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Review article

Mycobacterium bovis cervical lymphadenitis: A representative case and review

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ABSTRACT

Mycobacterium bovis is a tuberculosis causing bacterium that commonly presents with cervical lymphadenopathy. It is important to differentiate *M. bovis* from other Mycobacterial pathogens to ensure selection of correct anti-microbial therapy. This may decrease the number of treatment failures, the prevalence of anti-mycobacterial drug resistance patterns, and the need for surgical intervention. *M. bovis* has universal resistance to pyrazinamide and thus may not respond to typical first line mycobacterial drugs and may require surgical intervention. This case report and review of *M. bovis* cervical lymphadenitis demonstrates the need for accurate diagnosis as well as combined management with infectious disease and public health specialists.

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1. Introduction

According to the World Health Organization (WHO), tuberculosis bacillus (TB) is the second leading cause of death due to an infectious agent worldwide. Although the incidence of TB has declined by 1.5% every year since 2000 and mortality due to TB has dropped by more than 45% since 1990, the WHO estimates that in 2013, nearly 9 million people were infected with TB and 1.5 million died as a result [1,26]. *Mycobacterium bovis* is one of three species of *Mycobacterium* capable of causing TB—*M. tuberculosis*, *bovis*, and *africanum*. Together these three species are referred to as "typical" or "tuberculous mycobacteria," which are clinically distinct from the more than fifty other species of "atypical" or "non-tuberculous mycobacteria" (NTM) that usually only cause local infections.

One of the leading clinical manifestations of head and neck tuberculosis is cervical lymphadenopathy, which is present in up to 95% of patients with TB [2,3]. Among all of the causes of cervical lymphadenitis, approximately 8% is of mycobacterial origin of which more than 90% is caused by NTM [4]. *M. bovis* lymphadenitis is suspected from history, physical, and PPD testing. Similar to atypical forms, lymphadenopathy presentation predominates in the anterior cervical chains, most likely because the oral cavity is the primary site of inoculation and is preferentially drained by the anterior cervical chains. This is in contrast to the posterior cervical chain lymphadenopathy often seen in *M. tuberculosis* infections.

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Of all the mycobacterium that causes tuberculosis, *M. bovis* is especially concerning due to its multi-drug resistance. It also is frequently associated with HIV infection. As *M. bovis* is likely under-reported, it is difficult to quantify the actual prevalence of tuberculosis due to *M. bovis*. According to the National TB Genotyping Service of the CDC, the percentage of all TB infections in the United States attributed to *M. bovis* is 1–2% [6,41]. However, in regions of the country with greater concentrations of foreign-born individuals, the incidence of TB caused by *M. bovis* is even greater. In California, the overall occurrence of TB infections as a whole has decreased from 2003 to 2011. But cases of *M. bovis* in this same time period, have relatively increased from 3.4% to 5.4% of TB infections [6]. From 2001 to 2005, 10% of tuberculosis cases observed in San Diego, California – which, due to its bordering city Tijuana, Mexico, is the largest binational metropolitan region in the country – were caused by *M. bovis* infection. Almost all of the *M. bovis* cases reported were in Hispanic individuals [6,7]. *M. bovis* incidence in endemic, developing countries is often underreported because diagnosis requires specialized laboratory equipment and expertise that is costly and not readily available. Not only do these countries lack the infrastructure to perform routine testing but the implication of positive testing also increases cost due to need for vaccinate and the slaughter of infected animals [8]. Even in the United States, speciation beyond Mycobacterium complex (typical TB) is often not performed.

Historically, the epidemiological link between human and bovine TB has been well documented. TB was initially clinically described in the early 1800's among slaughterhouse workers. In 1882, Koch showed that TB in cattle could directly cause TB in humans. It has been postulated that cattle were the major culprits for the spread of *M. bovis* to humans from the Victorian Age and World War II. In England where, historically, TB was epidemic, more than 40% of cattle were infected with tuberculosis, pasteurization was not universal, and cattle slaughterhouses were within city limits. In the mid-1900's, however, control measures virtually eradicated the disease in industrialized countries [9–11]. Unfortunately, the past several decades have witnessed a resurgence of bovine TB. In countries like the United States and Great Britain, increased transportation of cattle across national borders has been associated with increased incidence of bovine TB, which can then be transmitted to humans [8,12].

