

# A Rare Complication of Intravesical Bacillus Calmette Guérin Therapy: Local Progressive Pelvic Inflammation

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## Abstract

It has been proven that intravesical Bacillus Calmette–Guérin (BCG) therapy prevents the recurrence and progression of carcinoma in situ and of superficial bladder cancers, although local and systemic complications have been reported. However, careful attention should be given to the timing and management of this therapy because complications that may delay possible definitive treatment may also be seen. A case characterized with extensive inflammation, observed rarely after BCG therapy, involving pelvic organs and leads up to the internal abdomen and mesenteric area in the superior and levator muscle and prepubic area in inferior is presented here.

Keywords: Bacillus Calmette–Guérin; bladder cancer; pelvic inflammation.

It has been proven that intravesical Bacillus Calmette–Guérin (BCG) therapy prevents the recurrence and progression of carcinoma in situ and of superficial bladder cancer. However, it has been associated with local and systemic side effects [1]. A case characterized with extensive inflammation observed rarely after BCG therapy and involving pelvic organs and leads up to the internal abdomen and mesenteric area in the superior and levator muscle and prepubic area in the inferior is presented here.

## Case Report

A 59-year-old male patient had transurethral bladder tumor resection for bladder cancer diagnosed as a 4-cm mass on urinary ultrasonography at an external center. Without a

second-look transurethral resection, BCG therapy was initiated with T1 high-grade (HG) pathological stage. A 6-week induction treatment was completed. Then, the patient was referred to our clinic. On evaluation, there were no additional comorbidities or other surgical procedures. On physical examination, inflammation and apparent hardness with palpation, including bilateral scrotum and testicles and reaching up to both the inguinal areas and prepubic area, were noted. On anamnesis, it was observed that these conditions persisted even before the last induction cure. Next, empirical quinolone treatment was initiated, and additional radiological and laboratory examinations and consultation to pulmonary and infection disease clinics were

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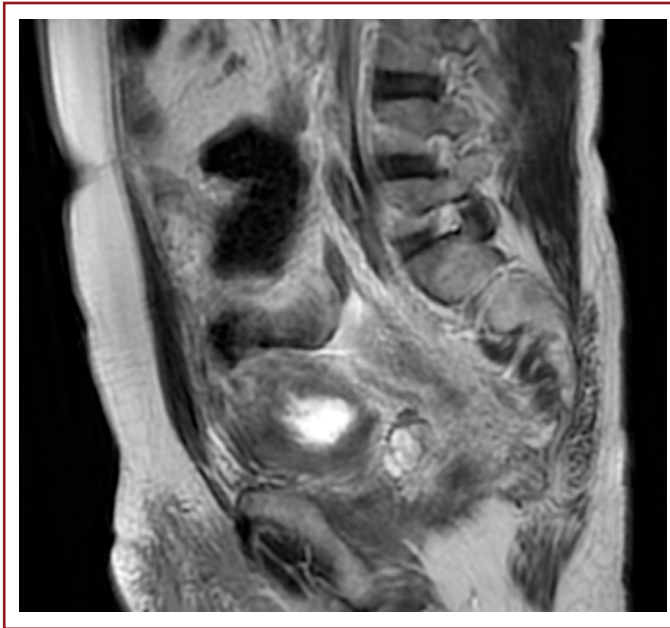
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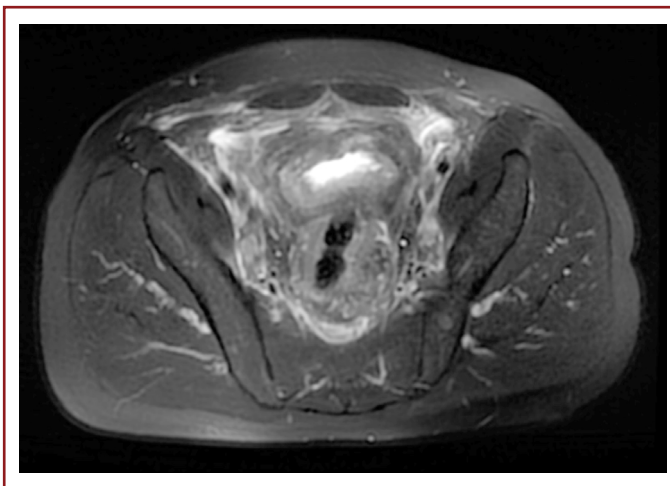
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requested. When the pathological samples were re-evaluated at our hospital, the pathological stage observed was T2HG. There was no pulmonary involvement. On radiological evaluation, an extensive, local, progressive, nontumoral inflammation involving the pelvic organs and leading up to the mesenteric area in the abdomen in the superior and levator muscle and prepubic area in the inferior was detected (Figs. 1, 2). A 6-month antituberculosis treatment (oral rifampin, isoniazid, and ethambutol) was planned for the patient and because of this condition, definitive treatment was deferred.



