Tularemia presenting as pulmonary nodules in an immunocompromised patient

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Tularemia is a zoonotic disease caused by *Francisella tularensis* that can be transmitted to humans when they handle rabbits, receive tick bites, consume contaminated water, or inhale aerosolized particles. We present the case of a 51-year-old white man with rheumatoid arthritis who was taking immunosuppressive medications and presented with tularemia. Our patient acquired the typhoidal form of tularemia, which is a severe systemic illness that manifests with fevers, headaches, myalgias, vomiting, diarrhea, and neurological symptoms, due to his immunocompromised state. The diagnosis was made through biopsy of a pulmonary nodule found incidentally on computed tomography scan.

CASE PRESENTATION

A 51-year-old white man with rheumatoid arthritis and Addison's disease came in to the emergency department complaining of generalized weakness, watery diarrhea, fever, and chest pain for 3 days. On the day of admission, he was confused and lethargic. His medications included a monthly infliximab infusion, leflunomide 5 mg orally two times daily for rheumatoid arthritis, and fludrocortisone 0.1 mg orally once daily for Addison's disease. He lived with his wife, children, and a dog on a ranch in Wichita Falls, Texas. At admission, his blood pressure was 130/70 mm Hg; heart rate, 103 beats per minute; and temperature, 101.9°F. Physical examination was unremarkable. His white blood cell count was 6100/μL and platelet count, 80,000/μL. Computed tomography (CT) showed multiple pulmonary parenchymal nodules bilaterally with mediastinal adenopathy and a right pleural effusion *(Figure)*.

He was started on intravenous vancomycin, cefepime, and metronidazole. On day 3, one of the pulmonary nodules was biopsied. Bactrim 80 to 160 mg/day was added on day 4, and he was discharged. One week later, he was informed by the state health department that the lung biopsy culture grew *Francisella tularensis.* He was then readmitted for intravenous infusion of gentamicin and oral ciprofloxacin. Further history revealed that he had found dead cottontail rabbits in his backyard several weeks earlier and had picked them up with his bare hands. Thereafter, he may have inhaled the aerosolized organism from mowing the lawn. His dog became sick after this and developed supraclavicular lymphadenitis that required incision and drainage along with intravenous antibiotics. He was treated with 3 weeks of intravenous gentamicin and oral ciprofloxacin. A repeat CT of the chest showed that the pulmonary nodules had decreased in size.

DISCUSSION

Tularemia is a zoonotic infection that is endemic in North America, continental Europe, Russia, Japan, and China. In 1911, McCoy and Chapin first isolated a gram-negative bacterium from ground squirrels suffering from a plague-like disease in Tulare County, California, and named it *Bacterium tularense* (1). The first documented case of human infection was in 1914, when this bacterium was isolated from a meat cutter who developed conjunctivitis and lymphadenopathy (2). Edward Francis reviewed about 800 cases of infections with this bacterium and published a paper describing the clinical characteristics of the disease in 1928 (3); the bacterium was renamed *Francisella tularensis* after him.

F. tularensis is gram-negative coccobacilli that can be contracted through an arthropod bite, the handling of an infected animal carcass, or the consumption of contaminated water and meat. Small rodents and lagomorphs (hares and rabbits) are the most common animal reservoirs. From 2005 to 2014, 95 to 203 cases of tularemia were reported per year in the United States (4). This condition is most prevalent in the Southwest region of the United States, including Arkansas, Kansas, Louisiana, Missouri, Oklahoma, and Texas. Men have contracted more than 70% of cases of tularemia, possibly due to exposure from hunting and landscaping (4).

Of the six described forms of tularemia, ulceroglandular tularemia is most common and is acquired through an infected skin lesion that leads to lymphadenopathy (5). This patient was diagnosed with the typhoidal form of tularemia, which usually presents with acute-onset fevers, headaches, myalgias, vomiting, diarrhea, and neurological symptoms including

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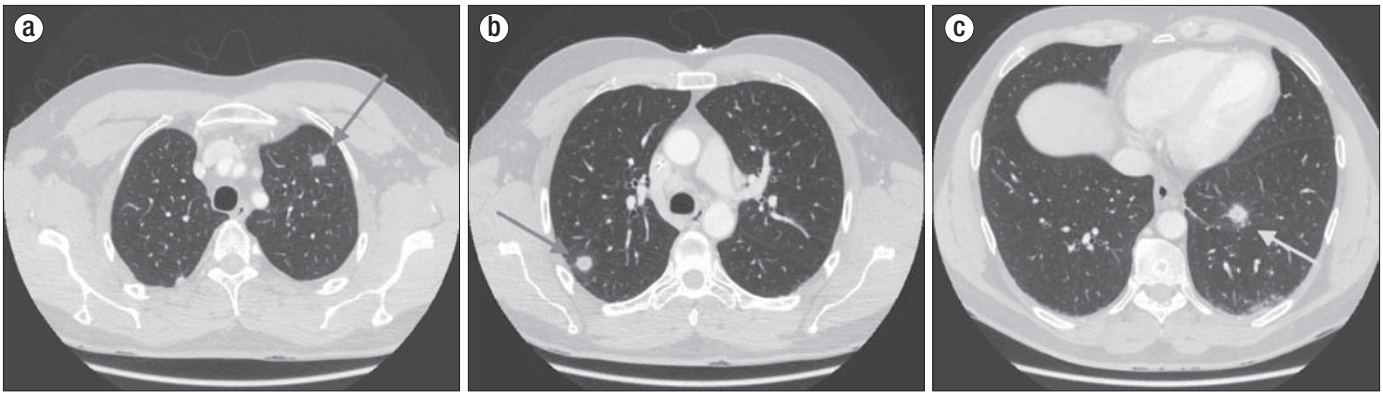

Figure. Cross-sectional CT shows pulmonary nodules (arrows) in the **(a)** left upper lobe measuring 1 cm, **(b)** right upper lobe measuring 1.3 cm, and **(c)** left lower lobe measuring 1.6 cm.

confusion. Pulmonary tularemia is a subacute or chronic infection that presents with fever, cough, weight loss, and mediastinal lymphadenopathy that mimics tuberculosis, lymphoma, or sarcoidosis (6). A distinctive feature of this case is that the patient was on immunosuppressive therapy for rheumatoid arthritis, which placed him at a higher risk for typhoidal tularemia than an average individual. This is an atypical presentation for tularemia because the patient presented with nonspecific symptoms and was found to have incidental pulmonary nodules on CT scan of the chest.

Blood cultures are usually falsely negative because *F. tularensis* is a fastidious organism that requires cysteine-enriched media, and the laboratory must be made aware of its possibility ahead of time. Serology with agglutination or enzyme-linked immunosorbent assay can be used for diagnosis with titers of 1:128 or 1:160. Antibodies may not be detectable until the second week of illness (7). Streptomycin is usually the drug of choice but is not readily available in most hospitals. Streptomycin and gentamicin have 97% and 86% cure rates, respectively, against *F. tularensis* (6).

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