Case Report

Asymptomatic renal granuloma diagnosed 3 years after Bacillus Calmette–Guérin intravesical injection: A case report and a literature review

Ibuki Tsuru,[1] Masaki Nakamura,[1] Taro Izumi,[1] Akihiro Ono,[1] Yoshio Masuda,[2] Masashi Kusakabe,[3] Teppei Morikawa,[2] Haruki Kume[4] and Yoshiyuki Shiga[1]

Departments of [1]Urology, [2]Diagnostic Pathology, and [3]Radiology, NTT Medical Center Tokyo, and [4]Department of Urology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

Abbreviations & Acronyms
BCG = Bacillus Calmette–Guérin
CT = computed tomography
MRI = magnetic resonance imaging
NR = not reported
RAPN = robot-assisted partial nephrectomy
RCC = renal cell carcinoma
VUR = vesicoureteral reflux

Correspondence: Masaki Nakamura M.D., Ph.D., Department of Urology, NTT Medical Center Tokyo, 5-9-22 Higashigotanda, Shinagawa-ku, Tokyo 141-8625, Japan. Email: masakin64@gmail.com

How to cite this article: Tsuru I, Nakamura M, Izumi T *et al*. Asymptomatic renal granuloma diagnosed 3 years after Bacillus Calmette–Guérin intravesical injection: A case report and a literature review. *IJU Case Rep*. 2023; 6: 377–381.

Received 31 January 2023; accepted 3 August 2023. Online publication 18 August 2023

Introduction: Intravesical Bacillus Calmette–Guérin immunotherapy is an effective treatment for non-muscle-invasive bladder cancer, which is occasionally associated with side effects and complications. The incidence of significant renal complications after intravesical Bacillus Calmette–Guérin immunotherapy is less than 2%. We report a case of renal granuloma after intravesical Bacillus Calmette–Guérin immunotherapy for bladder cancer, which radiologically resembled a papillary renal cell carcinoma.

Case presentation: A 65-year-old man, who had a medical history of urothelial carcinoma and received intravesical Bacillus Calmette–Guérin therapy, was referred to our Urology Department with a right renal tumor. Imaging findings suggested papillary renal cell carcinoma. Robot-assisted partial nephrectomy was performed, and the histopathological examination revealed epithelioid cell granuloma, which were considered to be Bacillus Calmette–Guérin-related renal granuloma.

Conclusion: Bacillus Calmette–Guérin-related renal granuloma mimicking papillary renal cell carcinoma have been reported. We should consider the possibility of renal granulomas when encountering image abnormalities for patients treated with intravesical Bacillus Calmette–Guérin therapy.

Key words: granuloma, kidney, nephrectomy, renal tuberculosis.

Keynote message

The incidence of renal complications such as renal granulomas after intravesical BCG immunotherapy is rare. However, BCG-related renal granuloma can mimic papillary RCC. We should consider the possibility of renal granulomas when encountering image abnormalities for patients treated with intravesical BCG therapy.

Introduction

Intravesical BCG immunotherapy is a treatment for non-muscle-invasive bladder cancer. Although it is effective, side effects and complications can occur. The most common local complications include cystitis, hematuria, bladder contracture, prostatitis, epididymitis, and ureteral obstruction.[1] Rarely, systemic infections such as granulomatous nephritis and abscesses, pneumonitis, hepatitis, osteomyelitis, and other life-threatening adverse events may develop.[1] The incidence of significant renal complications after intravesical BCG immunotherapy is less than 2%.[2]

Here, we report a case of renal granulomatosis after intravesical BCG immunotherapy for bladder cancer, which radiologically resembled a papillary renal cell carcinoma.

