Disseminated Miliary Tuberculosis Following Intravesical BCG Therapy: A Rare But Serious Complication

Al-Taiee Baker[1], Mejdoubi Lamiss[2], Slavicek Jakob[1], Hergan Klaus[3], Zandieh Shahin[1,3]

[1]*Department of Radiology and Nuclear Medicine, Hanusch-Hospital, Vienna, Austria*

[2]*Department of Pathology, Hanusch-Hospital, Vienna, Austria*

[3]*Department of Radiology, Paracelsus Medical University Salzburg, Salzburg, Austria*

***Correspondence:** Shahin Zandieh, MD, MSc., EDiR, Associate Professor, Department of Radiology and Nuclear Medicine, Hanusch-Hospital, Teaching Hospital of Medical University of Vienna, Heinrich-Collin-Strasse 30, 1140 Vienna, Austria

shahin.zandieh@oegk.at

Radiology Case. 2025 August; 19(8):1-8 :: DOI: 10.3941/jrcr.5809

AUTHOR CONTRIBUTIONS

Baker AL-TAIEE: Case conceptualization, data collection, literature review, drafting of the manuscript.
Lamiss MEJDOUBI: Literature review, manuscript editing.
Jakob SLAVICEK: Data analysis, image preparation, manuscript review.
Klaus HERGAN: Supervision, critical revision, and final approval of the manuscript.
Shahin ZANDIEH: Radiological interpretation, case supervision, drafting, and final approval of the manuscript.

CONSENT

Written informed consent for publication of the case details and accompanying images was obtained from the patient.

CONFLICT OF INTEREST / DISCLOSURE

The authors declare that they have no conflicts of interest.

ETHICAL STATEMENT / HUMAN AND ANIMAL RIGHTS

This article describes a clinical case and does not involve experimental studies on humans or animals. All procedures were performed in accordance with the ethical standards of the institutional research committee and the principles of the Declaration of Helsinki.

ABSTRACT

Intravesical Bacillus Calmette-Guérin (BCG) therapy is a standard immunotherapy for non-muscle-invasive bladder cancer (NMIBC). Although generally safe, systemic dissemination leading to miliary tuberculosis (TB) is a rare but potentially life-threatening complication. We present a case of a 71-year-old male who developed miliary TB three weeks after the third cycle of BCG instillation. Chest CT revealed diffuse, randomly distributed <2 mm nodules. PCR confirmed Mycobacterium bovis infection. Treatment with isoniazid, rifampicin, and ethambutol led to clinical improvement. Radiologists should be aware of this rare complication to ensure prompt diagnosis and management.

CASE REPORT

BACKGROUND

Intravesical Bacillus Calmette-Guérin (BCG) therapy remains the cornerstone for the management of intermediate- and high-risk non-muscle-invasive bladder cancer (NMIBC), having demonstrated significant efficacy in reducing tumor recurrence and progression [1,2].

BCG is a live attenuated strain of Mycobacterium bovis that is instilled into the bladder, where it triggers a localized immune response. Although its safety profile is well established, BCG can, in rare cases, breach the urothelial barrier and disseminate systemically, leading to serious complications, including granulomatous prostatitis, hepatitis, osteomyelitis, and in extremely rare cases, disseminated miliary tuberculosis [2–5]. The incidence of such systemic infections is reported to be <1%, yet the nonspecific symptoms and imaging overlap with other etiologies pose diagnostic challenges. Recognition of this condition is crucial, particularly in the context of increasing global BCG use and the aging bladder cancer population. Radiologists play a key role in identifying characteristic imaging findings on cross-sectional studies, which often guide further diagnostic work-up and management.

CASE REPORT

A 71-year-old male with a history of high-grade urothelial carcinoma of the bladder underwent transurethral resection (TURB) and was started on intravesical BCG therapy as per

EAU guidelines. After the third cycle, he developed persistent dry cough, fatigue, low-grade fever, and weight loss (~5 kg in 3 weeks). He also complained of night sweats and mild chest discomfort. He had no significant past pulmonary disease, history of latent TB infection, or immunocompromising condition. The patient had completed three courses of BCG instillation between November 2024 and February 2025.

