

#### Available online at www.sciencedirect.com

# **ScienceDirect**





## **Case Report**

# Mycobacterium bovis: An unusual cause of aortic graft infection ♣,★☆

Mark A. Colantonio, MD<sup>a,\*</sup>, Sushil Pokharel, MBBS<sup>a,1</sup>, Christopher Dionne, MD<sup>a,2</sup>, Sean Leibrock, B.S.<sup>b,3</sup>

#### ARTICLE INFO

## Article history: Received 23 August 2024 Revised 17 September 2024 Accepted 19 September 2024

Keywords: Mycobacterium bovis Aortic endovascular aneurysm repair Bacillus calmette-Guerin Aortic graft stent

## ABSTRACT

Mycobacterium has presented public health challenges since its inception, primarily affecting developing nations. Much less is known about M. bovis, a member of the mycobacterium family more frequently affecting zoonotic species. Infections postaortic aneurysm repair are rare, and few cases have reported infection secondary to the lesser-known mycobacterium member, M. bovis. Here, we present a case of aortic graft infection status-post aortic aneurysm repair secondary to M. bovis. We highlight the essential role multi-modal radiographic imaging played in establishing this diagnosis.

© 2024 The Authors. Published by Elsevier Inc. on behalf of University of Washington.

This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/)

## Introduction

Mycobacterium are well-known, gram positive bacterium of roughly 100 related species [1]. First isolated in the late 1800s

by Dr. Robert Koch, Mycobacterium are classified as nontuberculosis mycobacterium (NTM) or tuberculosis-causing mycobacterium [2]. Thought to be less pathogenic than tuberculosis-causing mycobacterium, NTM are found throughout the environment and more commonly affect immunocompromised

Abbreviations: BCG, Bacillus Calmette-Guerin; CBC, Complete blood count; CRP, C-reactive protein; CT, Computer tomography; EAVR, Aortic endovascular aneurysm repair; ED, Emergency department; ESR, Erythrocyte sedimentation rate; HIV, Human immunodeficiency virus; MRI, Magnetic resonance imaging; NTM, Nontuberculosis mycobacterium; WBC, White blood cell.

1930-0433/© 2024 The Authors. Published by Elsevier Inc. on behalf of University of Washington. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/)

<sup>&</sup>lt;sup>a</sup> Department of Medicine, West Virginia University, Morgantown, WV, USA

<sup>&</sup>lt;sup>b</sup> West Virginia University School of Medicine, Morgantown, WV, USA

<sup>\*</sup> Competing Interests: Each author certifies that he/she, a member of his or her immediate family, has no commercial association (i.e., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted manuscript. The authors have not used Generative Artificial Intelligence or Artificial Intelligence associated technologies.

<sup>☆☆</sup> Acknowledgments: None.

 $<sup>^{</sup>st}$  Corresponding author.

E-mail address: macolantonio@hsc.wvu.edu (M.A. Colantonio).

Sushil Pokharel MBBS, PO Box 9168s, Department of Medicine House Staff, 4th Floor HSC-N Morgantown, WV 26506

<sup>&</sup>lt;sup>2</sup> Christopher Dionne M.D., PO Box 9168, Department of Medicine House Staff, 4th Floor HSC-N Morgantown, WV 26506

<sup>&</sup>lt;sup>3</sup> Sean Leibrock B.S., PO Box 9100, 64 Medical Center Drive, Morgantown, WV 26506, West Virginia University School of Medicine https://doi.org/10.1016/j.radcr.2024.09.107

individuals [2]. This vastly differs from tuberculosis-causing mycobacterium, responsible for roughly 1.3 million deaths globally [3]. Four tuberculosis species are known to cause active tuberculosis, including Mycobacterium canettii, Mycobacteria microti, Mycobacterium bovis and Mycobacteria africanum [4]. M. bovis is an infrequent etiology of mycobacterium infection and is most common in zoonotic and bovine species [5]. A metaanalysis conducted by Taye et al found M. bovis responsible for 12.1% of cases word-wide, although this number is variable due to country-wide reporting differences [6]. Further analysis has found M. bovis responsible for 1.4% of pulmonary tuberculosis cases and nearly 12,000 annual tuberculosis-related mortalities [7]. Initially identified after transmission through unpasteurized milk, intestinal and extrapulmonary involvement can also occur [8]. Similar to other strains, M. bovis is transmitted via aerosolization of respiratory droplets, contact of infected cattle or dairy products [3,9]. Risk factors for M. bovis infection include occupational exposures, such as livestock farming, those with frequent wildlife exposure and those in the food industry, specifically raw-meat handlers [10]. Compared to other species of mycobacterium, M. bovis has a greater propensity to infect a broader range of hosts [5]. Clinically, M. bovis presents radiographically similar to M. tuberculosis infection. Extrapulmonary manifestations include lymph node, intra-abdominal, central nervous system and pleural involvement [11]. Diagnosis is also similar to M. tuberculosis, including acid-fast staining, culture, skin test and interferon-gamma assay [12]. Management involves pharmacotherapy, including isoniazid, rifampin and ethambutol for 2 months duration followed by rifampin and isoniazid for 7 months, whereas pyrazinamide is typically avoided due to documented resistance [13,14]. Interestingly, those with M. bovis have a worse prognosis compared to infection with M. tuberculosis [13,15]. Scott et al compared outcomes in those with M. bovis compared to M. tuberculosis in the United States, finding higher death rates in those infected with M. bovis [15]. It is clear that more attention should be paid to this lesser-known subtype of Mycobac-

