



Case Report

Successful treatment with low-dose oral steroids for contracted bladder after intravesical instillation of Bacillus Calmette–Guérin

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Abbreviations & Acronyms

BCG = Bacillus Calmette–Guérin
CT = Computed tomography
TURBT = transurethral resection of bladder tumor

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How to cite this article:

Katami A, Inoue T, Sakurai H *et al.* Successful treatment with low-dose oral steroids for contracted bladder after intravesical instillation of Bacillus Calmette–Guérin. *IJU Case Rep.* 2024; 7: 185–187.

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Received 16 November 2023; accepted 24 January 2024.
Online publication 2 February 2024

Introduction: Contracted bladder is a rare adverse effect of intravesical Bacillus Calmette–Guérin instillation, with an incidence of 0.2–3.3%. This report aimed to present a case of contracted bladder successfully treated with a low-dose oral steroid.

Case presentation: A 78-year-old man underwent a third transurethral resection of a bladder tumor. The pathological diagnosis was urothelial carcinoma in situ. After the fifth instillation of the second-line induction therapy of Bacillus Calmette–Guérin, the patient discontinued treatment because of increased urinary frequency and a continuous mean voiding volume of 80 mL. The patient was diagnosed with a contracted bladder based on computed tomography findings and a urination chart. After initiating oral prednisolone (20 mg/day), the patient experienced significant recovery within 2 weeks for both urinary frequency and mean voiding volume of 226 mL.

Conclusion: A patient with a contracted bladder after Bacillus Calmette–Guérin instillation was successfully treated with low-dose oral steroid therapy.

Key words: adverse event, BCG, bladder cancer, contracted bladder, steroid.

Keynote message

A low-dose oral steroid is effective in treating contracted bladder as an adverse event after intravesical BCG instillation.

Introduction

Contracted bladder is a rare but severe adverse event after intravesical BCG instillation, with an incidence of 0.2–3.3%.^{1–3} Conservative treatment with antituberculosis drugs, steroids, and bladder hydrodistension is the first treatment option for contracted bladder. However, cystectomy can be performed in cases in which conservative treatment achieved no improvement. Steroid pulse therapy has been reported to be effective. However, few reports have described the effectiveness of low-dose oral steroid therapy.⁴ This report aimed to present a case of a patient with a contracted bladder after intravesical instillation of BCG, who was successfully treated with low-dose oral steroid therapy.

Case report

A 78-year-old man presented to our hospital with a complaint of gross hematuria. Cystoscopy was performed and showed redness. The patient underwent TURBT and was pathologically diagnosed with noninvasive urothelial carcinoma (pTa, G2, high grade). Induction therapy with BCG bladder instillation was performed for six doses. Four years later, cystoscopy showed a red area of less than 5 mm in diameter, and the patient was suspected of recurrence. The patient underwent TURBT, which revealed no malignant findings.

After 8 months, cystoscopy showed a red area approximately 2 cm in diameter. The patient was suspected of recurrence, and TURBT was performed. The pathological diagnosis was urothelial carcinoma in situ (pTis, G3, high grade). Second-line induction therapy of BCG bladder instillation was initiated. The sixth instillation of BCG was discontinued because of persistent urinary frequency and pain during urination.

The patient was instructed to document his symptoms in a voiding diary. The average number of daily voids over 14 days was 15, with an average of four nocturnal voids. The mean voiding volume was approximately 80 mL, and the maximum voiding volume was 130–150 mL. Blood and urine tests showed no abnormalities. Cystoscopy revealed multiple sites of redness on the mucosa. Urine cytology was class II. CT showed thickening of the bladder wall without clear signs of bladder cancer recurrence (Fig. 1a).

After 1 month, levofloxacin (500 mg/day) was administered for 21 days, and 3 months later, ciprofloxacin (100 mg/day) was administered for 28 days without improvement in symptoms. The patient refused to receive antituberculosis drugs because the tuberculosis polymerase chain reaction, smear, and liquid culture tests for urine were all negative. Urine sediment examination showed negative results for protein and bacteria, Red Blood Cell (RBC) of 30–49 per high-power field, and White Blood Cell (WBC) of 30–49 per high-power field. The bladder findings on the CT scan did not improve, and the patient was clinically diagnosed with a contracted bladder.