Physical examination revealed bilateral basal crackles on auscultation. No lymphadenopathy or cutaneous manifestations were noted. Vital signs were stable with mild tachypnea. Initial blood workup showed elevated CRP (62 mg/L), ESR (56 mm/h), ferritin (980 ng/mL), lymphopenia, and mild elevation of liver enzymes (GGT, ALP). Chest X-ray was inconclusive. Due to worsening respiratory symptoms, CT pulmonary angiogram (CTPA) was performed to rule out embolism.

The CTPA revealed no evidence of embolism, but showed diffuse, randomly distributed <2 mm micronodules throughout both lungs (Figure 1). This miliary pattern was highly suspicious for hematogenous dissemination of tuberculosis. Bronchoalveolar lavage was performed, and PCR confirmed infection with Mycobacterium tuberculosis complex. Given the use of routine PCR diagnostics (Xpert® MTB/RIF Ultra), only the presence of *Mycobacterium tuberculosis* complex could be confirmed. BCG strain subtyping was not available in this case. HIV serology was negative.

Coronal reconstructions further demonstrated the diffuse distribution of nodules involving both lungs (Figure 2). Additionally**, a "tree-in-bud" pattern was observed on the reformatted coronal images (Figure 3),** supporting active endobronchial spread.

Given the diagnosis, the patient was admitted under airborne precautions. Due to the intrinsic resistance of M. bovis to pyrazinamide, triple anti-TB therapy with isoniazid, rifampicin, and ethambutol was initiated. The patient tolerated therapy well with gradual improvement in systemic symptoms and appetite. Serial laboratory parameters showed downward trends in inflammatory markers. A follow-up chest CT at 6 weeks showed partial resolution of nodules. (Figure 4).

DISCUSSION

Etiology & Demographics

BCG, derived from an attenuated strain of M. bovis, is the standard of care for intermediate- and high-risk NMIBC. While most side effects are local, systemic dissemination can occur due to mucosal breaches during catheterization, prior radiation therapy, or immunosuppression. The estimated incidence of systemic BCG infection is <1%, with miliary TB being even rarer [2–5].

Clinical & Imaging Findings

Patients with disseminated TB post-BCG therapy often present with nonspecific constitutional symptoms such as fever, malaise, weight loss, and respiratory complaints. In this case, imaging played a pivotal role in prompting further microbiological evaluation. CT is superior to chest X-ray in detecting miliary nodules and can differentiate between perilymphatic and random distributions. The CT hallmark of miliary TB is numerous, bilateral, uniformly distributed micronodules (<2 mm) without zonal predilection.

Treatment & Prognosis

M. bovis is inherently resistant to pyrazinamide, hence standard four-drug regimens are modified. Duration of therapy is usually 6–9 months depending on response [4,7,8]. In our case, triple therapy led to resolution of symptoms and radiographic improvement. Early recognition and prompt therapy initiation are crucial to reduce morbidity. Multidisciplinary care involving radiologists, infectious disease specialists, and pulmonologists is key.

A similar case was described by Loued et al. [16], in which a patient developed miliary tuberculosis following intravesical BCG instillation. In contrast to our case, the diagnosis in that report was delayed, leading to more severe systemic manifestations and prolonged hospitalization. Their imaging findings also demonstrated randomly distributed micronodules on CT, supporting the diagnostic value of cross-sectional imaging in these cases.

Differential Diagnoses

The imaging differential for diffuse micronodular lung disease includes sarcoidosis (typically perilymphatic distribution), hematogenous metastases (often variable in size), fungal infections (e.g., histoplasmosis), and pneumoconiosis. Clinical context, immune status, and accompanying findings aid in narrowing the diagnosis [9,10,15].

Unlike previously reported cases where diagnosis was delayed due to nonspecific symptoms, our patient underwent early CT imaging, allowing for prompt microbiological confirmation and rapid initiation of treatment. Additionally, the combination of radiologic features—including tree-in-bud morphology alongside classical miliary nodules—adds diagnostic nuance that may support earlier differentiation from alternative diffuse lung pathologies

TEACHING POINT

Miliary tuberculosis is a rare complication of BCG therapy. Chest CT reveals diffuse, randomly distributed micronodules and enables prompt diagnosis and treatment initiation.