Case

A 65-year-old man was referred to our Urology Department with a right renal tumor. He had a medical history of urothelial carcinoma of the urinary bladder, and he was treated

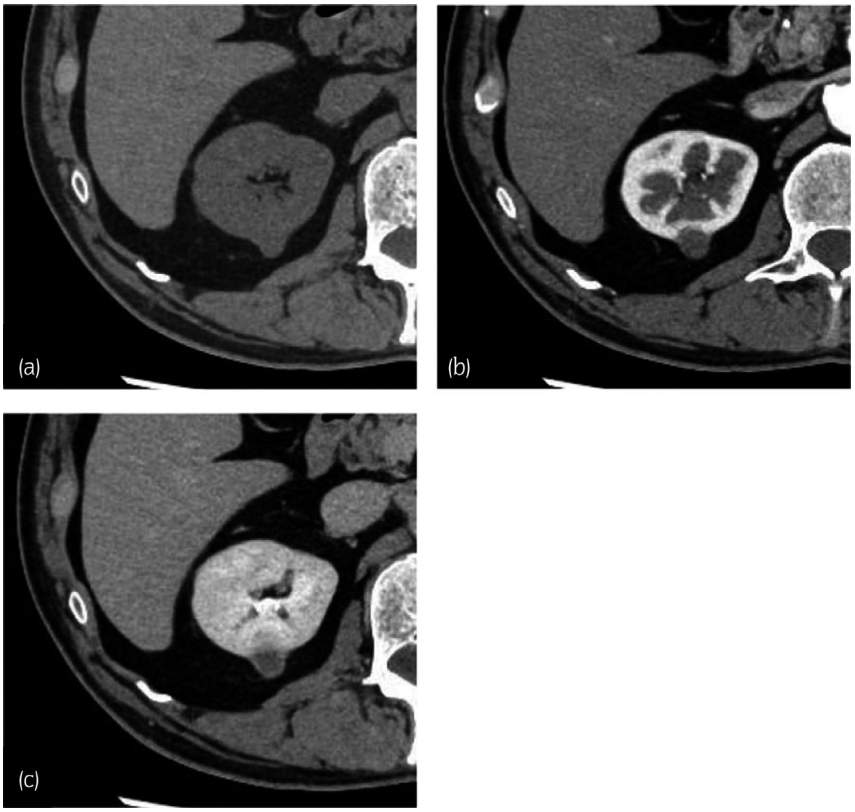

Fig. 1 CT images of the right kidney. (a) In the non-contrast phase, it is isodense with the renal parenchyma. (b) Corticomedullary phase and (c) excretory phase show that gradual and weak enhancing effects are suspected in the periphery of the tumor.

with transurethral resection and intravesical BCG immunotherapy consisting of 6-weekly instillations at the age of 62. A CT performed 2 years before showed no recurrence or metastasis. However, recent dynamic contrast-enhanced CT showed a 1 cm dorsal renal tumor. Gradual and weak enhancing effects were suspected in the periphery of the tumor (Fig. 1). MRI fat-saturated T2-weighted images showed slightly low signal intensity, suggesting renal cell carcinoma (Fig. 2). The suggested differential diagnoses were a papillary renal cell carcinoma, a complicated cyst, and an angiomyolipoma. However, only the tumor periphery was stained. The finding did not seem to be typical of papillary renal cell carcinoma.

After discussion with radiologists, we decided to perform a partial nephrectomy. RAPN was done through the retroperitoneal approach without renal artery clamping and renorrhaphy. The tumor was resected with margin using sharp incision and blunt dissection. During resection, white pus came out from the tumor (Fig. 3a,b). The operative time was 104 min, and the estimated blood loss was 10 mL.

Histopathological examination revealed an epithelioid cell granuloma with necrosis of the right kidney, which were considered to be changes after BCG therapy for bladder cancer. Numerous lymphocytes and Langhans giant cells are observed (Fig. 3c). The lesion extended from the renal cortex to the peripheral fat tissue, with no evidence of fungi with periodic acid–Schiff stain or Grocott's stain or of acid-fast bacilli with Ziehl–Neelsen's stain.

Discussion

Renal granuloma is an extremely rare condition that develops in 0.1% of BCG-treated bladder cancer cases.[2] The patients may present with various associated symptoms, including low-grade fever, chills, night sweats, flank pain, vomiting, and pain on urination.[2–9] However, our patient remained asymptomatic during and after the course of the intravesical BCG immunotherapy. There were no symptoms suggestive of pyelonephritis, such as fever or back pain. Also, there was no pyuria.

