**Brucella Meningitis**

KATHRYN R. CHALLONER, MD,* KEITH B. RILEY MD,†
ROBERT A. LARSEN MD‡§

A 36-year-old Hispanic man came into the emergency department with nonspecific symptoms (headache, myalgias, low-grade temperature, and low white blood cell count) and was diagnosed with brucella meningitis. The patient said he had consumed unpasteurized goat's milk and cheese in Mexico, and had been treated 3 months previously for a febrile illness diagnosed as *Malta fever* (brucellosis). Cultures of both the blood and cerebrospinal fluid yielded *Brucella melitensis*. Blood agglutinin results for *B abortus* were positive at >1:160. Unpasteurized milk and cheese are consumed in many countries where brucellosis is endemic. Emergency physicians are occasionally confronted with patients from developing countries with diseases that require rapid and specific diagnosis for optimal treatment (Am J Emerg Med 1988;8:40-42 ©1990 by W.B. Saunders Company.)

The incidence of brucella infection has decreased in the United States. The number of reported cases declined from 6,521 in 1945 to 154 cases in 1982 with the implementation of the Federal-State Cooperative Brucellosis Eradication Program coupled with the mandatory pasteurization of milk. From 1985 to 1987, the number of cases increased from 106 to 153 per year; most of these occurred in people with occupational exposure to infected animals. However, brucellosis remains a problem in many of the South and Central American countries, the Mediterranean area, and the Middle East.

Brucellosis is frequently misdiagnosed because signs and symptoms are nonspecific. However, if there is a history of recurrent febrile illness and either occupational exposure to infected pigs, goats, or cows, or the consumption of unpasteurized milk or cheese, brucellosis should be included in the differential diagnosis. The onset may be acute or insidious with patients complaining of malaise, chills, fever, chills, sweats, weakness, myalgias, arthralgias, anorexia, and weight loss. Physical abnormalities are few although lymphadenopathy, splenomegaly, hepatomegaly, orchitis, and epididymitis may be present.

Neurobrucellosis can take diverse forms, such as meningitis, meningooencephalitis, subarachnoid hemorrhage, myelitis, and neuritis. Recovery of the Brucella organism from the cerebrospinal fluid (CSF) is very rare, with less than 40 cases reported in the world literature. A case of brucella meningitis that occurred in 1987 in a patient from Mexico is reported here.

### CASE REPORT

A 36-year-old Mexican man entered the emergency department at the Los Angeles County/University of Southern California Medical Center complaining that during the past week he had experienced photophobia, fever, chills, nausea, and vomiting. A headache that had begun 1 month prior to admission was increasing in severity. Over the last 7 days, he had developed a dry nonproductive cough and diffuse myalgias. In the last 48 hours, he noted increased dizziness on standing, decreased urine volume, and dark urine. He denied dysuria, diarrhea, chest or abdominal pain, shortness of breath, or skin rash. One day prior to admission another physician had diagnosed malaria and prescribed chloroquine, even though a blood smear had not been done. The patient had a history of similar symptoms 3 months previously, diagnosed as *Malta fever* (brucellosis), that resolved after treatment with an intramuscular injection.

The patient had come to Los Angeles 1 month earlier from a rural village near Leon, Mexico. He described the village as primitive, lacking basic sanitation and a safe water supply. The area is endemic for malaria, and he had taken no malaria prophylaxis. He also denied a history of tuberculosis (TB) but had never had a TB skin test. He said that he had consumed unpasteurized goat's milk and cheese during his stay in Mexico.

The patient was married with six children and no one else in the family was ill. He had no history of intravenous (IV) drug abuse, homosexuality, or blood transfusions. There was no history of alcohol abuse, trauma, previous surgeries, or other medical illnesses.

On examination, the patient was alert but appeared to be acutely ill and in a toxic condition. Vital signs were blood pressure, 88/40 mm Hg; pulse, 90/min; respirations, 24/mm; and oral temperature 101.0°F (38.3°C). His eyes were sunken and the conjunctivae were injected. Pupils were equal and reactive to light. Fundoscopic examination results were normal. His mucous membranes were dry. Tympanic membranes were normal. His neck was not stiff but he experienced some pain on forward flexion. Kernig’s and Brudinski’s signs were positive but all the muscles were tender on manipulation. There was no lymphadenopathy. His lung fields were clear to auscultation and percussion. There was a soft systolic murmur located at the left precordial border that radiated to the apex. The liver was palpable four finger breadths below the right costal margin; a spleen tip was felt. The abdomen was not tender and had decreased bowel sounds. Rectal examination results were normal; stool occult blood result was negative. Genitalia were normal. There was tenderness to palpation along the lower thoracic spine. There was no costovertebral angle tenderness. He had mild clubbing of the fingers with no splinter hemorrhages. His skin had no rash but turgor was decreased. The neurological examination showed no focal deficits. Reflexes were normal and symmetrical.

