Scientific Research Publishing

Case Reports in Clinical Medicine, 2025, 14(7), 347-353
https://www.scirp.org/journal/crcm
ISSN Online: 2325-7083
ISSN Print: 2325-7075

Case Report: A Diagnostic Odyssey Unveiling BCGosis in an Elderly Patient

Venkata Chekuri[1*], Georgina Trotter[2]

[1]Department of General Medicine, Armadale Health Service, Mount Nasura, Australia
[2]Department of General Medicine, Kalgoorlie Health Campus, Kalgoorlie, Australia
Email: *venkata.chekuri@health.wa.gov.au, *drkrishnaraju@yahoo.com, georgina.trotter@health.wa.gov.au

How to cite this paper: Chekuri, V. and Trotter, G. (2025) Case Report: A Diagnostic Odyssey Unveiling BCGosis in an Elderly Patient. *Case Reports in Clinical Medicine*, **14**, 347-353.
https://doi.org/10.4236/crcm.2025.147046

Received: April 10, 2025
Accepted: July 13, 2025
Published: July 16, 2025

Abstract

Background: Bacillus Calmette-Guérin (BCG) immunotherapy is a widely used treatment for non-muscle invasive bladder cancer (NMIBC). While generally safe, rare systemic complications such as BCGosis—disseminated infection with *Mycobacterium bovis*—can occur, posing significant diagnostic and therapeutic challenges. **Case Presentation:** We report the case of a 73-year-old male with multiple comorbidities who presented with prolonged constitutional symptoms, including fever, weight loss, and lethargy, several months after completing intravesical BCG therapy for bladder transitional cell carcinoma. Extensive workup, including infectious, oncologic, and autoimmune investigations, was inconclusive. Imaging revealed granulomatous changes and hypermetabolic lesions in the urinary tract and multiple organs. Blood cultures eventually grew *M. bovis*, confirming BCGosis. The patient was successfully treated with a six-month course of antimycobacterial therapy, with clinical resolution. **Discussion:** This case highlights the importance of considering BCGosis in patients with systemic symptoms and a history of BCG therapy, even with delayed onset. The diagnosis is often challenging due to nonspecific clinical and imaging findings and low yield of microbiological tests. Early recognition and prolonged antimycobacterial treatment are crucial to prevent serious morbidity. **Conclusion:** Clinicians should maintain a high index of suspicion for BCGosis in patients with unexplained systemic illness and prior BCG immunotherapy. Thorough history, clinical vigilance, and multidisciplinary collaboration are essential for timely diagnosis and management.

Keywords

BCGosis, Bacillus Calmette-Guérin Therapy, BCG Immunotherapy Side Effects, Delayed BCG Complication, Multisystem Involvement in BCGosis, *Mycobacterium bovis* Infection, Systemic BCG Infection

1. Introduction

In clinical medicine, diagnostic challenges frequently arise that demand meticulous investigation to unravel complex cases. These challenges are often heightened in elderly patients with multiple comorbidities, where atypical presentations can obscure the underlying diagnosis. We present the case of a 73-year-old gentleman with a multifaceted medical history, whose presentation with constitutional symptoms and abnormal laboratory findings prompted an extensive diagnostic workup. The eventual diagnosis of Bacillus Calmette-Guérin (BCG)osis, highlights the importance of considering uncommon aetiologies in patients with atypical presentations and delayed onset following treatment. This case also underscores the need for clinicians to maintain a high index of suspicion for rare infectious complications, especially in patients with complex medical backgrounds.

2. Background

BCG immunotherapy has been a cornerstone in the treatment of non-invasive bladder cancer for several decades, reducing the risk of tumour recurrence by approximately 40% - 50% and delaying or preventing progression to muscle-invasive disease [1]-[3]. Originating from an attenuated strain of *Mycobacterium bovis*, BCG works by stimulating a robust immune response within the bladder mucosa, inducing cytotoxic effects against cancer cells. While generally well tolerated, BCG therapy is associated with a spectrum of side effects, ranging from mild local irritative symptoms to rare but serious systemic complications [4]. BCGosis, defined as the systemic dissemination of the BCG organism. The incidence of BCGosis is low, reported in approximately 0.4% to 1% of treated patients [5] [6]. Risk factors include mucosal breaches during catheterization, overdosage, immunosuppression, or improper administration techniques [7] [8]. Understanding these risks is critical, given the increasing global burden of non-muscle invasive bladder cancer and the widespread use of BCG therapy.

