Chronic Brucella Empyema*

Nabil Mili, M.D.;‡ Raymond Auckenthaler, M.D.;‡ and Laurent Pierre Nicod, M.D.§

Brucellosis rates have decreased in developed countries in recent years, but the pathologic condition still occurs in developing countries and well-known endemic areas such as the Mediterranean and Middle Eastern countries. A Portuguese patient presented in Switzerland with long-term pleural empyema, which was later diagnosed as Brucella empyema through positive cultures of Brucella melitensis. Brucellosis should be considered in patients who have traveled to Middle Eastern countries or any other areas where brucellosis is more frequently encountered. (Chest 1993; 103:620-21)

Chronic pleural exudate may represent a difficult clinical problem. We report the case of chronic Brucella empyema. This etiology is rarely mentioned in developed countries where the incidence of brucellosis has markedly decreased. However, this pathologic condition may have to be recalled not only for patients from well known endemic areas such as the Mediterranean and Middle Eastern countries, but also from most developing countries.

CASE REPORT

A 39-year-old man was hospitalized on April 5, 1989, for treatment of an anal fistula. The pulmonary service was called for the evaluation of a chronic left pleural exudate.

This Portuguese patient resided in Switzerland since 1980 when left pleural thickening was discovered on a routine chest roentgenogram. The tuberculin skin test yielded a 20 mm reaction, and six months of prophylaxis with isoniazid (300 mg/dl) was given. On a routine chest roentgenogram April 16, 1983, the pleural opacity was three times thicker while the patient reported no symptoms, and his weight was unchanged. The pleural fluid WBC value was 1,300/cu mm, with mostly polymorphonuclear cells, protein value of 67 g/L, and a LDH value of 1,680 U/ml. The culture for aerobic bacteria after four days and for Mycobacteria remained negative.

In the pleural biopsy specimens, nonspecific granulomatoses tissue was described, but no organism was noted with the Zielh coloration on two occasions. Trithrapy with isoniazid, rifampicin, and ethambutol was prescribed and stopped four months later. In May 1984, a mild cholestatic icterus was investigated. The work-up included a liver biopsy. The mild fibrosis and inflammation were attributed to alcohol abuse. The follow-up was discontinued in July 1985, the chest roentgenogram being unchanged, and the patient having no complaints.

In April 1989, the patient presented without chest pain, cough, fever, or chills, but had a mild tremor and a subicterus. The physical examination revealed a mild dullness on the left side with a few crackles. There was no hepatosplenomegaly. On the chest roentgenogram, the pleural thickening was slightly enhanced on the left side (Fig 1 left), with some interstitial markings adjacent to it. The hemocrit value was 43 percent. The WBC was 7,200/cu mm, with 58 percent neutrophils, 8 percent monocytes, and 28 percent lymphocytes. The platelet count was 327,000/cu mm. Aspartate aminotransferase value was 330 U/L, and alanine aminotransferase, 628 U/L. The prothrombin time was normal. A left pleural puncture revealed a hemorrhagic exudate with RBC of 2.2×10¹⁰/cu mm; WBC, 4,500/cu mm, with 88 percent neutrophils, 9 percent lymphocytes, and 3 percent macrophages. The protein value was 72 g/L; glucose, 0.5 mmol/L; and LDH, 3,251 U/L. Routine cultures were performed on 5 percent sheep blood agar, chocolate agar, and brain heart infusion broth incubated in 5 percent CO₂. Growth on agar plates was negative; however, routine subcultures of the broth after one week on chocolate agar revealed growth of Gram-negative catalase and oxidase-positive coccobacilli.

The strain was identified by the Swiss reference center as Brucella melitensis biochemically, with growth on Petragrani medium and agglutination with monospecific antisera anti-A and anti-M (FAO-WHO collaborating Center for Reference and Research as Brucellosis, Central Veterinary Laboratory, United Kingdom).