Radiological findings of renal granulomas on CT scan could be diverse. Some can appear as a segmental tumor associated with minimal perinephric stranding, while others can appear quite expansile.[4] Renal granulomas are solid masses that mimic papillary renal cell carcinoma and have been reported to appear hypovascular on CT.[10]

Renal granulomas may show preservation of the calyx center on CT scan, and the "unaffected calyx" sign may be a specific feature of renal granulomas.[3]

An overview of published reports of renal granuloma related to BCG is described in Table 1. When a definitive diagnosis is made by needle biopsy, patients had typically undergone antituberculotic therapy for at least 3 months and up to 1 year.[1,3,4,6–9,11–14] All patients were responsive to antituberculotic therapy, showing complete cure of renal granuloma and accompanying symptoms.[11] However, conservative management was also successful in asymptomatic cases with non-expansile renal lesions.[2,4,12,15,16] Patients who received

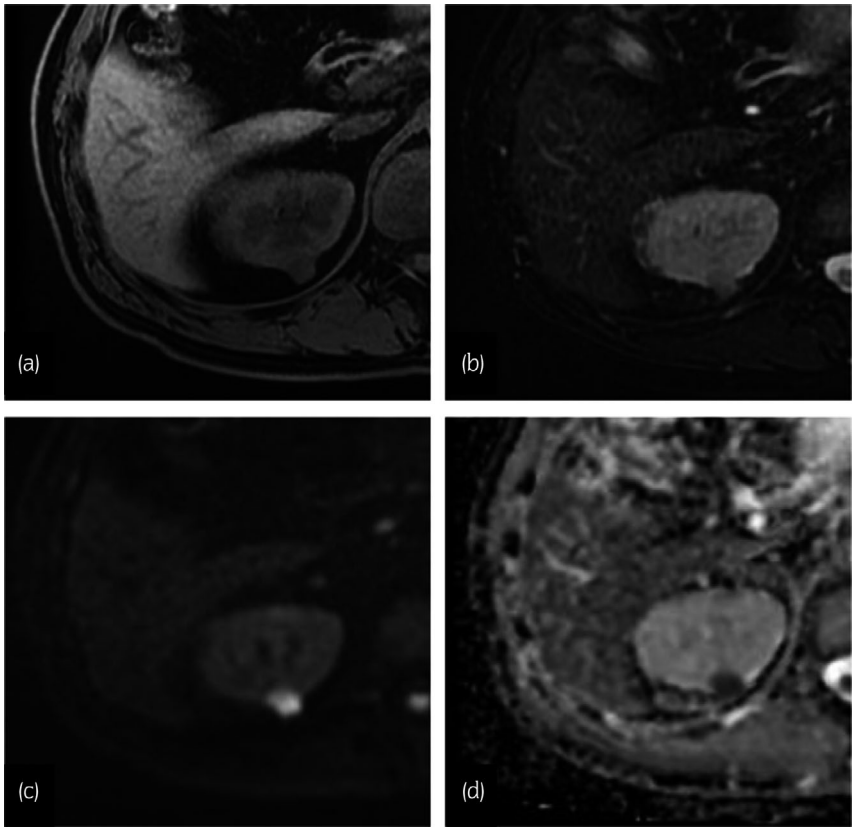

Fig. 2 MRI images of the right kidney. (a) Fat-saturated T1-weighted imaging shows low signal intensity, (b) fat-saturated T2-weighted imaging shows slightly low signal intensity. (c) Diffusion-weighted imaging shows strong high intensity, and (d) apparent diffusion coefficient value is low.