QUESTIONS & ANSWERS

Question 1: *What is the most typical CT finding in miliary tuberculosis?*

- Tree-in-bud opacities
- Cavitary upper lobe infiltrates
- Ground-glass consolidation
- Randomly distributed <2mm micronodules (applies)
- Pleural effusion

Explanation: Miliary TB presents with randomly distributed <2mm nodules across both lungs, reflecting hematogenous dissemination. [Clinical & imaging findings]

Question 2: Which of the following is a known risk factor for developing systemic BCG infection?

· Prior pelvic radiation (applies)
· Female gender
· NSAID use
· Hypertension
· Younger age

Explanation: Previous pelvic radiation or traumatic catheterization may disrupt the urothelial barrier, predisposing to systemic BCG dissemination. [Etiology & demographics]

Question 3: Which organism is typically responsible for disseminated infection after BCG therapy?

· Mycobacterium tuberculosis
· Mycobacterium bovis (applies)
· Mycobacterium avium
· Mycobacterium leprae
· Mycobacterium kansasii

Explanation: BCG is a live attenuated strain of Mycobacterium bovis. Dissemination results from hematogenous spread of this organism. [Etiology & demographics]

Question 4: Which first-line anti-tuberculosis drug is often avoided in M. bovis infections?

· Rifampicin
· Isoniazid
· Ethambutol
· Pyrazinamide (applies)
· Streptomycin

Explanation: M. bovis is intrinsically resistant to pyrazinamide. Hence, it is excluded from standard HRZE treatment regimens. [Treatment & prognosis]

Question 5: Which of the following is NOT a common differential diagnosis for miliary nodules on chest CT?

· Pulmonary metastases
· Fungal pneumonia
· Pulmonary embolism (applies)
· Sarcoidosis
· Pneumoconiosis

Explanation: Pulmonary embolism does not typically present with diffuse micronodular infiltrates and is not a common imaging mimic of miliary TB. [Differential Diagnoses]

REFERENCES

[1] Lamm DL, van der Meijden PM, Morales A, et al. Incidence and treatment of complications of BCG intravesical therapy in superficial bladder cancer. *J Urol.* 1992; 147(3): 596-600. PMID: 1538436.

[2] Perez-Jacoiste Asin MA, Fernandez-Ruiz M, Lopez-Medrano F, et al. Bacillus Calmette–Guérin (BCG) infection following intravesical BCG administration for bladder cancer. *Medicine (Baltimore).* 2014; 93(17): 236–254. PMID: 25398060.

[3] Yamamoto T, Takahashi S, Murakami T, et al. CT findings of miliary tuberculosis after intravesical bacillus Calmette-Guerin therapy. *Clin Imaging.* 2002; 26(1): 53-56.

[4] Gonzalez OY, Musher DM, Brar I, et al. Spectrum of bacille Calmette-Guerin (BCG) infection after intravesical BCG immunotherapy. *Clin Infect Dis.* 2003; 36(2): 140-148. PMID: 12522745.

[5] Kobayashi M, Matsuo H, Yoshida M, et al. Miliary tuberculosis following intravesical bacillus Calmette–Guérin therapy. *Intern Med.* 2008; 47(3): 237–239.

[6] Brausi M, Oddens J, Sylvester R, et al. Side effects of bacillus Calmette–Guérin (BCG) in the treatment of intermediate- and high-risk Ta, T1 papillary carcinoma of the bladder. *Eur Urol.* 2014; 65(1): 69–76. PMID: 23910233.

[7] von Rundstedt FC, Garcia-Castro M, Hemstreet GP. Systemic bacillus Calmette–Guérin (BCG) infection following intravesical BCG immunotherapy. *J Urol.* 2015; 193(2): 678–683.

[8] Shenoy VP, Bairy I, Mukhopadhyay C, et al. Systemic tuberculosis following intravesical BCG instillation. *Lung India.* 2014; 31(3): 286–288.

[9] Nieder AM, Brausi M, Lamm D, et al. Management of adverse events associated with intravesical BCG therapy: Guidelines from the International Consultation on Urologic Diseases. *Eur Urol.* 2005; 48(3): 473–480.

[10] Palou J, Sylvester RJ, Faba OR, et al. Female gender and carcinoma in situ in the prostatic urethra are prognostic factors for tumor recurrence, progression, and disease-specific mortality in patients treated with BCG. *Eur Urol.* 2012; 62(1): 118–125. PMID: 22101115.