Cultures for Mycobacteria performed on Bactec, Loewenstein, and Middlebrook media remained negative. The immunoserology was positive in a single serum sample with an elevated titer of 1/160 by tube agglutination. A sonogram of the abdomen showed no liver or pancreatic abnormality. Scintigraphy revealed no osteo-articular involvement. The patient was treated with doxycycline, 100 mg/d for six weeks in association with gentamicin, 3×80 mg/d for two weeks. The surgical cure of the anal fistula was uneventful, and the histologic findings showed only a nonspecific inflammatory tissue. The liver function test results were normal two months later.

The chest roentgenogram during the following year revealed a marked decrease of the left pleural thickening (Fig 1 right). The Brucella serology decreased to a titer of 1/40.

DISCUSSION

This case illustrates a rare cause of empyema. However, this etiology has to be considered in patients with recent travel to Middle Eastern countries such as Kuwait, where the incidence of brucellosis reaches 70/100,000 inhabitants or to Mediterranean countries such as Spain, where 22.3 cases per 100,000 inhabitants are reported. If brucellosis is also frequent in Latin America or in Asia, the annual incidence rates for human brucellosis ranged from 0.4 to 0.9 cases per million in the United States between 1983 and 1989. Transmission to humans usually occurs by direct

*From the Anesthesiology Division, ‡Infectious Diseases Division, and §Respiratory Division, University Hospital, Geneva, Switzerland.

Reprint requests: Dr. Nicod, Centre Antituberculeux, Hospital Cantonal, Geneva, Switzerland 1211
contact with infected animals or by ingestion of unpasteurized milk or dairy products from infected animals. The clinical manifestations may vary from acute systemic or localized infections to chronic infections. The most common symptoms are fever, sweats, chills, and musculoskeletal pain. Any organ may be affected, and the spectrum varies from arthritis and carditis to neurobrucellosis. Respiratory symptoms are reported in up to 25 percent of patients. Cough, dyspnea, and flu-like disease occurred in 87 (23 percent) of 379 patients in a recent series. On chest roentgenogram, the findings were a localized or general haziness in 24 cases, a pneumonia in five, and a solitary granuloma in one. In the remaining 54 patients, no abnormalities were found. In Greer's study, nodular lesions were reported in 8 out of 27 cases and a miliary pattern in four. The most characteristic changes were perihilar thickening or peribronchial infiltrates. Pleural empyema has, however, been reported on at least ten occasions, three of which were long-term empyema.

A definitive diagnosis of brucellosis is made by recovering the organism in blood, fluids, or tissue specimens. If blood cultures are often positive in acute cases, they remain most often negative in subacute or chronic cases. The specimen may need up to six weeks to grow the organisms on appropriate media. A serology with the standard tube agglutination test of 1/160 or greater, or a fourfold rise in titer is considered presumptive evidence of past or recent infection with brucelae.

The present patient entered Switzerland in 1980 with a thickened pleura and a positive skin test for tuberculosis. He completed a six-month prophylactic regimen of isoniazid for having been infected with tuberculosis with probable pleural sequellae. He travelled several times to Portugal since 1980, where he consumed goat cheese and unpasteurized milk. He may have contracted brucellosis in 1983, when a pleural effusion appeared. He may have been treated partially with rifampicin. A patient with brucellosis, treated with rifampicin alone, has indeed a 10 to 40 percent chance of suffering relapse. A definitive diagnosis was made only in 1989 when pleural cultures were kept long enough to grow the organisms.

A year after proper treatment, the serology titers dropped from 1/160 to 1/40, and the pleura markedly decreased in thickness. This case illustrates how Brucella melitensis can produce a chronic pleural empyema. Some of the poorly defined symptoms may have been attributed to the alcoholism of the patient, and this may explain the protracted course before the diagnosis was made.

Many regimens have been used for treating patients with brucellosis. Treatment with a single agent is often complicated by relapses. Previous guidelines recommended the combination therapy of tetracycline and streptomycin. Currently, doxycycline, 200 mg/day, plus rifampicin, 600 to 900 mg/day given for six weeks, is considered the regimen of choice by the World Health Organization.

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