2. Case report

A 23-month old Hispanic female presented with a 3 day history fever and redness overlying a 2 × 2 cm left submandibular neck mass (Fig. 1). Previously treated with 4 weeks of cephalexin, the mass had been increasing in size. Both parents were PPD converters in the past with a normal CXR. There was no history of travel, animal, or unpasteurized dairy product. There was history of a recent visit from a grandmother from Mexico. Initial work-up revealed a temperature of 37 °C, WBC 11.9, ESR 50, normal CXR, and a strongly positive 20 mm wheal from PPD testing. FNA yielded acid-fast bacilli (Fig. 2). INH, RMP, EMB, PZA, and Azithromycin were started and the public health department was notified for direct observed therapy (DOT). Within 3 weeks, the mass showed improvement. After 5 weeks, final cultures had shown *Mycobacterium* complex sensitive to INH and RMP but resistant to PZA. Azithromycin and PZA were discontinued and the specimen was sent for PCR identification. Over the next 3 months, the mass slowly enlarged and overlying skin changes worsened with extension into the posterior cervical lymph node chain. CT scan showed a 3 × 2 cm mass in the posterior chain (Fig. 3). The patient was observed for possible paradoxic upstaging reaction by the primary care physical but she was eventually referred to Otolaryngology for surgical consultation. It was discovered that

Fig. 1. A 23 month old female with *M. bovis* presenting as submandibular neck mass.

DOT was not documenting EMB administration—thus the patient was only receiving INH and RMP. *M. bovis* diagnosis was recognized based on the previously documented PZA resistance. At this point, considering the patient had not had resolution for approximately 4 months, the size of the neck mass, and the recognizance of *M. bovis*, surgery was offered. The patient was taken to the operating room for excision of 2.5 × 1.7 × 1 cm mass and two necrotic nodes deep to the mass. Pathology again showed AFB and caseous necrosis. Post-operatively, the surgical wound healed well. INH, RMP, and EMB were continued for 9 additional months. On last follow up, over 2 years post-treatment, there have been no signs of recurrence.

3. Discussion

Before the advent of anti-TB drugs, BCG (bacillus Calmette–Guerin) vaccination and animal control measures were standard techniques to control TB incidence. Since the 1950's, control measures have virtually eradicated human bovine TB in developed

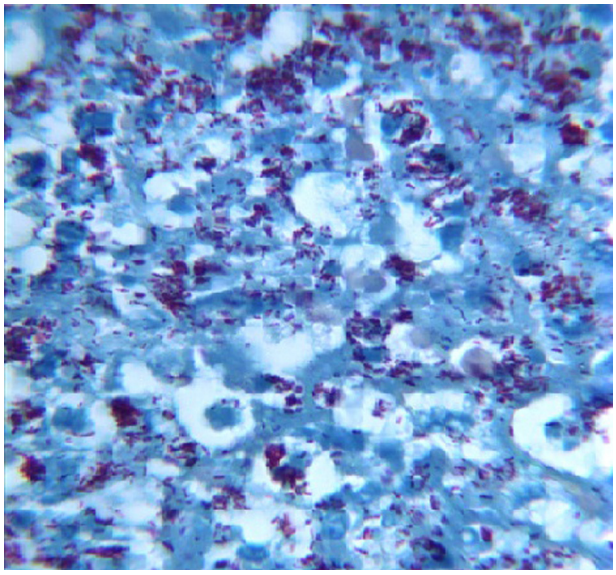

Fig. 2. Acid-fast staining bacilli demonstrated in tissue biopsy.