

***Arcanobacterium pyogenes* Sepsis in Farmer, Brazil**

To the Editor: *Arcanobacterium pyogenes* is a normal inhabitant of the mucous membranes of domestic animals, such as cattle, sheep, swine, and goats (1). Diseases caused by this agent have been reported for persons who live in rural areas and have underlying illnesses such as cancer and diabetes (2–4). A recent literature review (3), elicited by a case of *A. pyogenes* endocarditis, found 13 unequivocal cases of human infection with this agent; many patients had a history of close contact with domestic animals. However, septicemia was not reported.

In June 2006, a 27-year-old immunocompetent man was hospitalized in Campinas (São Paulo, Brazil) for fever, cough with purulent bloody sputum, and discharge from and pain in both ears. The patient was a farmer who lived in the rural Amazon area and had extensive contact with cattle and swine. For the past 3 days he had been taking amoxicillin, 1.5 g/day, for chronic otitis media. At the time of hospital admission, his temperature was 38.9°C, respiratory rate 24 breaths/min, and blood pressure 100/70 mm Hg. He had palpable hepatosplenomegaly, but no murmur was detected in the precordium. Computed tomography (CT) scan of his chest showed multiple pulmonary nodules and alveolar infiltrates with small cavities suggestive of septic infarctions. Abdominal CT scan confirmed hepatosplenomegaly with focal lesions in the spleen. CT scan of the middle ear showed bilateral cholesteatoma and mastoiditis. No abnormalities were found during 2 transthoracic echocardiography procedures. Laboratory values were PaO₂ 63.4 mm Hg, hemoglobin 11.9 g/dL, thrombocytes 109 × 10³/mm³, leukocytes 11.05 × 10³/mm³ with a left shift, serum albumin 2.6

g/dL, alanine aminotransferase 108 U/L, and total bilirubin 2.57 mg/dL. Blood and the ear secretion were submitted for culture. Cefepime was prescribed, 2 g/twice a day.

Three blood cultures grew gram-positive bacilli, initially identified as *Corynebacterium* spp., sensitive to penicillin, ampicillin, ceftriaxone, gentamicin, clindamycin, vancomycin, and resistant to erythromycin, as determined by disk-diffusion test. Ear discharge culture grew *Proteus mirabilis*, sensitive to β-lactams, cephalosporins, and aminoglycosides. Subcultures of the gram-positive bacilli on sheep blood agar grew pinpointed, grayish, β-hemolytic colonies, identified as *A. pyogenes* by use of API Coryne 2.0 kit (bioMérieux, Durham, NC, USA; code 4732761). Although susceptibility standards are not available for this organism, it was considered susceptible to penicillin and ampicillin by combining the disk-diffusion test with the MICs, as determined by the Etest (0.06 mg/L for penicillin, 0.023 mg/L for ampicillin).

Partial 16S rDNA was amplified by using primers p27f and BAC1401r and sequenced by using primers 1100r, 765fs, and 10f. Sequences were compared with those available in GenBank by using gapped BLASTN 2.0.5 software (5). Identification to the species level was defined as a 16S rDNA sequence identity ≥97%. Phylogenetic analysis was performed by using MEGA version 4.0 (6) after multiple alignments of data by ClustalX (7); gaps were treated as missing data. Clustering was performed by the neighbor-joining method (8). Bootstrap analysis was used to evaluate tree topology of the neighbor-joining data by performing 1,000 resamplings (9). BLASTN analysis of the 16S sequence of the isolate showed 99% identity with the 16S sequence of *A. pyogenes* (accession no. X79225). Phylogenetic analyses with MEGA grouped this isolate with *A. pyogenes* NCTC 5224 in a branch separated from other species;

this grouping supported the phenotypic identification.

During the 7 days after admission, the patient's condition worsened, cefepime was withdrawn, and ampicillin 6 g/day plus gentamicin 240 mg/day were prescribed. The patient became afebrile, gradually recovered, and was discharged after 28 days of therapy.

Our patient had otitis media that progressed to sepsis, which was diagnosed by clinical, laboratory, and imaging findings. The causative agent may have been undetectable in ear discharge if it was overshadowed by a strain of *P. mirabilis*, a fastidious organism that also colonizes or co-infects this site. Endocarditis could not be ruled out because transesophageal echocardiography was not available.

