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Intravesical BCG therapy-induced granulomatous prostatitis in a patient with non-muscle invasive bladder cancer and prostate adenocarcinoma

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A B S T R A C T

Granulomatous prostatitis (GP) is a rare inflammatory condition that may mimic prostate cancer (PC) progression. We present the case of a 64-year-old man with low-risk PC on active surveillance who developed Bacillus Calmette-Guérin (BCG)-induced GP following intravesical therapy for non-muscle invasive bladder cancer. Clinical and imaging findings suggested PC progression, but biopsy confirmed granulomatous inflammation without malignancy upstaging. This case underscores the similarities in clinical presentation, as well as the importance of histopathological evaluation in differentiating GP from PC.

1. Introduction

Granulomatous prostatitis (GP) is an uncommon prostate condition characterized by inflammatory granulomatous lesions.[1] Epstein and Hutchins classified GP into nonspecific, specific, post-surgical, and secondary to systemic granulomatous diseases with causes including infections and allergic reactions to surgical interventions.[2] Systemic or genitourinary tuberculosis is a well-documented infectious cause of GP.[3] Studies have also pointed to intravesical Bacillus Calmette-Guerin (BCG) treatment for non-muscle invasive bladder cancer (NMIBC) as a source of GP.[4–7] Additionally, BCG-related GP has been associated with reduced malignancy risk in lesions classified as PI-RADS 3, 4, or 5 on MRI, complicating prostate cancer (PC) risk assessments.[8]

The clinical presentations of GP often mimic those of prostate cancer, making differentiation difficult without histopathological examination. Common findings include a hard, fixed nodule on digital rectal exam (DRE), elevated serum prostate-specific antigen (PSA) levels, and MRI abnormalities similar to those seen with PC. Here, we present a case of intravesical BCG therapy-induced GP in a patient with existing PC, highlighting diagnostic and therapeutic challenges.

2. Case presentation

A 64-year-old man with a medical history of coronary artery disease, hyperlipidemia, and hypertension was initially diagnosed with localized PC with a Gleason Score (GS) of 6 (3 + 3) and an associated PSA of 3.6 ng/mL. The patient underwent active surveillance (AS) over the next twelve years comprised of serial MRIs, PSA measurements, and biopsy. Repeat prostate biopsy at year four showed unchanged disease state (GS 3 + 3). Due to PSA increase (10.3 ng/mL), a magnetic resonance imaging (MRI) of the prostate was obtained at year twelve which showed three suspicious lesions including a 1.3 cm lesion in the right (R) mid gland, a 1.2 cm lesion in the left (L) anterior transition zone, and a 0.9 cm lesion in the L anterior/posterolateral peripheral zone mid-gland. A repeat biopsy up-staged the PC to GS 7 (3 + 4, corresponding to the R mid gland lesion seen on the MRI), indicating more aggressive disease. Potential treatment options discussed included AS, radiation therapy, and surgery. The patient opted to continue AS. PSA remained stable (8–11 ng/mL) and a repeat MRI in year thirteen showed stable prostate lesions (1.4 cm, 1.2 cm, and 0.9 cm respectively) (Fig. 1A and B).

In year fourteen, the patient developed hematuria. Computer tomography (CT) of the abdomen/pelvis and cystoscopy revealed a 2 cm bladder mass on the left lateral wall; a trans-urethral resection of bladder tumor revealed high grade, NMIBC. The patient underwent intravesical gemcitabine instillation followed by six weeks of intravesical BCG treatment, with negative surveillance cystoscopies post treatment.

However, an MRI of the prostate 5 months post BCG treatment showed significant increase in the R mid-gland (from 1.4 cm to 4.2 cm), with extension in the left peripheral zone and left apex. The lesions in the L mid-gland and left anterior transition zone remained stable (Fig. 1C and D), with a new, non-specific, 0.6 cm R pelvic sidewall lesion