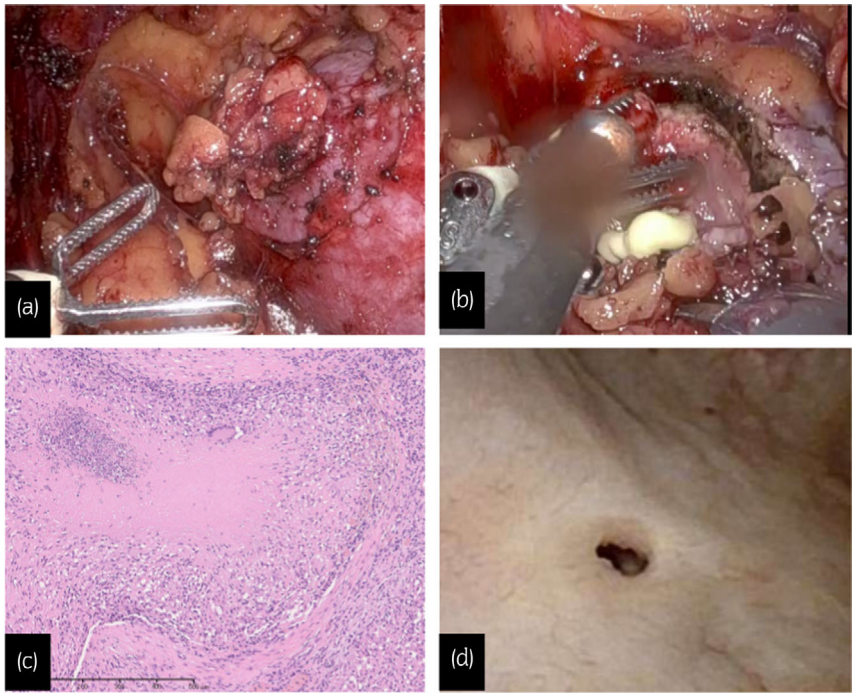

Fig. 3 (a, b) Intraoperative imaging of RAPN. (b) White pus came out from the tumor during resection. (c) Histopathological examination revealed epithelioid cell granuloma with necrosis of the right kidney. A Langhans giant cell was observed (arrow). (d) Postoperative cystoscopy showed enlargement of the right ureteral orifice.

conservative treatment tended to have a longer time from intravesical BCG administration (median: 19.5 months [range 0–28]). As our case was asymptomatic and had a small solitary lesion, the disease could have been treated conservatively. However, there is no consensus regarding the appropriate management of renal granuloma.

The possible routes of BCG dissemination to the kidney include retrograde urinary infection due to VUR and

Table 1 Patient and tumor characteristics in the literature

Number of cases	24
Median age (range)	66.5 (45–79)
Location of urothelial carcinoma	
Upper urinary tract	4 (16.7)
Bladder	20 (83.3)
Chief complaint, *n* (%)	
Asymptomatic	12 (50.0)
Fever	7 (29.2)
Other	2 (8.3)
NR	3 (12.5)
Median tumor size, mm (range)	28 (10–57)
Tumor multiplicity, *n* (%)	
Single	9 (37.5)
Multiple	7 (29.2)
NR	8 (33.3)
Time after intravesical BCG therapy, *n* (%)	
<3 months	6 (25.0)
3 months≤, <12 months	5 (20.8)
12 months≤	8 (33.4)
NR	5 (20.8)
Tumor biopsy, *n* (%)	
Yes	15 (62.5)
No	9 (37.5)
Treatment, *n* (%)	
Conservative treatment	6 (25.0)
Antituberculotic therapy	14 (58.3)
Surgery	4 (16.7)

hematogenous infection. Transurethral resection of bladder tumors close to the ureteral orifices occasionally cause VUR.[11] In this case, the bladder tumor was located near the right ureteral orifice, and postoperative cystoscopy showed enlargement of the right ureteral orifice (Fig. 3d). Although the presence of VUR was not confirmed, retrograde urinary infection could have led to the renal granulomatosis.

Intravesical BCG-related complications such as renal granuloma occasionally occur and mimic renal tumors. Clinicians should consider this possibility when image abnormalities are encountered in bladder cancer patients treated with intravesical BCG therapy. A review of a larger number of similar cases is required to establish appropriate management strategies for renal granulomatosis.

Conclusion

Here, a case of an intravesical BCG-related renal granuloma mimicking papillary RCC has been reported. Clinicians should consider the possibility of renal granuloma that resembles cancer when encountering image abnormalities in patients treated with intravesical BCG therapy for bladder carcinoma.

Acknowledgments

We thank Drs. Yasushi Inoue, Hiroki Inatsu, Ryo Amakawa, and Tadashi Yoshimatsu for informative discussions and the critical review of our article. We thank NAI for English language editing.

Author contributions

Ibuki Tsuru: Writing – original draft. Masaki Nakamura: Supervision; writing – original draft; writing – review and editing. Taro Izumi: Writing – review and editing. Akihiro Ono: Writing – review and editing. Yoshio Masuda: Writing – review and editing. Masashi Kusakabe: Writing – review and editing. Teppei Morikawa: Writing – review and editing. Haruki Kume: Supervision. Yoshiyuki Shiga: Supervision.