**Figure 1.** Widespread inflammation extending to the prepubic and perirectal area and left levator muscle.



**Figure 2.** Diffuse thickening of the bladder wall, especially at the right anterolateral wall. This thickening on the right anterolateral wall keeps the entire wall and infiltrates the perivesical fatty planes.

## Discussion

BCG therapy, which is frequently used in medium- and high-risk superficial bladder cancer and carcinoma, decreases their recurrence rates and delays progression [2]. It exhibits these effects through the development of T-cell-mediated immune response in the bladder [3]. It causes local inflammation after instillation and tumor cell damage.

Local complications, such as hematuria, dysuria, and cystitis, are common after BCG application. In the literature, the reported incidence is 57%–91% for hematuria, 26%–55% for cystitis, and 28%–73% for fever [4]. Nonsteroidal anti-inflammatory, antipyretic, and antispasmodic drugs may be commonly used to treat spontaneously recovering local complications with a mild course.

Post-BCG systemic complications have been reported but are relatively rare. Systemic complications occur with hematogenous spreading of the bacteria due to predisposing conditions, such as damaged and/or inflamed urothelium caused by extreme tumor resection, diabetes, immunosuppression, liver function disorder, traumatic catheterization, and bladder perforation [5]. General condition disorder, myalgia, arthralgia, headache, fever, pneumonia, abscess, and sepsis may also be observed. Complications, such as psoas abscess, septic shock, peritonitis, disseminated intravascular coagulation, and diffused granulomatous mesenteric disease have also been reported [6, 7].

Aseptic conditions should be maintained during BCG application to prevent the occurrence of secondary complications, and the application should be delayed in case of inflammatory disease, macroscopic hematuria, and cystitis. BCG should be applied at least 2 weeks after transurethral operation and traumatic catheterization. BCG should not also be applied in case of immunosuppression, pregnancy, or previous hypersensitivity. While some researchers recommend isoniazide prophylaxis to prevent these complications, others indicate that this application decreases the antitumoral effect of BCG or fails to prevent these complications [8]. Low-dose BCG application has been attempted by many researchers with the same concern, but the results remain controversial.

BCG instillation should be immediately cut when systemic complications occur, and patients with high fever should be immediately hospitalized [9]. Systemic BCG infection treatment is a 6-month regimen, including isoniazide (300 mg/24 h), rifampicin (600 mg/24 h), and ethambutol (1200 mg/24 h) [3]. Although the use of corticosteroids is risky during treatment, they may be administered in case of high fever, sudden hypotension, and hypersensitivity.

It is proclaimed that a single transurethral resection (TUR) may not be enough to extract the ill tissue, especially in multiple and invasive tumors, and may cause early recurrence and stage advancement despite additional intravesical treatment<sup>[10]</sup>. Another fact that should not be ignored is that intravesical treatment provided in addition to TUR does not compensate the inadequate resection in TUR<sup>[11]</sup>. Therefore, second TUR (re-TUR) should be applied after 2–6 weeks in these patients. In the literature, residual tumor detection ratios in re-TUR range from 28% to 74% and understating ratios from 1.7% to 64%<sup>[12, 13]</sup>. Schwaibold et al.<sup>[14]</sup> evaluated 136 patients with T1 ( $\pm$ CIS) tumor who had re-TUR and observed upstaging in re-TUR in 28 patients (21%) whose first resection was reported to be standard TUR<sup>[15]</sup>. In the same study, it was found that re-TUR applied before BCG prevented upstaging with an additional ratio of 27% compared with BCG alone. Thus, re-TUR is recommended in multifocal disease, large tumor ( $\geq$ 3 cm), incomplete resection, and T1HG pathological stage.

In our case, the pathological stage for standard TUR operation applied in an external center was evaluated as T1HG, and BCG treatment was applied because re-TUR was regarded unnecessary due to complete resection. The patient was referred to our center due to the development of progressive pelvic inflammation because of BCG. Muscular invasion was observed on histopathological re-evaluation by an experienced uropathologist at our center. Although we believed that cystectomy should be immediately performed in this young high-risk patient without long-term metastasis, the definitive treatment decision had to be delayed due to BCG-related intense pelvic and mesenteric inflammation.

## Conclusion

Although BCG therapy has a rare local and systemic side effect, it is an effective treatment for carcinoma in situ and superficial bladder cancer. However, complications that may delay possible definitive treatment, as in this case, may also be observed. Therefore, particularly regarding re-TUR indication, we believe that it should be performed in pathologically and radiologically noninvasive patients, and this will not result in delay in the possible definitive treatment.

**Informed Consent:** Written informed consent was obtained from the patient for the publication of the case report and the accompanying images.

**Peer-review:** Externally peer-reviewed.

**Conflict of Interest:** None declared.

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