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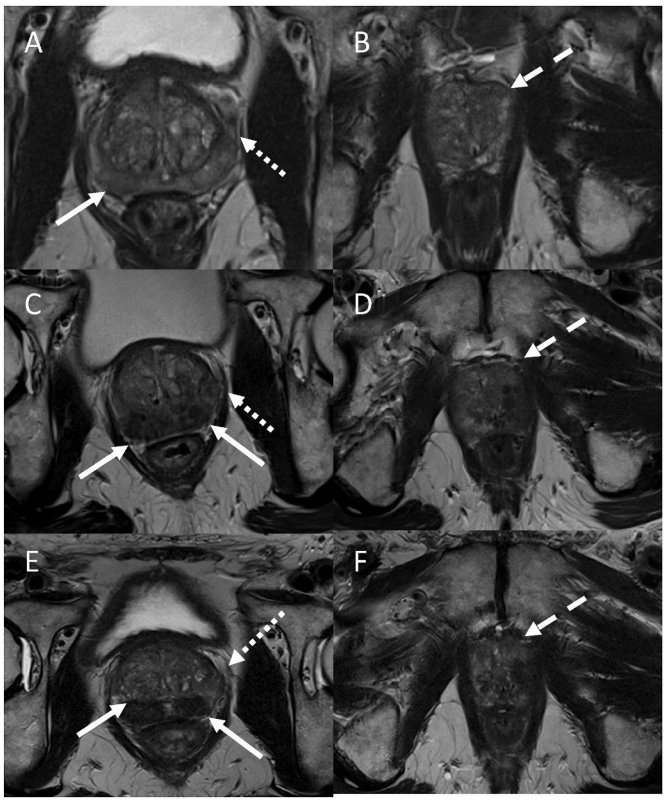

Fig. 1. Magnetic resonance imaging (mpMRI) was performed for active surveillance, including axial T2-weighted imaging. Three T2 hypointense lesions were identified. A and B. 1.4 cm lesion in the right peripheral zone (PZ) midgland (solid arrows), a 1.2 cm left anterior transition zone (TZa) (thick dashed arrow) and 0.9 cm lesion in the left PZ midgland (small dashed arrow), corresponding to PI-RADS 4, 3, and 4 lesions, respectively. C and D. Interval increase in size of the previously noted right PZ midgland lesion, now measuring 4.2 cm and extending into the left PZ (solid arrows). This lesion did not demonstrate enhancement on DCE-MRI (not shown), with corresponding necrosis at subsequent pathology. The 1.2 cm left TZa lesion (small dashed arrow) and the 0.9 cm left PZ midgland lesion (thick dashed arrow) remained stable. E and F. Interval decrease in size of the right PZ midgland lesion, now measuring 3.4 cm with reduction of extension into the left PZ (solid arrows). The 1.2 cm left TZa lesion (small dashed arrow) and the 0.9 cm left PZ midgland lesion (thick dashed arrow) remained stable.

(not shown). Prostate MRI at 8 months post BCG installation showed improvement: shrinkage of the R mid-gland (from 4.2 cm to 3.4 cm), stable appearance of L anterior transition zone lesion and left mid-gland lesion, and resolution of the right pelvic side wall lesion (Fig. 1E and F). CT of the chest/abdomen/pelvis and bone scan were negative for distant metastasis. Subsequent prostate biopsy was not consistent with PC progression: only 1 out of 15 biopsy cores showed prostate adenocarcinoma, down-staged from GS 7 (3 + 4) to GS 6 (3 + 3, Fig. 2A). All other targeted and random cores, including the large R mid-gland lesion, showed prostate tissue with necrosis, acute, chronic, and granulomatous inflammation (Fig. 2B–C). Acid-fast bacilli (AFB) staining was negative.

Based on BCG exposure, discordance between findings on MRI and prostate cancer grade, severe granulomatous inflammation on prostate biopsy, and improvement on subsequent MRIs without therapeutic intervention, we conclude the patient developed BCG-associated GP superimposed on his existing PC.

3. Discussion

Granulomatous prostatitis is rare, accounting for <1 % up to 6 % of benign lesions in the prostate.[1,3,9–13] The coexistence of GP and PC is an even rarer, with most patients presenting as case reports and documented concurrent diagnoses.[10,11,14–16] This patient offers a unique perspective with longstanding PC subsequently developing BCG-induced GP. Particularly, the case highlights several diagnostic and therapeutic challenges in the context of GP mimicking PC progression.