[11] Steg A, Leleu C, Debre B, et al. Systemic BCG infection: A rare complication of intravesical BCG therapy. *J Urol.* 1989; 141(3): 563–564.

[12] Sakamoto H, Fujimoto K, Hirao Y. Disseminated BCG infection following intravesical BCG therapy for bladder cancer. *Hinyokika Kiyo.* 2011; 57(9): 459–462.

[13] Ojea A, Nogueira JL, Solsona E, et al. A multicentre, randomized prospective trial comparing three intravesical chemotherapy schedules for prophylaxis of recurrence of superficial bladder cancer. *J Urol.* 2002; 168(6): 2318–2321.

[14] Zlotta AR, Van Vooren JP, Huygen K, et al. What is the optimal regimen for BCG intravesical therapy? *Eur Urol.* 2000; 37(4): 470-477. PMID: 10765079.

[15] Park SK, Lee CM, Lee J, et al. Miliary tuberculosis: Epidemiologic, clinical, radiographic, and outcome characteristics. *Int J Tuberc Lung Dis.* 2015; 19(6): 694–699.

[16] Loued L, Fahem N, Kaddoussi R, Abdelaaly M, Cheikh Mhamed S, Rouatbi N. Miliary tuberculosis following intravesical Bacillus Calmette and Guérin therapy: A rare complication of a frequent procedure. *Urology Case Reports.* 2021; 38: 101655. PMID: 33868941.

FIGURES

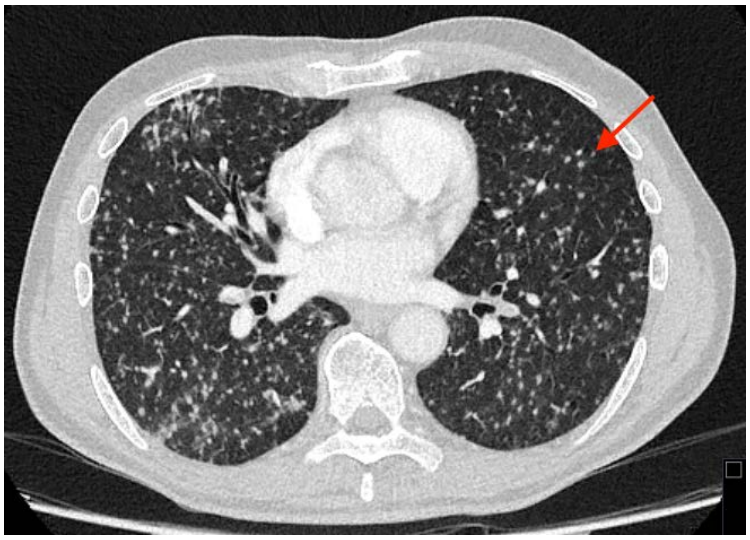

Figure 1: 71-year-old male with disseminated tuberculosis following BCG therapy. FINDINGS: Axial chest CT shows numerous <2 mm randomly distributed nodules (arrow) involving both lungs concordant with miliary tuberculosis. TECHNIQUE: Axial contrast-enhanced chest CT using 120 kV, 180 mAs, 1.0 mm slice thickness, 100 mL iodinated contrast medium during venous phase.