Conflict of interest

The authors declare no conflict of interest.

Approval of the research protocol by an Institutional Reviewer Board

Not applicable.

Informed consent

Written informed consent for publication was obtained from the patient.

Registry and the Registration No. of the study/trial

Not applicable.

References

1 Bhat S, Srinivasa Y, Paul F. Asymptomatic renal BCG granulomatosis: an unusual complication of intravesical BCG therapy for carcinoma urinary bladder. *Indian J. Urol.* 2015; **31**: 259–61.
2 Tran-Harding K, Nair RT, Ganesh H. Renal granulomatosis post intravesical Bacillus Calmette–Guerin therapy for non-muscle-invasive bladder cancer. *J. Clin. Imaging Sci.* 2018; **8**: 18.
3 Senés AT, Badet L, Lyonnet D, Rouvière O. Granulomatous renal masses following intravesical Bacillus Calmette–Guérin therapy: the central unaffected calyx sign. *Br. J. Radiol.* 2007; **80**: e230–3.
4 Ma W, Kang SK, Hricak H, Gerst SR, Zhang J. Imaging appearance of granulomatous disease after intravesical Bacille Calmette–Guerin (BCG) treatment of bladder carcinoma. *Am. J. Roentgenol.* 2009; **192**: 1494–500.
5 Sikpa KH, Danjou P, Mahjoubi Z, Makke S, Bernard A, Chaabane C. Incidental discovery of a case of renal tuberculoma after intravesical BCG treatment. *Urol. Case Rep.* 2022; **45**: 102177.
6 Cheremisin D, Andropova P, Gavrilov P. A case of renal tuberculosis following BCG therapy for bladder cancer. *QJM* 2019; **112**: 797–8.
7 Selmi Y, Kheder-Elfekih R, Jebali H *et al*. A case of renal granulomatosis with polyangiitis following intravesical Bacillus Calmette–Guérin therapy. *Saudi J. Kidney Dis. Transpl.* 2018; **29**: 185.
8 Kobayashi S, Hori J, Okazaki S *et al*. A case report of suspected tuberculous granuloma in the kidney after BCG perfusion therapy for urothelial carcinoma of the renal pelvis. *Hinyokika Kiyo* 2016; **62**: 25–8.
9 Higashioka K, Miyake N, Nishida R *et al*. Bilateral granulomatous renal masses after intravesical BCG therapy for non-muscle-invasive bladder cancer and carcinoma in situ of the upper urinary tract: a case study. *Kansenshogaku Zasshi* 2015; **89**: 481–4.
10 Wada Y, Sugiyama Y, Kikukawa H *et al*. Isolated renal tuberculosis following intravesical Bacillus Calmette–Guérin therapy for bladder cancer. *Urol. Int.* 2004; **72**: 257–60.
11 Bajramovic S, Alic J, Skopljak E *et al*. Renal tuberculosis following intravesical Bacillus Calmette–Guérin (BCG) immunotherapy for the treatment of bladder cancer. *Med Arch.* 2020; **74**: 146–50.

12 Narita K, Akita H, Kikuchi E *et al*. Biopsy-diagnosed renal granuloma after intravesical Bacillus Calmette–Guérin therapy for bladder carcinoma: a case series and review of the literature. *BJR Case Rep.* 2019; **5**. https://doi.org/10.1259/bjrcr.20190012.
13 Kuramoto T, Nishikawa T, Nanpou Y. A case report of granulomatous renal masses following intravesical instillation of Bacillus Calmette–Guerin therapy. *Acta Urol. Jpn.* 2018; **64**: 225–30.
14 Sihra N, Diasuke N, Thurairaja R, Khan MS, Malde S. Renal tuberculosis following intravesical Bacillus Calmette–Guérin for high-grade non–muscle-invasive bladder cancer. *Urology* 2018; **107**: e3–4.
15 Al-Qaoud T, Brimo F, Aprikian AG, Andonian S. BCG-related renal granulomas managed conservatively: a case series. *Can. Urol. Assoc. J.* 2015; **9**: E200-3.
16 Marks J, Argyres M, Lloyd G. BCG renal granuloma. *Urology* 2019; **127**: e10.