PC and GP are clinically indistinguishable, both manifesting with urinary symptoms, serum PSA changes, and abnormal and/or worsening prostate nodules on physical exam and MRI. Several large case series of GP are summarized in Table 1[1,3,11–15] A majority of patients present with clinical symptoms (83–100 %), abnormal DRE (77–100 %) and a PSA ranging from normal up to 28.8 ng/mL (Table 1). In most studies, PC was high on the differential based on clinical and laboratory evaluations, but only 4 of the 336 evaluable patients had concurrent PC diagnosis.[1,3,10–13] GP should be on the differential when evaluating prostate-related symptoms in patients with risk factors such as certain bacterial/fungal/parasitic/viral infections (i.e., urinary tract infections, tuberculosis, syphilis, coccidiidiomycosis, schistosomiasis, herpes simplex virus), recent surgical intervention (i.e., TURP or biopsy), systemic granulomatous diseases (i.e., sarcoidosis) and intravesical BCG therapy.[12] If GP is confirmed, treating the underlying cause is usually sufficient.

Intravesical use of BCG, a live attenuated strain of Mycobacterium bovis, has become a standard adjuvant therapy for NMIBC.[4–7] The incidence of BCG-associated GP was highlighted by Oates et al. where GP was found in all 13 patients who underwent prostate biopsy for clinical indications (i.e. prostate nodularity) post intravesical BCG.[6] In the study by LaFontaine et al., 9 of the 12 patients (75 %) who underwent cystoprostatectomy following BCG therapy developed GP, while more recent studies from Soda et al. and Kim et al. describe GP incidence rates of 10–25 % following BCG treatment.[6,17,18] Balasar et al. evaluated 472 patients with BPH symptoms who underwent TURP and found none of the 459 without prior BCG therapy developed GP, whereas 3/13 (23 %) of the patients who received prior BCG therapy developed GP.[7] Although BCG was the likely culprit in all studies, AFB within the prostate was detected only in 23–78 % of the cases.[5,6] This is echoed in our case study, where the fit stain for AFB was negative but all clinical and pathological evidence supported BCG-induced GP. The timing of

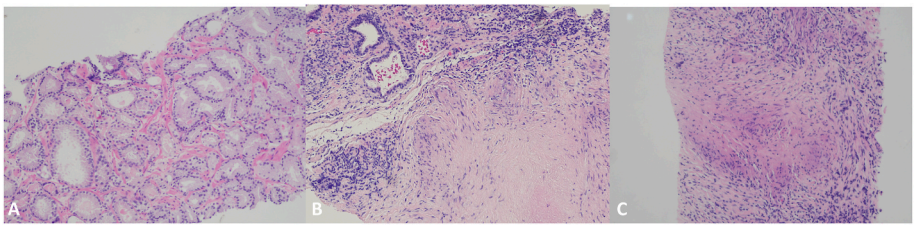

Fig. 2. Hematoxylin and eosin (H & E) staining of representative prostate tissue biopsies, which was performed after surveillance MRI post-BCG treatment for NMIBC revealed an enlarging right peripheral zone prostate lesion. A. Left medial mid gland, Gleason score 3 + 3 prostate adenocarcinoma. B. Right medial peripheral zone, prostate tissue with necrotizing granulomas, which most likely corresponds to the enlarged lesion identified at MRI. C. Left lateral base peripheral zone, prostate tissue with granulomatous inflammation and early focus of necrosis.

Table 1
Histopathological evaluation of granulomatous prostatitis in published case series.

Study	GP (N)	Incidence	Clinical/Urinary Symptoms[a]	Abnormal DRE % (N)	PSA range (ng/mL)	Clinical Suspicion for PC % (N)	Pathologic Diagnosis of PC (N)
Tanner et al.	37	3.3 %	–	–	–	–	–
Kalalis et al.	70	6.4 %	83 %	77 % (54) – –	–	77 % (54)	0
Stillwell et al.	200	0.8 %	–	–	0.8–20.94	59 % (118)	3
Mohan et al.	20	1.4 %	100 %	100 % F&N: 75 % (15) H&F: 25 % (5)	2.2–18.2[b]	35 % (7)	1
Shanggar et al.	9	0.65 %	–	–	–	–	0
Shukla et al.	22	1.9 %	100 %	100 % F&N: 36 % (8) H&F: 64 % (14)	0.88–19.22	36 % (8)	0
Kumbar et al.	17	1.4 %	100 %	100 % F&N: 35 % (6) H&F: 65 % (11)	2.8–28.8	41 % (7)	0

DRE: digital rectal exam; F&N: firm and nodular; GP: granulomatous prostatitis; H&F: hard and fixed; N: number of cases; PC: prostate cancer; PSA: prostate specific antigen.
[a] Including fever, frequency, urgency, irritative voiding, obstruction, and/or hematuria.
[b] PSA of the patient diagnosed with PC was excluded.