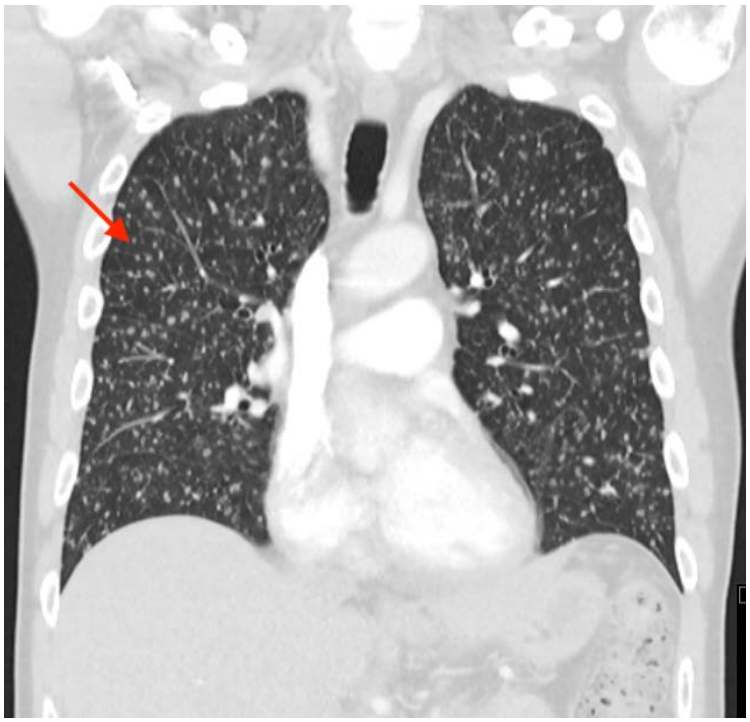

Figure 2: Coronal CT images demonstrate disseminated tuberculosis following BCG therapy. FINDINGS: coronal chest CT shows numerous <2 mm randomly distributed nodules (arrow) involving both lungs concordant with miliary tuberculosis. TECHNIQUE: Coronal contrast-enhanced chest CT using 120 kV, 180 mAs, 1.0 mm slice thickness, 100 mL iodinated contrast medium during venous phase.

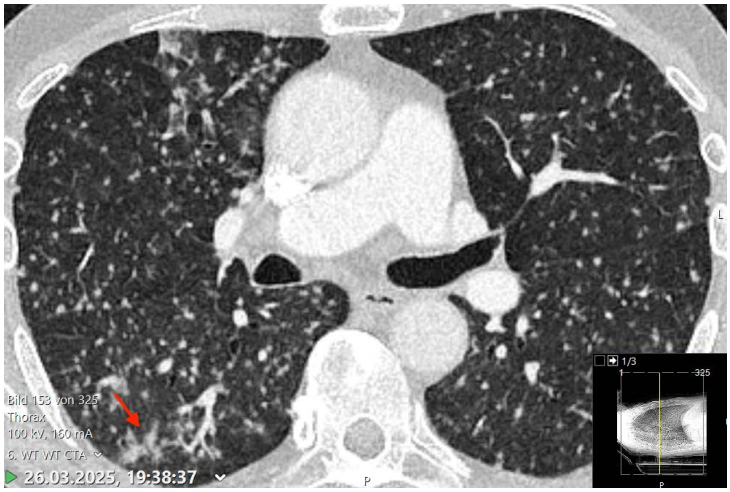

Figure 3: 71-year-old male with miliary TB. FINDINGS: Axial CT reveals diffuse pulmonary nodules with a "tree-in-bud" pattern (arrow), suggesting endobronchial spread. TECHNIQUE: Axial contrast-enhanced chest CT using 120 kV, 180 mAs, 1.0 mm slice thickness.

