem diseases, showing wide clinical polymorphism, which frequently leads to misdiagnosis and treatment delays, further increasing the complication rate (11).

The prevalence of brucellosis is more than 10 per 100 000 population in some endemic countries. Although the disease is seen widely throughout the world, it is hyperendemic in the Mediterranean Basin, the Arabian Peninsula, India, Mexico, and Central and South America (12). Brucellosis is also an endemic disease in Turkey, where the annual incidence is 23 per 100 000 population

(13). It is especially frequent in the rural areas of the middle and southeastern regions of the country, and *Brucella melitensis* is the most prevalent strain (14). In the presence of uremia complicated by brucellosis, neutrophils show reduced killing capabilities and modulated spontaneous apoptosis, and macrophages show inhibited NO synthesis (15). Those factors set the stage for the development of peritoneal infections in CAPD patients.

Peritonitis is a rare complication of brucellosis. Most cases of *Brucella* peritonitis reported in the literature (Table 1) are spontaneous bacterial peritonitis in the setting of cirrhosis (2–6). Of 5 patients with CAPD-related *Brucella* peritonitis reported in the literature, 4 were from Turkey (8). In 4 of the 5 patients, there was history of contact with animals and animal products, and of use of unpasteurized milk. Interestingly, fever at presentation was present in only 1 case. The most common presenting symptom was abdominal pain.

Brucellosis requires laboratory testing for diagnosis. Isolation of the organism from blood samples or other clinical specimens is the confirmatory test for the disease; however, the sensitivity of this technique depends on the stage of the illness and on other factors. Furthermore, culture does not provide a rapid result (16). Irmak *et al.* (16) showed that *Brucella* IgM and IgG flow assays had high sensitivity and specificity. That rapid and simple diagnostic test may be used to confirm brucellosis in patients living in an area endemic for the disease and clinically suspected of having it. Tests for *Brucella* IgM and IgG have been reported only by us and by Ozisik *et al.*, and although results were positive in our case, results in the case reported by Ozisik *et al.* were negative (8). The local nature of the infection in the Ozisik *et al.* case may be the reason for the negative test results.

In the isolated peritoneal *Brucella* infection reported by Ozisik *et al.* (8), blood and serologic markers of systemic disease were absent, although the peritoneal fluid was shown to be infected with *Brucella* species. In all other reported cases (including the present case), evidence of systemic involvement was present. Our isolated peritonitis case may be a result of contamination through direct contact. Interestingly, the case reported by Alothman *et al.* (9) showed persistent positive serology despite long-term treatment and was considered to be chronic *Brucella* peritonitis.

In 3 of 5 cases, the Tenckhoff catheter was removed, but in the other 2 cases, the infection was treated with the catheter *in situ*. With our case included, the catheter removal rate is 50%. In the case of chronic *Brucella* peritonitis reported by Alothman *et al.* (9), recurrence

TABLE 1
Clinical and Laboratory Findings in Reported Cases of Brucella Peritonitis in Continuous Ambulatory Peritoneal Dialysis

Reference	Age (years)	Sex (M/F)	Previous symptoms and history	Predisposing factors	ESR (mm/h)	Effluent white blood cells	Gram stain	Cultures Effluent	Blood	Serum agglutinin titer	Per	Treatment	IgG	IgM	Catheter removal
Taskapan <i>et al.</i> , 2002 (10)	47	M	Fatigue Sweating Back pain Cloudy effluent Fever 38.2°C No history of previous peritonitis	Ingestion of unpasteurized, unsalted cheese made from fresh goat's milk	—	300/mm ³ Neutrophil predominance Increased to 1400/mm ³ with empirical treatment Lymphocyte predominance	No organisms shown	<i>B. melitensis</i> , 6th day	<i>B. melitensis</i> , 6th day	1:2560?	NR	Doxycycline 100 mg twice daily, rifampin 600 mg daily	NR	NR	(+) Recur- rence after 6 weeks' treat- ment while catheter in situ
Ozisik <i>et al.</i> , 2006 (8)	39	F	Nausea Abdominal pain Fever 37.3°C History of 4 peritonitis episodes	Direct contact with animal	—	3140/μL 80% neutrophils After empirical treatment 24 300/μL	No organisms shown	<i>B. melitensis</i> , 21st day	Negative	Negative	1:160	Doxycycline 100 mg twice daily, rifampin 450 mg daily	(-)	(-)	(+)
Alothman <i>et al.</i> , 2008 (9)	67	M	Change of effluent color Abdominal pain Lower limb edema History of previous peritonitis?	History of raw milk ingestion	63	3356/mm ³ 8% lymphocytes 85% neutrophils After empirical treatment: 11/mm ³ 62% lymphocytes 12% neutrophils	No organisms shown	Grew <i>Brucella</i> spp., 6th day	NR	<i>B. melitensis</i> : 1/2560 <i>B. abortus</i> : 1/640???	NR	Doxycycline 100 mg, rifampin 600 mg once daily	NR	NR	(+) Recur- rence after 8 weeks' treat- ment while catheter in situ

TABLE 1 (cont'd.)