BCG-induced GP is not well defined, but commonly falls within the 3–12 months range.[19] Our patient developed GP within 5 months of BCG therapy completion with subsequent improvement at 8 months.

Given the relatively high incidence of BCG-related GP detected at imaging or through histopathology, a patient should undergo thorough history and physical with or without laboratory evaluation (i.e. screening PSA) prior to BCG therapy to identify pre-existing prostate abnormalities. If a patient develops new or worsening prostate-associated symptoms, especially within 12 months of BCG therapy, GP should be considered. A prostate biopsy with histological evaluation is warranted to confirm suspicion and to rule out malignancy.

Accurate diagnosis and treatment are difficult in the rare circumstance of a patient with existing PC on AS who then develops BCG-induced GP. This is further challenged by the overlap in imaging appearance between BCG-induced GP and PC on MRI. Aside from the patient presented here, there is a paucity of published reports, which include a 78-year-old male with GS 6 (3 + 3) PC on AS developed GP 14 months post BCG therapy for NMIBC.[20] In both cases, there was an increase in PSA but no up-staging of PC at the time of GP diagnosis, and both patients continued AS with decrease in their follow-up PSA without other complications. As such, in a patient with existing PC, clinical exam, PSA, and CT and/or MRI should be undertaken prior to BCG therapy initiation to establish baseline. If GP develops, treatment should be standard of care based on the stage and extent of PC; if AS is chosen, regular interval follow-up imaging should be performed to monitor for GP improvement/resolution.

4. Conclusions

We have presented a rare case of BCG-induced GP that mimicked PC progression in a patient with low-risk PC on AS. Abnormal clinical (i.e., DRE), PSA, and MRI findings should be interpreted with caution in a patient with new prostate symptoms in the post BCG-therapy setting, and GP should remain high on the differential. Given the clinically indistinguishable nature of the GP and PC at clinical presentation and MRI, prostate biopsy and histological evaluation may be warranted to confirm diagnosis and direct therapeutic options.

CRediT authorship contribution statement

Ryan Yu: Writing – review & editing. **Qian (Janie) Qin:** Writing – original draft. **George K. Haines:** Data curation, Formal analysis. **William K. Oh:** Conceptualization, Supervision, Writing – review & editing. **Sara Lewis:** Supervision, Writing – review & editing.

Ethics statement

This case report was conducted in compliance with ethical standards. This report has been anonymized to ensure the patient's privacy and confidentiality. No identifying information is disclosed in this manuscript.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

1. Tanner FH, McDonald JR. Granulomatous prostatitis: a histologic study of a group of granulomatous lesions collected from prostate glands. *Arch Pathol Lab Med*. 1943;36:358–370.
2. Epstein JI, Hutchins GM. Granulomatous prostatitis: distinction among allergic, nonspecific, and post-transurethral resection lesions. *Hum Pathol*. 1984 Sep;15:818–825. https://doi.org/10.1016/s0046-8177(84)80142-2.
3. Shanggar K, Zulkifli MZ, Razack AH, Dublin N. Granulomatous prostatitis: a reminder to clinicians. *Med J Malaysia*. 2010 Mar;65:21–22. PMID: 21265242.
4. Bahnson RR. Elevation of prostate-specific antigen from Bacillus Calmette-Guérin-induced granulomatous prostatitis. *J Urol*. 1991 Nov;146:1368–1369. https://doi.org/10.1016/s0022-5347(17)38098-9.
5. Oates RD, Stilmant MM, Freedlund MC, Siroky MB. Granulomatous prostatitis following bacillus Calmette-Guérin immunotherapy of bladder cancer. *J Urol*. 1988 Oct;140:751–754. https://doi.org/10.1016/s0022-5347(17)41803-9.
6. LaFontaine PD, Middleman BR, Graham Jr SD, Sanders WH. Incidence of granulomatous prostatitis and acid-fast bacilli after intravesical BCG therapy. *Urology*. 1997 Mar;49(3):363–366. https://doi.org/10.1016/s0090-4295(96)00507-9.
7. Balasar M, Doğan M, Kandemir A, et al. Investigation of granulomatous prostatitis incidence following intravesical BCG therapy. *Int J Clin Exp Med*. 2014 Jun 15;7(6):1554–1557. PMID: 25035779.
8. Rodríguez Cabello MA, Méndez Rubio S, Vázquez Alba D, Aulló González C, Platas Sancho A. Effect of Bacillus Calmette-Guérin exposure on prostate cancer detection using magnetic resonance imaging: a cohort study. *Clin Genitourin Cancer*. 2024 Oct;22(5), 102130. https://doi.org/10.1016/j.clgc.2024.102130.