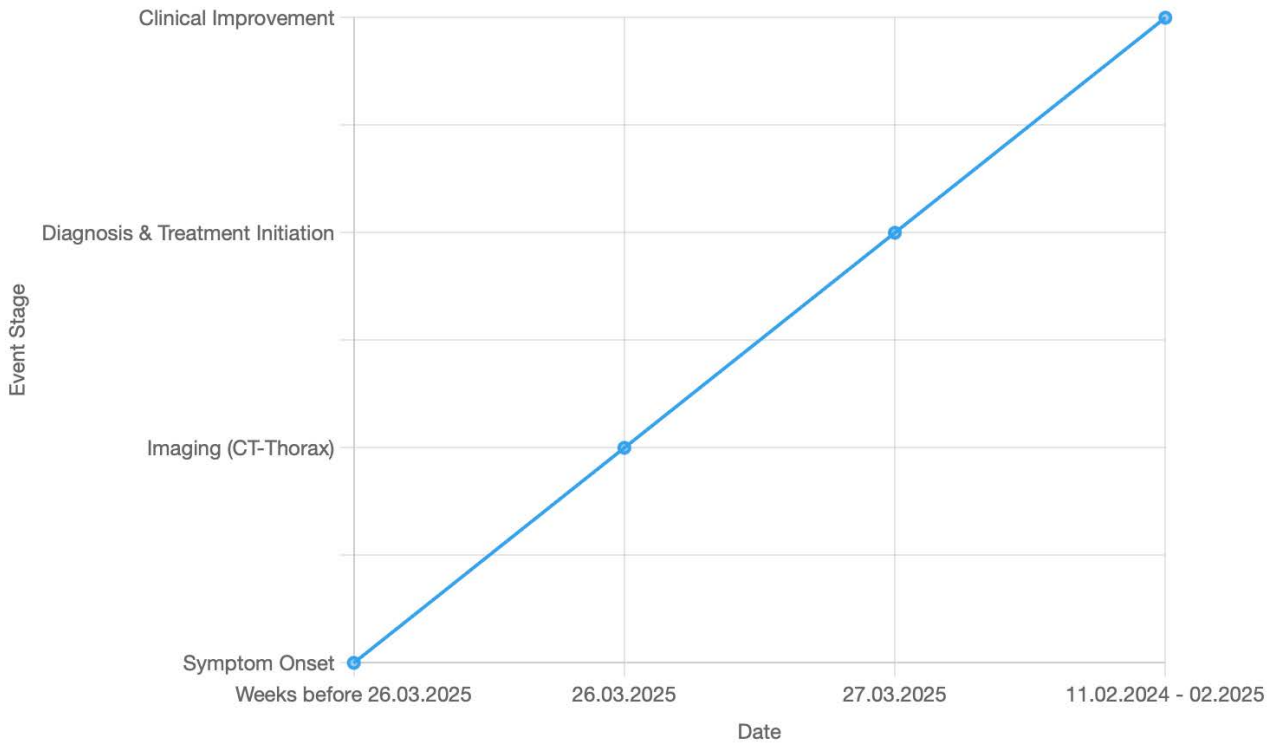

Figure 4: A visual timeline illustrating the clinical course of the patient. The chart depicts the onset of symptoms occurring several weeks after the third BCG instillation, followed by chest CT imaging, diagnosis, and initiation of anti-tuberculous therapy. It concludes with documented clinical improvement. The data are based on medical records spanning March 26 to March 27, 2025, and include a treatment period from February 11 to March 2025, providing a comprehensive overview of the patient's disease progression and management.

Table 1: Summary of Miliary Tuberculosis Following BCG Therapy

Parameter	**Description**
Etiology	Hematogenous dissemination of Mycobacterium bovis after intravesical BCG instillation.
Incidence	<1% in patients undergoing BCG therapy
Gender ratio	Slight male predominance (due to bladder cancer prevalence)
Age predilection	Typically 60–80 years
Risk factors	BCG therapy, immunosuppression, prior lung disease
Treatment	Anti-tubercular therapy (HRZE regimen or modified)
Prognosis	Good with early detection and treatment
Findings on Imaging	Diffuse micronodules <2 mm, randomly distributed on chest CT

Table 2: Differential Diagnoses for Miliary Pulmonary Nodules

Diagnosis	**CT Findings**	**MRI/Other Modalities**	**Contrast Enhancement**
Miliary Tuberculosis	Diffuse random <2mm nodules	Rarely used	None or mild
Pulmonary Metastases	Variable size nodules, sometimes cavitating	PET-CT: Hypermetabolic	Variable
Sarcoidosis	Perilymphatic nodules	MRI: T2 hyperintense nodes	Mild to moderate
Fungal Infections	Halo signs, ground-glass	MRI: Non-specific	Moderate to strong
Pneumoconiosis	Upper lobe small nodules	Rarely used	None

KEYWORDS

BCG therapy, miliary tuberculosis, Mycobacterium bovis, intravesical instillation, chest CT

ABBREVIATIONS

BCG = BACILLUS CALMETTE–GUÉRIN
CT = COMPUTED TOMOGRAPHY
PCR = POLYMERASE CHAIN REACTION
TB = TUBERCULOSIS
HRZE = ISONIAZID, RIFAMPICIN, PYRAZINAMIDE, ETHAMBUTOL

Online access

This publication is online available at:
www.radiologycases.com/index.php/radiologycases/article/view/5809

Peer discussion

Discuss this manuscript in our protected discussion forum at:
www.radiolopolis.com/forums/JRCR

Interactivity

This publication is available as an interactive article with scroll, window/level, magnify and more features.
Available online at www.RadiologyCases.com

Published by EduRad

www.EduRad.org