Reference	Age (years)	Sex (M/F)	Previous Symptoms and history	Predisposing factors	ESR (mm/h)	Effluent white blood cells	Gram stain	Cultures Effluent	Blood	Serum agglutinin titer	Treatment	IgG	IgM	Catheter removal
Unal <i>et al.</i> , 2009 (7)	38	M	Abdominal pain Nausea, vomiting Cloudy effluent Fever 37.3°C No history of previous peritonitis	Farmer; history of unpasteurized cheese consumption	30	1600/mm ³ Neutrophil predominance After empirical treatment: >100/mm ³ Lymphocyte predominance	No organisms shown	<i>B. melitensis</i> , 5th day	<i>B. melitensis</i>	1:640	Doxycycline 100 mg twice daily, rifampin 600 mg daily	NR	NR	(-)
Unal <i>et al.</i> , 2009 (7)	52	M	Severe abdominal pain Nausea, vomiting Joint pain Cloudy effluent Fever 37.2°C No history of previous peritonitis	Absent	130	5100/mm ³ Neutrophil predominance After empirical treatment: 1500/mm ³	No organisms shown	<i>B. melitensis</i> , 6th day	<i>B. melitensis</i>	1:640	Doxycycline 100 mg twice daily, rifampin 600 mg daily	NR	NR	(-)
Present report	48	M	Abdominal pain Abdominal bloating Constipation Previous peritonitis episode?	Contact with sheep and cattle	69	820/mm ³ 84% lymphocytes 1% neutrophils	No organisms shown; numerous leucocytes	<i>Brucella</i> spp.	Yielded no organisms	1:5120	Ceftriaxone 1 g twice daily, plus rifampin 600 mg daily	+	+	(-)

M/F = male/female; ESR = erythrocyte sedimentation rate; IgG = immunoglobulin G; IgM = immunoglobulin M; NR = not reported.

after 2 months of antibiotic treatment necessitated removal of the peritoneal catheter. Consequently, those authors suggested that removal of the peritoneal catheter should be strongly considered once CAPD *Brucella* peritonitis is diagnosed. However, we were able to treat our patient with the catheter *in situ*. In our opinion, the factors to rely on when deciding on catheter removal can include the presence of local peritonitis [as in the case reported by Ozisik *et al.* (8)] or the presence of severe systemic disease [as in the case reported by Taskapan *et al.* (10)]. In the latter case, the *Brucella* bacilli most probably entered through the catheter by direct contact, and thus colonization of the catheter may have occurred. Recurrence of the peritonitis after clinical and biochemical improvement lend further support to that mode of spread. If a culture of the peritoneal fluid yields *Brucella* bacilli, and if systemic involvement is lacking (blood cultures and *Brucella* IgM and IgG antibodies in blood are all negative), then it may be prudent to remove the catheter early in the infective course to prevent recurrence and treatment failure, because it seems difficult to eradicate *Brucella* bacilli from a contaminated catheter. Nevertheless, given that only a few cases have been reported to date, the choice to remove the catheter or to leave it in place should be judged according to the features of the individual case.

Although not reported to date in developed countries, *Brucella* peritonitis should be kept in mind in endemic countries. Patients living in rural areas who are involved in the care of domestic animals or who consume unpasteurized milk products are especially at risk for CAPD *Brucella* peritonitis. In Turkey, nephrologists prefer peritoneal dialysis for patients residing rural areas distant from hemodialysis facilities. Most of these patients are at risk for brucellosis, a factor that may hold true for other endemic countries.

One point that should be noted is the susceptibility of most strains of *Brucella* to ceftriaxone treatment. Because ceftriaxone is one of the empiric antibiotic options in the treatment of CAPD-related bacterial peritonitis, an initial partial response to empiric treatment may delay the diagnosis of *Brucella* peritonitis. If lymphocyte predominance in a WBC differential of peritoneal effluent coupled with incomplete clinical remission is encountered, then *Brucella* should be included with tuberculosis in the differential diagnosis.

DISCLOSURES

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