A. pyogenes is usually susceptible to benzyl penicillin, ampicillin, gentamicin, and macrolides and resistant to trimethoprim/sulfamethoxazole, streptomycin, and tetracyclines (10). The isolate from this patient was sensitive to β-lactams, ceftriaxone, and gentamicin. However, susceptibility standards are not available because *A. pyogenes* rarely causes disease in humans. The patient had taken oral amoxicillin before admission, but his condition had not improved; subsequent addition of cefepime was also unsuccessful. The organism was probably sensitive to ampicillin, considering the low MIC and the expected serum concentration of the drug, but diffusion into the middle ear may have been poor or the local conditions caused by the cholesteatoma may have influenced the poor outcome of initial therapy. Treatment with intravenous ampicillin plus gentamicin produced full recovery.

Clinical laboratories do not routinely attempt to identify this organism. However, even in the absence of substantial concurrent illness, *A. pyogenes* must be considered as an etiologic agent of several human infections, especially septicemia, for patients with a

history of close contact with domestic animals, mainly cattle and swine.

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Reactivation of Bovine Tuberculosis in Patient Treated with Infliximab, Switzerland

To the Editor: Increased risk for reactivation of tuberculosis (TB) after treatment with tumor necrosis factor (TNF) antagonists, particularly infliximab, is well documented (*1*). We describe a case of peritoneal TB, probably resulting from reactivation of *Mycobacterium bovis* infection after infliximab treatment. In retrospect, reactivation might have been preventable had physicians been aware of the patient's history of regularly drinking fresh cow's milk from a local farm in Switzerland during 1944–45, when bovine TB was prevalent.

The patient was a 69-year-old Swiss woman who was examined for weakness, abdominal pain, increasing abdominal girth, and weight loss in April 2008. Her history included a diagnosis of Crohn disease in 1978 and treatment with glucocorticoids, cyclosporine, and mercaptopurine. In November 2007, during a recurrence of Crohn disease and while receiving treatment with azathioprine, the patient had a negative interferon

gamma release assay (IGRA) result (QuantiFERON-TB in Tube test; Celltestis International, Carnegie, Victoria, Australia) and an unremarkable chest radiograph. On November 30, 2007, she was given prednisone (40 mg/d for 2 weeks, then tapered) and prescribed 3 doses of infliximab because of severe inflammation seen during colonoscopy (5 mg/kg on November 30, 2007, January 4, 2008, and February 15, 2008). She was hospitalized on April 25, 2008, at which time she had ascites; the fluid contained $1.4 \times 10^9/L$ leukocytes (79.5% lymphocytes) but was negative for acid-fast bacilli on direct examination and PCR testing for *Mycobacterium tuberculosis* complex. Laparoscopy on May 2, 2008, showed extensive peritoneal inflammation. Peritoneal biopsy samples contained acid-fast bacilli and caseating granulomas; PCR for *M. tuberculosis* complex was positive. At this time, results of a repeat QuantiFERON-TB in Tube test and a tuberculin skin test (TST) were negative, but a T-SPOT.TB (Oxford Immunotec, Abingdon, UK) test was positive (6-kDa early secretory antigenic target [ESAT-6], >20 spots; 10-kDa culture filtrate protein [CFP-10], 11 spots). *M. bovis* ssp. *bovis* was grown in cultures of peritoneal biopsy samples. For culture, the MGIT 960 automated culture system (Becton Dickinson, Sparks, MD, USA) was used. The isolate was identified by use of a multiplex PCR-based, solid-phase, reverse-hybridization assay (GenoType MTBC, Hain Lifescience GmbH, Nehren, Germany), excluding *M. bovis* BCG (*2*). The patient was discharged May 30, 2008. In January 2009, she was much improved after treatment with isoniazid/rifampin/ethambutol for 3 months and moxifloxacin/rifampin for 5 months.

This case of presumed reactivation of peritoneal TB caused by *M. bovis* in a patient treated with infliximab highlights the need to be aware of local epidemiology with regard to transmissible infectious diseases.