3. Case Presentation

A 73-year-old gentleman with a medical history of coronary artery bypass grafting, hypertension, dyslipidaemia, type 2 diabetes mellitus, and chronic obstructive pulmonary disease presented and was admitted on 29/08/2023. He reported a five-week history of intermittent fevers, flu-like symptoms, persistent productive cough, lethargy, loss of appetite, reduced oral intake, and activity levels, accompanied by a 10 kg weight loss. His baseline functional status prior to symptom onset was independent, with active engagement in daily activities and community involvement. Notably, there were no urinary or bowel symptoms, and he denied any recent travel or known infectious exposures. Differential diagnoses initially included relapsing malaria due to his history of residing in Africa from 2000 to 2013; however, he had not travelled there since, and malaria screening was negative. Further investigations included serology for Coxiella burnetii (Q fever), which was negative, and abdominal ultrasound revealing mild splenomegaly and fatty infiltration of liver. During his

inpatient stay, broad-spectrum antibiotics were administered targeting respiratory and systemic symptoms, including a productive cough, persistent lethargy, and loss of appetite. He was discharged on 08/09/2023 with pending results of other infectious aetiology and scheduled outpatient follow-up. Prior to admission and during hospitalization, he had received multiple courses of antibiotics, including broad-spectrum antibiotics and doxycycline in view of suspected common respiratory bacterial infections.

When seen in the outpatient (OP) follow-up clinic on 19/09/2023, the patient continued to report decreased mobility, generalized weakness, and ongoing anorexia, prompting re-admission for further evaluation and management. Given the combination of weight loss, iron deficiency anaemia, hypercalcemia, and deranged liver function tests, a broad differential diagnosis was considered. This included gastrointestinal malignancies (such as colorectal, gastric, or pancreatic cancer), haematological malignancies (notably lymphoma and multiple myeloma), disseminated infections (including tuberculosis and BCGosis), granulomatous diseases like sarcoidosis, infiltrative liver diseases, inflammatory bowel disease, and metabolic or endocrine causes such as primary hyperparathyroidism. As part of the workup, a gastroscopy and colonoscopy were performed on 22/09/2023. Gastric biopsy showed chronic gastritis with atrophy and antral inflammation, while colonoscopy revealed multiple polyps with low-grade dysplasia. Additional investigations included serum protein and urine electrophoresis, Quantiferon-TB Gold test, serum ACE levels, autoimmune serologies (ANA, ANCA), and assessment of serum calcium, PTH, and vitamin D levels. Hypercalcemia was managed with intravenous hydration and vitamin D supplementation, and iron deficiency was corrected with intravenous iron infusion on 21/09/2023. Although the patient remained afebrile throughout admission, sarcoidosis was considered, and a PET scan was arranged for further evaluation. While PET imaging did not show any focal site of infection, it revealed intense tracer uptake in the bladder and ureters, retrospectively interpreted as consistent with inflammation related to prior BCG therapy. Additional uptake was observed in the bowel, testes, and lung bases. On further history, the patient disclosed a past diagnosis of bladder transitional cell carcinoma (TCC) in September 2020, treated with 12 cycles of intravesical BCG from February 2021 to May 2022. This prompted a shift in diagnostic focus toward BCG-related complications, and blood and urine cultures were sent for mycobacterial studies.

4. Unravelling the Mystery

Extensive infectious disease workup, including hepatitis A, B, C, HIV, and CMV, returned negative. Presence of both Epstein-Barr virus (EBV) IgG and IgM antibodies, raising the possibility of recent infection; however, a negative EBV heterophile antibody test and anti-EBV nuclear antigen negativity effectively excluded active EBV disease. Imaging with computed tomography (CT) of the chest, abdomen, and pelvis demonstrated calcified pulmonary granulomas, mosaic attenuation of lung parenchyma, prominent but non-enlarged mediastinal and hilar lymph

nodes, and splenomegaly. These findings raised suspicion for atypical infection, sarcoidosis, or relapse of bladder cancer. The PET scan, performed electively, did not support sarcoidosis or lymphoma [9]. Given the patient's complex presentation and imaging, the differential diagnosis was broadened to include mycobacterial infections, and the history of prior BCG therapy became pivotal. This case illustrates the challenge of diagnostic bias, where initial consideration was given to more common infections or malignancies before rare aetiologies like BCGosis were investigated.

5. BCGosis Revelation

The turning point occurred when blood cultures, reported on Christmas Day 2023, grew *Mycobacterium bovis*, confirming systemic BCG infection. Urine cultures remained negative, likely due to insufficient sampling or low bacterial load. The diagnosis was further supported by the clinical picture of constitutional symptoms, abnormal liver function tests, unexplained hypercalcemia, and PET scan findings, consolidating the diagnosis of BCGosis. This rare complication typically occurs during or shortly after BCG instillation; however, our patient's delayed presentation highlights the variable latency period and the need for ongoing vigilance in patients with a history of BCG therapy.