The patient was given 400 mL of intravenous normal saline after which the blood pressure rose to 110/80 mm Hg. Serum electrolytes were: sodium, 132 mmol/L; potassium, 3.4 mmol/L; and bicarbonate, 20 mmol/L; glucose level was 114/mg/dL. Hematocrit was 13.9 g/dL. The hemoglobin was 13.9 g/dL, the hematocrit was 40%; the white blood cell count (WBC) was 4.6 x 10^9/L (WBC 4,600) with 38% segmented neutrophils, 1% bands, 40% lymphocytes, and 11% monocytes. No malarial parasites were seen in the peripheral smear. The erythrocyte sedimentation rate (ESR) was 40 mm/h. The results of the urinalysis were normal except for a trace of...
ketones. A chest roentgenogram and electrocardiogram (ECG) were normal. He was admitted to the Infectious Disease Service where blood was sent for culture, and to be tested for brucella antibodies, and febrile agglutinins. Lumbar puncture showed an opening pressure of 170 mm H2O; the fluid was clear. Cerebrospinal fluid (CSF) glucose was 45 mg/dL; protein was 54 mg/dL; gram stain results were negative. CSF cell count was 96 WBC/mm3 with 75 monocytes and 21 segmented neutrophils. Cerebrospinal fluid latex fixation results for Streptococcus pneumoniae and Neisseria meningitidis serogroups A, B, C, W135 antigens were negative. Cerebrospinal fluid was sent for brucella culture and antibodies, a mycobacterial four times a day to be continued for 2 months. On a follow-up visit diagnostic range can be encountered with cholera, typhoid fever, tularemia, yersinia infection, or vaccination against these diseases. Of particular interest in our patient was a positive Well-Felix reaction to OX 2 and OX 19 and a positive Widal reaction to salmonella group D. Cross reactions of the brucella antigen with rickettsial diseases has not been previously reported. Positive blood cultures occur in 10% to 30% of cases and may be higher with B melitensis infection. The CSF characteristically shows increased protein level, low sugar concentration, and a lymphocytic or mononuclear cell pleocytosis. Isolation of the brucella from the CSF is uncommon. In his study of 24 patients since 1975, reported positive CSF cultures in 8% of cases. If the CSF fluid or the infected central nervous system tissue obtained at the time of operative exploration is cultured, the retrieval of the brucella organism has been reported to occur in 45% of cases.

In 1897, Hughes first isolated B melitensis from the brain tissue of a patient with a fatal case of brucellosis. In 1951, Nichols reviewed the world literature and reported 22 cases where brucella was cultured from either the CSF or the brain tissue. Since then there have been random reports in the literature of 13 additional cases where a CSF culture was positive for brucellosis. Cerebrospinal fluid antibodies may be detected but were absent in our patient.

Traditional antimicrobial management of patients with brucellosis is with tetracycline alone or in combination with streptomycin. However, in the setting of neurobrucellosis this combination has been associated with frequent relapse, possibly because tetracycline is bacteriostatic and streptomycin does not cross the blood brain barrier. Alternatives to traditional therapy have not been well studied. Rifampin has excellent in vitro antibrucella activity and clinically has been used with limited success. Emergence of resistance has been postulated as a reason for the 8% to 15% rate of relapse when rifampin is used as a single agent. However, rifampin has good CSF penetration and may play a role in combination therapy. Trimethoprim-sulfamethoxazole has been used with increasing frequency for neuro-cerebral Brucella infection. Clinical experience using both trimethoprim-sulfamethoxazole and rifampin for treatment of neurobrucellosis is limited; one study including five patients noted a 20% relapse rate. The medical literature has yet to describe an ideal regimen except to recommend combination or triple therapy. The combination of tetracycline, rifampin, and trimethoprim-sulfamethoxazole was successful in curing this man with culture-proven neurobrucellosis, and there has been no evidence of relapse 3 months after treatment was stopped.

**SUMMARY**

A patient from Mexico came in to the emergency department with nonspecific symptoms. The diagnosis of B melitensis meningitis was made based on the patient's history and CSF findings; empiric treatment with triple antibiotics was begun. One week later, the diagnosis was confirmed by positive results from the blood and CSF cultures.

**REFERENCES**

7. Nichols E: Meningo-encephalitis due to brucellosis with the report of a case in which B. abortus was recovered from the cerebrospinal fluid and a review of the literature. Ann Intern Med 1951;35:673-693