Aortic endovascular aneurysm repair (EVAR) is a common technique used for the repair of aortic aneurysms [16]. Infection after repair is uncommon and found in 0.6% of cases [16]. Risk factors for infection include infected adjacent foci, immunosuppression and chronic diseases predisposing to infection, including diabetes and renal insufficiency [16]. Gram positive organisms are responsible for 47% of graft infections, with Staphylococcus aureus, Beta hemolytic streptococci, Staphylococcus epidermidis and cornebacterium as the most common sources [16]. Few case reports have described graft infections due to mycobacterium. Here, we present an endovascular graft infection secondary to M. bovis.

#### Case presentation

The patient is a 83 year old male with past medical history of left psoas abscess with fistulization to the lower left back, abdominal aortic aneurysm status-post aorto-biliac endograft repair in April of 2023, high-grade nonmuscle invasive bladder cancer status-post transurethral bladder tumor resection in August of 2021, bladder cancer in remission status-post treatment with Bacillus Calmette-Guerin (BCG) in November

of 2021, coronary artery disease, hypertension and hyperlipidemia who initially presented to the emergency department (ED) with endorsements of yellow-tinged fistula drainage ongoing for 3 weeks. Initial complete blood count (CBC) revealed a white blood cell (WBC) of 9.7  $\times$  10<sup>3</sup>/uL, c-reactive protein (CRP) of 25.9 mg/L and erythrocyte sedimentation rate (ESR) of 42 mm/hr. Of note, the patient had multiple, prior emergency department (ED) visits due to similar endorsements. The patient had a recent drain placement 1 week prior to hospitalization due to evidence of an organized fluid collection at the left psoas muscle space. This abscess was found incidentally during management of endoleak repair. Interestingly, the patient underwent abscess aspiration 1 year prior at an outside facility and cultures were found positive for mycobacterium tuberculosis complex with a positive genotype for M. bovis. At most recent presentation, increased drainage was noted, along with fever, chills, and fatigue. The patient also endorsed taking doxycycline 100 mg twice daily for "several weeks" prior to presentation. The patient was admitted to the medicine service for further management. Upon admission, antibiotics were initially held for the possibility of a biopsy and culture of the abscess. Blood cultures revealed 2+ gram positive cocci and infectious disease was consulted due to concerns of a superimposed bacterial infection. Per infectious disease, prior positive M. bovis cultures were thought to be secondary to BCG treatment. The patient was started on a 9-month total antimicrobial therapy including rifampin 600 mg daily, isoniazid 1100 mg daily and pyridoxine 50 mg daily for 2 months followed by rifampin 600 mg daily, isoniazid 300 mg daily and pyridoxine 50 mg daily for the following 7 months. An MRI of the lumbosacral spine was ordered for further infectious workup and revealed a large iliopsoas abscess contiguous with the native lumen of the known intrarenal abdominal aortic aneurysm with bi-iliac aortic stent graft. Two fistulous tracts were visualized extending to the posterior skin surface. The fluid collection was visualized extending to the anterior L3 vertebral body, concerning for osteomyelitis. After further discussion with the patient regarding risks and benefits of removal of the infected graft, the patient opted nonsurgical treatment. At this time, the patient was not amenable to PICC line and long-term IV antibiotics nor a surgical or procedural intervention. The patient ultimately underwent CTguided drain placement in the setting of the patient's chronically seeded aortic EVAR. The patient tolerated this procedure without complications and was ultimately discharged with a plan for re-evaluation of abscess with interval imaging 4 weeks.