6. Resolution and Beyond

Antituberculosis treatment was initiated using a standard regimen excluding pyrazinamide, to which *Mycobacterium bovis* is inherently resistant [1] [7]. The patient tolerated the treatment well and completed the recommended six-month course. Although an additional three months of therapy was advised based on evidence and European and American guidelines recommending a nine-month duration for pyrazinamide-resistant cases, the patient declined extended treatment. A tuberculosis specialist supported this decision, considering the patient's stable clinical condition and lack of symptoms. Continued clinical and laboratory monitoring, including regular liver function tests to detect hepatotoxicity, renal function assessment, full blood counts to monitor for cytopenias, and vigilance for peripheral neuropathy, rash, gastrointestinal upset, and visual changes (associated with ethambutol), were planned during monthly outpatient follow-ups to promptly identify any adverse effects, relapse, or treatment failure. Following completion of therapy, the patient has continued to remain clinically stable, with no evidence of disease recurrence or treatment failure.

7. Discussion

This case demonstrates the diagnostic complexities surrounding BCGosis, a condition that can mimic multiple infectious and inflammatory disorders. Typically, BCGosis manifests soon after BCG instillation; however, delayed presentations such as in this patient are documented but rare [10]. The nonspecific systemic

symptoms of fever, weight loss, and malaise, combined with granulomatous inflammation on imaging, pose significant diagnostic challenges. Negative results on conventional microbiological testing further complicate diagnosis. Literature reports vary on the timing of BCGosis onset, ranging from days to years post-treatment, emphasizing the need for clinicians to maintain suspicion regardless of elapsed time [11] [12].

BCGosis results from hematogenous dissemination of *Mycobacterium bovis* following urothelial disruption or reflux during BCG instillation. Clinical manifestations can involve multiple organ systems, including pulmonary infiltrates, hepatitis, osteoarticular involvement, vascular lesions such as mycotic aneurysms, and genitourinary inflammation. Diagnosis often depends on a combination of clinical suspicion, imaging, histopathology demonstrating granulomatous inflammation, and culture or molecular identification of *M. bovis*. Treatment requires prolonged antimycobacterial therapy with isoniazid, rifampicin, and ethambutol, excluding pyrazinamide, alongside possible corticosteroids in cases of severe inflammation [13].

The rarity of BCGosis necessitates awareness of risk factors such as traumatic catheterization, immunosuppression, concurrent urinary tract infections, and dosing errors. Preventive measures include careful patient selection, gentle catheterization techniques, and close post-treatment monitoring. Given the increasing use of BCG therapy worldwide, particularly in aging populations, the incidence of such complications may rise, making this case pertinent for clinicians across disciplines.

The following table depicts the timeline of events.

Timeline	Events
Sep. 2020	Diagnosis of bladder TCC
Feb. 2021-May 2022	Completed 12 cycles of intravesical BCG therapy
Late Jul./Early Aug. 2023	Symptom onset: intermittent fevers, cough, lethargy, weight loss over 5 weeks
29 Aug. 2023	First hospital admission for constitutional symptoms
8 Sep. 2023	Discharged with outpatient follow-up and pending infectious workup
19 Sep. 2023	Re-admitted due to persistent anorexia, weight loss, and weakness
21 Sep. 2023	Received IV iron and vitamin D supplementation
22 Sep. 2023	Gastroscopy and colonoscopy performed
Late Sep. 2023	CT chest/abdomen/pelvis performed (showed granulomas, splenomegaly)
Oct. 2023	PET scan showed bladder/ureter inflammation, bowel and lung base uptake
Dec. 2023	History of prior BCG instillation revealed
25 Dec. 2023	Blood culture grew *Mycobacterium bovis*, confirming BCGosis

Continued

Late Dec. 2023	Anti-tubercular treatment initiated (isoniazid, rifampicin, ethambutol—no pyrazinamide)
Jun. 2024	Completed 6-month anti-tubercular regimen
Jun. 2024 onwards	The patient remains clinically well with no signs of relapse and continues to be monitored by his general practitioner on an outpatient basis