At 4 months, the patient was recommended to undergo pulse steroid therapy. However, he refused due to concerns about susceptibility to infection. Therefore, oral steroids at 30 mg/day were suggested based on previous reports.⁴ However, he also refused, so the patient was treated with prednisolone at 20 mg/day. Subsequently, over 14 days, the average

number of daily voids significantly decreased from 14 times daily before prednisolone initiation to 8 times after initiation. Furthermore, the average number of nocturnal voids reduced significantly from 4 times nightly to two times (Fig. 2a, $p < 0.001$, Mann–Whitney U -test). The mean voiding volume significantly increased from 132 to 226 mL (Fig. 2b, $p < 0.001$, Mann–Whitney U -test).

After 5 weeks of prednisolone initiation, the dose was gradually reduced to 10 mg, and then, the dose was reduced to 5 mg in 6 weeks after initiation. Even after discontinuing prednisolone after 10 weeks, no worsening of urinary symptoms was observed. CT revealed no recurrence of carcinoma or contracted bladder (Fig. 1b). At 40 months, cystoscopy showed no carcinoma recurrence.

Discussion

The cause of the contracted bladder after BCG instillation remains unclear. However, it has been suggested that severe inflammatory reactions that persist over the long-term⁵ low bladder capacity after partial cystectomy or frequent TURBT, and many BCG instillations² may be possible factors associated with contracted bladder. Nagayama *et al.*⁶ reported that it is important to promptly consider administering antituberculosis drugs or steroids in patients with persistent severe bladder irritation symptoms and significantly decreased bladder capacity. Antituberculosis therapy is recommended according to

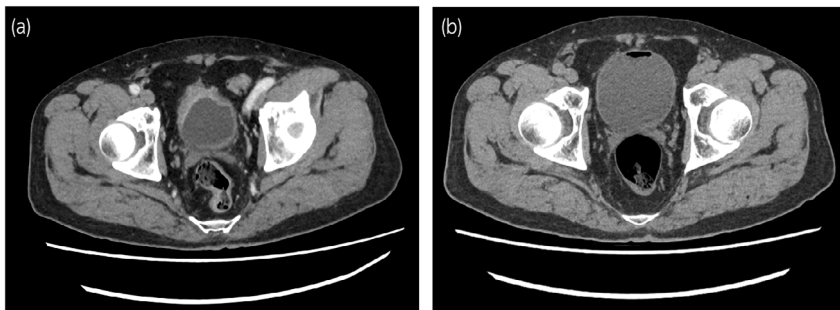


Fig. 1 (a) CT images before steroid therapy. (b) CT images after steroid therapy.