9. Kelalis PP, Greene LF, Harrison Jr EG. Granulomatous prostatitis. A mimic of carcinoma of the prostate. *JAMA*. 1965 Jan 25;191(4):287–289. https://doi.org/10.1001/jama.191.4.287.
10. Stillwell TJ, Engen DE, Farrow GM. The clinical spectrum of granulomatous prostatitis: a report of 200 cases. *J Urol*. 1987 Aug;138(2):320–323. https://doi.org/10.1016/s0022-5347(17)43134-x.
11. Mohan H, Bal A, Punia RP, Bawa AS. Granulomatous prostatitis–an infrequent diagnosis. *Int J Urol*. 2005 May;12(5):474–478. https://doi.org/10.1111/j.1442-2042.2005.01068.x.
12. Kumbar R, Dravid N, Nikumbh D, Patil A, Nagappa KG. Clinicopathological overview of granulomatous prostatitis: an appraisal. *J Clin Diagn Res*. 2016 Jan;10(1):EC20–E23. https://doi.org/10.7860/JCDR/2016/15365.7146.
13. Shukla P, Gulwani HV, Kaur S. Granulomatous prostatitis: clinical and histomorphologic survey of the disease in a tertiary care hospital. *Prostate Int*. 2017 Mar;5(1):29–34. https://doi.org/10.1016/j.prnil.2017.01.003.
14. Val-Bernal JF, Zaldumbide L, Garijo MF, González-Vela MC. Nonspecific (idiopathic) granulomatous prostatitis associated with low-grade prostatic adenocarcinoma. *Ann Diagn Pathol*. 2004 Aug;8(4):242–246. https://doi.org/10.1053/j.anndiagpath.2004.06.002.
15. Gujral S, Gillatt DA. A peculiar case of granulomatous prostatitis: a cause for concern. *Br J Urol*. 1998 May;81(5):775. https://doi.org/10.1046/j.1464-410x.1998.00579.x.
16. Murugan P, Brown RE, Zhao B. Nonspecific granulomatous prostatitis with prostatic adenocarcinoma. *Indian J Pathol Microbiol*. 2010 Jan-Mar;53(1):152–154. https://doi.org/10.4103/0377-4929.59211.
17. Kim TJ, Yu YD, Hwang SI, et al. Analysis of risk factors for post-bacillus Calmette–Guerin-induced prostatitis in patients with non-muscle invasive bladder cancer. *Sci Rep*. 2020 Jun;10:9763. https://doi.org/10.1038/s41598-020-66952-4.
18. Soda T, Tashiro Y, Koike S, Ikeuchi R, Okada T. Evaluation of incidence, predictive factors and treatment considerations for asymptomatic genitourinary granulomas after intravesical bacillus Calmette-Guérin therapy. *Actas Urol Esp*. 2023 Jun;47(5):317–326. https://doi.org/10.1016/j.acuroe.2022.09.003.
19. Kim CY, Lee SW, Choi SH, et al. Granulomatous prostatitis after intravesical Bacillus calmette-guérin instillation therapy: a potential cause of incidental F-18 fdg uptake in the prostate gland on F-18 fdg PET/CT in patients with bladder cancer. *Nucl Med Mol Imaging*. 2016 Mar;50(1):31–37. https://doi.org/10.1007/s13139-015-0364-y.
20. Logan JK, Walton-Diaz A, Rais-Bahrami S, et al. Changes observed in multiparametric prostate magnetic resonance imaging characteristics correlate with histopathological development of chronic granulomatous prostatitis after intravesical Bacillus Calmette-Guerin therapy. *J Comput Assist Tomogr*. 2014 Mar-Apr;38(2):274–276. https://doi.org/10.1097/RCT.0b013e3182aac58a.