8. Conclusion

BCGosis, although an uncommon complication, should always be considered in patients with a history of BCG immunotherapy who present with systemic symptoms and inflammatory changes, regardless of the time elapsed since treatment. Early recognition and timely initiation of appropriate antimycobacterial therapy are vital to preventing significant morbidity and mortality. This case highlights the importance of comprehensive clinical assessment, detailed history taking, and an open diagnostic approach to rare but serious complications in patients with complex medical histories. Long-term vigilance post-BCG therapy, especially in elderly or immuno-compromised patients, is essential for optimal outcomes. When diagnosed early and treated adequately—typically with a six- to nine-month regimen of isoniazid, rifampicin, and ethambutol—BCGosis generally has a favourable prognosis, with most patients achieving full recovery. Recurrence is uncommon, with reported rates under 5% - 10%, but may occur in those with delayed diagnosis, incomplete treatment, or immunosuppression [5] [14] [15]. As such, close follow-up for at least 12 months after treatment is recommended to detect any signs of relapse or treatment failure.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Babjuk, M., Burger, M., Capoun, O., Cohen, D., Compérat, E.M., Dominguez Escrig, J.L., *et al.* (2022) European Association of Urology Guidelines on Non-Muscle-Invasive Bladder Cancer (Ta, T1, and Carcinoma *in Situ*). *European Urology*, **81**, 75-94. https://doi.org/10.1016/j.eururo.2021.08.010

[2] Basu, S. and Alameh, M. (2020) BCG Immunotherapy for Bladder Cancer: An Update on Mechanism of Action and Therapeutic Applications. *International Journal of Urology*, **27**, 667-677.

[3] Lamm, D.L. (2000) Efficacy and Safety of Bacille Calmette-Guérin Immunotherapy in Superficial Bladder Cancer. *Clinical Infectious Diseases*, **31**, S86-S90. https://doi.org/10.1086/314064

[4] Liatsos, G.D., Mariolis, I., Hadziyannis, E., Bamias, A. and Vassilopoulos, D. (2025) Review of BCG Immunotherapy for Bladder Cancer. *Clinical Microbiology Reviews*, **38**, e00194-23. https://doi.org/10.1128/cmr.00194-23

[5] Powles, T., Kockelbergh, R. and Woodhouse, C. (2007) Bacillus Calmette-Guérin Treatment of Non-Muscle-Invasive Bladder Cancer: A Review of Complications and Treat-

ment Guidelines. *European Urology Supplements*, **6**, 379-385.

[6] Zlotta, A.R., Fleshner, N.E. and Jewett, M.A. (2014) Complications of BCG Immunotherapy for Bladder Cancer: A Review. *Canadian Urological Association Journal*, **8**, 356-361.

[7] Di Lorenzo, G., Perdona, S., Autorino, R., Palazzo, A. and De Placido, S. (2006) Bacillus Calmette-Guérin (BCG) Complications Associated with Intravesical Treatment of Bladder Cancer: The Role of Antituberculous Therapy. *Cancer Treatment Reviews*, **32**, 532-537.

[8] Peters, N., Kümmerlen, C. and Ludwig, W.D. (2009) BCG Infection after Intravesical Therapy: Case Report and Review of Literature. *European Urology*, **55**, 1273-1276.

[9] Brans, B., Goehrs, J.M. and Schillaci, O. (2015) Role of 18F-FDG PET/CT in Mycobacterial Infections. *European Journal of Nuclear Medicine and Molecular Imaging*, **42**, 1213-1221.

[10] Hotta, Y., Yoshioka, N., Sakamoto, A., Inagaki, M., Ito, R., Shiraki, K., *et al.* (2025) Late-Onset Disseminated BCG Infection with Hepatosplenomegaly after Intravesical BCG Immunotherapy in a Non-Immunocompromised Patient. *Clinical Journal of Gastroenterology*, **18**, 337-342. https://doi.org/10.1007/s12328-024-02086-8

[11] Cabas, P., Rizzo, M., Giuffrè, M., *et al.* (2020) BCG Infection (BCGitis) Following Intravesical Instillation for Bladder Cancer and Time Interval between Treatment and Presentation: A Systematic Review. *Urologic Oncology: Seminars and Original Investigations*, **39**, 85-92. https://doi.org/10.1016/j.urolonc.2020.11.037

[12] Liaw, F., Tan, Y.Y. and Hendry, D. (2017) Systemic BCG-Osis Following Intravesical BCG Instillation for Bladder Carcinoma. *Clinical Case Reports*, **5**, 1569-1572. https://doi.org/10.1002/ccr3.1129

[13] Meeks, J.J., Kassouf, W. and Konety, B. (2023) AUA 2023: Optimizing BCG Therapy/Managing BCG Toxicity. American Urological Association.

[14] Dalbagni, G., Zhang, Z.F., Lacombe, L. and Herr, H.W. (1999) Bacillus Calmette-Guérin Immunotherapy for Bladder Cancer: Long-Term Follow-Up. *The Journal of Urology*, **161**, 188-193.

[15] Smith, M., Nguyen, L. and Jones, P. (2021) *Mycobacterium bovis* Infections Following Intravesical Bacillus Calmette-Guérin Instillation for Bladder Cancer in Western Australia: A 22-Year Retrospective Review. *Australian and New Zealand Journal of Public Health*, **45**, 210-217.