#### Discussion

M. bovis is an infrequent cause of mycobacterium infection with a prevalence of roughly 12.1% [6]. Typically, M. bovis is associated with zoonotic animals with transmission from cattle to human, leading to nearly 12,300 deaths annually [5]. Although commonly associated with infection, Albert Calmette and Camille Guérin demonstrated protection against tuberculosis via a re-cultured strain termed M. bovis Calmette-Guérin [17]. Further studies demonstrated efficacy of this strain in

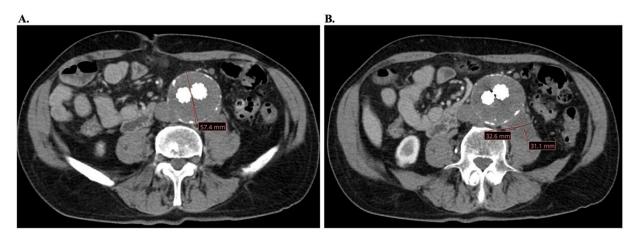


Fig. 1 – (A) CT imaging demonstrating stable aorto-iliac vascular Endo graft with a lumen of 5.7 cm. Absence of graft leak and/or fistulizing tract to the vascular graft. (B) A fluid collection of 3.2 x 3.1 cm is visualized adjacent to the Endo graft. Absence of air within the vascular graft or iliopsoas muscle. T1, T2, T1.

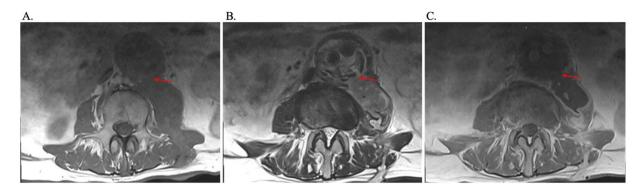


Fig. 2 – (A-C) MRI lumbosacral spine with and without contrast demonstrating a contiguous, rim enhancing fluid collection compatible with left psoas muscle abscess measuring  $2.4 \times 4.4 \times 9.2$  cm in transverse, anterior-posterior and longitudinal directions, respectively. Evidence of 2 fistulous tracts extending from fluid collection to the posterior skin surface. (A) represents the T1 spine without contrast, (B) represents the T2 spine without contrast and (C) represents the T1 spine with contrast.

management of bladder cancer in the late 1970s [17]. To this date, BCG continues to be the gold-standard for the management of invasive bladder cancer for prevention of progression and recurrence [17]. Studies have demonstrated a 5-year recurrence free rate of 80% when managed with BCG versus 48% in those without treatment [18]. Although infrequent, complications secondary to BCG therapy can occur [18]. Most common, skin irritation and fever occur in 39% of cases [18]. Infection is reported secondary to BCG treatment in as little as 1% of cases including hepatitis and mycotic aneurysm infection [18]. Per infectious disease, infection of the patient's bi-iliac aortic graft was thought to be secondary to prior BCG therapy for invasive bladder cancer.

Literature has reported 15 cases of vascular graft infection [19]. Of the cases, the abdominal aorta was the most common vascular site affected and the most common specimen sampled included abscess drainage, like our case [19]. Interestingly, of the 15 cases described, duration and choice of therapy differed. The shortest duration of therapy included 6 months of isoniazid and rifampin, while the longest duration

was 30 months of isoniazid, rifampin and ethambutol [19]. Our case included a 9-month duration of therapy. Further research should focus on appropriate antibiotic duration for M. bovis graft infection. Diagnostic imaging played an important role in our case. Initial CT revealed left psoas abscess without evidence of sinus tract, as shown in Fig. 1. Further imaging with MRI was needed for visualization of abscess contiguous with bi-iliac aortic graft stent, demonstrated in Fig. 2. Arsuffi et al. demonstrated a diagnostic yield of 93.3% for CT scan diagnosis of vascular graft infection. If initial CT imaging is negative, graft infection should not be ruled out. Our case demonstrated the importance of multimodal imaging with CT and MRI when M. bovis graft infection is suspected. Our case also highlights the persistent risk for M. bovis infection even years after initial treatment with BCG [20]. In our case, our patient underwent BCG treatment for bladder cancer in 2021 and found to be culture positive for M. bovis 2 years later. In patients with prior graft infection and treatment with prior BCG therapy, infection of graft secondary to BCG should be remain high on the differential.

#### Conclusion

Mycobacterium infections remain a global-health crisis, most commonly individuals in developing countries [3]. M. bovis Calmette-Guérin remains the gold standard of therapy management of invasive bladder cancer [17]. Infectious complications from therapy are uncommon, occurring in as few as 1% of cases affecting those with prior vascular grafts [18]. As initial CT scan was negative, our case highlights the importance of multimodal imaging for the diagnosis of graft infection secondary to M. bovis BCG as well as maintaining vigilance for this rare infection secondary to BCG therapy even years after initial treatment.