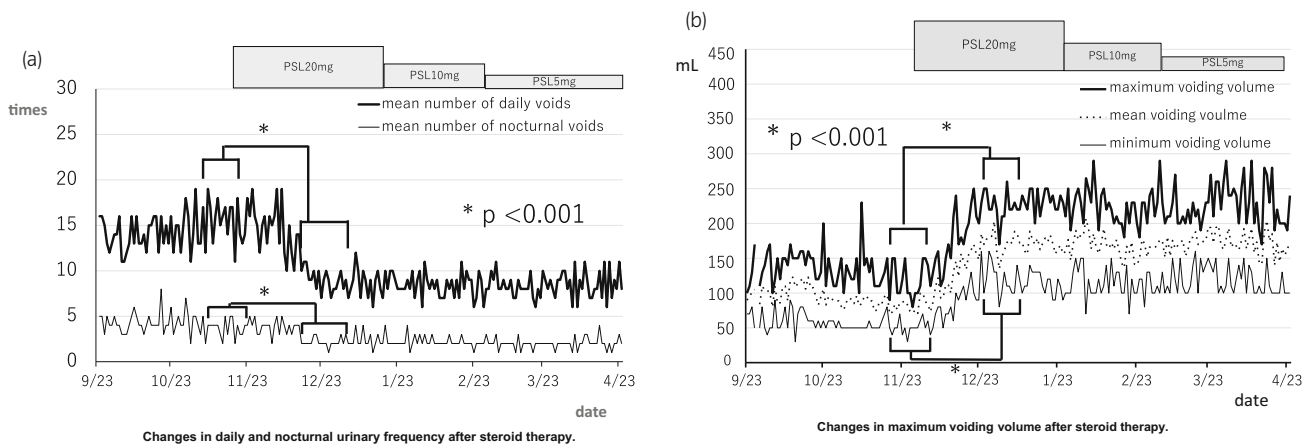


Fig. 2 (a) Changes in daily and nocturnal urinary frequency after steroid therapy. (b) Changes in maximum voiding volume after steroid therapy.

standard tuberculosis treatment for cases in which BCG is detected in urine with a contracted bladder after BCG instillation.⁶ However, even if the urinary BCG becomes negative after antituberculosis treatment, the contracted bladder cannot usually be treated in many cases.⁶

Kimura *et al.*⁷ reported that hypersensitivity reactions to BCG may be the cause of contracted bladder. They recommended using pulse steroid therapy (500–1000 mg/day for 3 days) within 2–4 weeks after the last BCG instillation before the complete formation of fibrosis and granuloma. They reported a patient with a voiding volume of 15–30 mL before pulse steroid therapy, which increased to approximately 100 mL on the fifth day of treatment, and the voiding volume continued to increase to 200–250 mL.

This report presents a patient with persistent frequent urination and dysuria due to a significant decrease in the mean voiding volume (approximately 80 mL) after the second induction course of BCG instillation. The patient was clinically diagnosed with a contracted bladder based on the persistent symptoms, including frequency and difficulty of urination for 4 months, and significant bladder wall thickening on CT. The patient was treated with low-dose oral prednisolone (20 mg/day), which significantly improved urinary frequency and bladder capacity (226 mL).

In this case, it is possible that the reason for the effective treatment was because of early steroid therapy (within 4 months) before the completion of irreversible tissue fibrosis and granulation formation. However, Wittes *et al.*⁴ reported a patient with a bladder capacity of 35–125 mL who was treated with oral prednisolone (30 mg/day) after 2 years of BCG instillation, which increased the bladder capacity to 250 mL. This case report creates controversy in the discussion regarding whether the timing of treatment initiation may be a factor in treatment success.⁴

For steroid-resistant contracted bladder, Sawada *et al.*⁸ and Numakura *et al.*⁹ reported that bladder hydrodistension therapy was effective after confirming the absence of malignant findings and BCG infection.

Currently, there is no clear consensus on objective indicators demonstrating irreversible contracted bladder, which is diagnosed only clinically based on frequent urination and decreased voiding volume. Furthermore, reports on contracted bladder after BCG instillation vary in severity, lack pathological diagnoses, and have no established definitions.

Although few studies have reported the effectiveness of low-dose oral steroid therapy, this treatment may be helpful because of its minimal invasiveness. The accumulation of experiences will establish a working definition of the condition, appropriate examinations, and sequence for various treatments, including low-dose oral steroid therapy.

Acknowledgment

We thank Mr. Takehiko Inoue, the presented patient and the corresponding author's biological father, for providing a detailed voiding diary.

Author contributions

Akinobu Katami: Data curation; formal analysis; investigation; writing – original draft. Takamitsu Inoue: Conceptualization; funding acquisition; investigation; methodology; project administration; writing – review and editing. Hiromichi Sakurai: Data curation. Mizuki Onozawa: Software; validation; visualization. Shin-ichi Hisasue: Supervision. Koji Kawai: Supervision. Jun Miyazaki: Supervision.

Conflict of interest

The authors declare no conflict of interest.

Approval of the research protocol by an Institutional Reviewer Board

The study protocol was approved by the Ethics Committee of the International University of Health and Welfare Narita Hospital (No. 22-Nr-007).

Informed consent

Written informed consent was obtained from the patient for the publication of this case report.

Registry and the Registration No. of the study/trial

Not applicable.

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