#### Patient consent

The patient consented to his medical course being used for a case report and educational purposes.

#### REFERENCES

- [1] Cook GM, Berney M, Gebhard S, Heinemann M, Cox RA, Danilchanka O, et al. Physiology of mycobacteria. Adv Microb Physiol 2009;55:81–182 318-189.
- [2] Sharma SK, Upadhyay V. Epidemiology, diagnosis & treatment of non-tuberculous mycobacterial diseases. Indian J Med Res 2020;152(3):185–226.
- [3] Tobin EH, Tristram D. Tuberculosis. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024.
- [4] Jilani TN, Avula A, Zafar Gondal A, Siddiqui AH. Active tuberculosis. StatPearls. Treasure IslandFL: StatPearls Publishing; 2024.
- [5] Guimaraes AMS, Zimpel CK. Mycobacterium bovis: from genotyping to genome sequencing. Microorganisms 2020;8(5).
- [6] Taye H, Alemu K, Mihret A, Wood JLN, Shkedy Z, Berg S, et al. Global prevalence of Mycobacterium bovis infections among human tuberculosis cases: systematic review and meta-analysis. Zoonoses Public Health 2021;68(7):704–18.
- [7] Bagcchi S. WHO's Global Tuberculosis Report 2022. Lancet Microbe 2023;4(1):e20.
- [8] Smith RM, Drobniewski F, Gibson A, Montague JD, Logan MN, Hunt D, et al. Mycobacterium bovis infection, United Kingdom. Emerg Infect Dis 2004;10(3):539–41.

- [9] Torres-Gonzalez P, Soberanis-Ramos O, Martinez-Gamboa A, Chavez-Mazari B, Barrios-Herrera MT, Torres-Rojas M, et al. Prevalence of latent and active tuberculosis among dairy farm workers exposed to cattle infected by Mycobacterium bovis. PLoS Negl Trop Dis 2013;7(4):e2177.
- [10] Vayr F, Martin-Blondel G, Savall F, Soulat JM, Deffontaines G, Herin F. Occupational exposure to human Mycobacterium bovis infection: a systematic review. PLoS Negl Trop Dis 2018;12(1):e0006208.
- [11] Torres-Gonzalez P, Cervera-Hernandez ME, Martinez-Gamboa A, Garcia-Garcia L, Cruz-Hervert LP, Bobadilla-Del Valle M, et al. Human tuberculosis caused by Mycobacterium bovis: a retrospective comparison with Mycobacterium tuberculosis in a Mexican tertiary care centre, 2000-2015. BMC Infect Dis 2016;16(1):657.
- [12] Pong A, Moser KS, Park SM, Magit A, Garcia MI, Bradley JS. Evaluation of an interferon gamma release assay to detect tuberculosis infection in children in San Diego, California. J Pediatric Infect Dis Soc 2012;1(1):74–7.
- [13] LoBue PA, Moser KS. Treatment of Mycobacterium bovis infected tuberculosis patients: San Diego County, California, United States, 1994-2003. Int J Tuberc Lung Dis 2005;9(3):333–8.
- [14] Nahid P, Dorman SE, Alipanah N, Barry PM, Brozek JL, Cattamanchi A, et al. Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America Clinical Practice Guidelines: treatment of drug-susceptible tuberculosis. Clin Infect Dis 2016;63(7):e147–95.
- [15] Scott C, Cavanaugh JS, Silk BJ, Ershova J, Mazurek GH, LoBue PA, et al. Comparison of sputum-culture conversion for Mycobacterium bovis and m. tuberculosis. Emerg Infect Dis 2017;23(3):456–62.
- [16] Kim YW. Aortic endograft infection: diagnosis and management. Vasc Specialist Int 2023;39:26.
- [17] Guallar-Garrido S, Julián E. Bacillus Calmette-Guérin (BCG) therapy for bladder cancer: an update. Immunotargets Ther 2020;9:1–11.
- [18] Jiang S, Redelman-Sidi G. BCG in bladder cancer immunotherapy. Cancers (Basel) 2022(13):14.
- [19] Arsuffi S, Cambianica A, Di Filippo E, Ripamonti D, Tebaldi A, Arosio MEG, et al. Vascular graft infections caused by Mycobacterium bovis BCG after BCG immunotherapy for non-muscle-invasive bladder cancer: case report and review of literature. J Clin Tuberc Other Mycobact Dis 2023;31:100360.
- [20] Ciofani L, Milani R, Giordano J, Cevolani M. Aortobisiliac graft thrombosis in bacillus Calmette-Guérin disseminated infection with graft involvement. J Vasc Surg Cases Innov Tech 2024;10(4):101504.