

# A rare reason of PSA elevation seen during intravesical BCG therapy: Granulomatous prostatitis

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## Dear Editor,

Prostatitis accounts for approximately 10-14% of cases of urinary system infections admitted to urologists (1). Acute bacterial prostatitis (98-99%) is the most common type of prostatitis. Granulomatous prostatitis, which differs from chronic bacterial prostatitis, constitutes less than 1% of all prostatitis cases. Etiology is not exactly known (2). When the literature is examined, it is seen that the diagnosis of granulomatous prostatitis is often made after surgical interventions of the prostate, intravesical administration of Bacillus Calmette-Guérin (BCG) in the treatment of bladder cancer, iatrogenic interventions or prostate biopsy performed under transrectal ultrasound (TRUS) guidance in patients having prostate-specific antigen (PSA) elevation. BCG treatment may increase dysuria and irritative symptoms, especially in patients with voiding dysfunction (3). In this article, we aimed to present a case of granulomatous prostatitis who was diagnosed with bladder cancer, had PSA elevation during intravesical BCG therapy, and underwent prostate biopsy under TRUS guidance.

A 64-year-old male patient was admitted to our polyclinic with the complaint of painless hematuria with passage of clots. Abdominal ultrasonography revealed an approximately 3.5 cm papillary mass extending to the lumen in the left wall of the bladder. The patient underwent cystoscopy under regional anesthesia. The mass which was seen in a single focus during cystoscopy underwent total transurethral resection. Histopathological evaluation was reported as superficial bladder tumor (T1) with lamina propria invasion and without muscle layer invasion. Intravesical BCG therapy was decided to be administered.

Severe lower urinary tract symptoms began 1 week after the last dose of BCG, although no side effects were seen

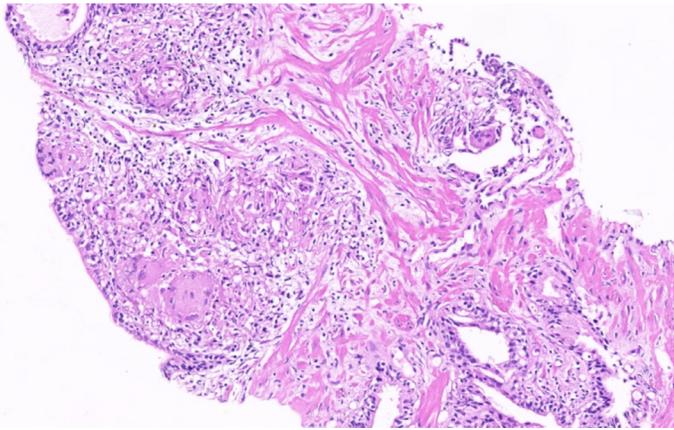
during weekly BCG treatments for the first 6 weeks. The patient had no fever or systemic infection sign. In this period, urinalysis revealed abundant leukocytes and microscopic hematuria. Urine cultures showed no growth. Serum total PSA and free PSA values were measured as 6 and 0.8 ng/dL, respectively. In the digital rectal examination, the prostate was soft. As a result of the patient's uroflowmetry, Qmax 16 residual urine volume was measured as 40 cc. Leukocytosis and hematuria resolved following administration of fluoroquinolone antibiotics to the patient. However, there was a slight increase in PSA values while they were expected to decrease (total PSA/free PSA: 7.1/0.9 ng/dL). Since it was considered that the patient might have prostate cancer, twelve core prostate biopsy was performed under transrectal ultrasound (TRUS) guidance.

Histopathological examination is periglandular granulomas consisting of epithelioid histiocytes, lymphocytes and giant cells in 3 of 12 prostate core needle biopsy (Figure 1). Pathology result was reported as granulomatous prostatitis. Therefore, intravesical administration of BCG was discontinued. Screening for acid-alcohol resistant bacilli (AARB) in urine was negative. The PPD skin test was negative. Intravesical BCG therapy was interrupted for 1 month. Since the patient who was assessed by the Division of Infectious Diseases did not have systemic tuberculosis signs, he was decided to be followed up without antituberculosis therapy. After one month, it was observed that serum total PSA and free PSA values decreased dramatically to 1.7 and 0.6 ng/dL, respectively. Because the mass was not detected by cystoscopy and the side effects of intravesical BCG were observed, the patient was decided to be followed up without additional intravesical therapy.

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**Figure 1.** Multiple granulomas around prostatic acini (H&E, x50)

The incidence of prostate infections is close to benign prostatic hyperplasia and prostate cancer. While most cases of prostatitis occur as acute prostatitis, granulomatous prostatitis accounts for approximately 0.8-1% of all prostatitis cases (1). When the literature is screened, it is seen that the majority of cases are male patients over 40 years of age. Our case was over 40 years old and male patient.

Although the etiology of the disease has not yet been elucidated, the most frequently accused factors are surgical interventions of the prostate and intravesical administration of *Bacillus Calmette-Guérin* (BCG) (2). It has been also reported that it is incidentally detected in prostate biopsies performed under TRUS guidance in patients having PSA elevation (1).

Granulomatous prostatitis occurs rarely due to specific causes (bacteria, fungi), but more often due to nonspecific factors. In literature, the most important factor for the formation of granulomatous prostatitis appears to be iatrogenic causes (3,4). We have not found a specific cause in our case.

In a study by Leibovici et al., they reported that serum PSA levels were elevated by 75% after intravesical BCG therapy and that this was associated with granulomatous prostatitis (5). In our case, PSA elevation was detected during intravesical BCG therapy.

Granulomatous prostatitis was first described by Tanner and McDonald in 1943 (6). Then, Hedelin et al. first described GP in 6 patients who underwent transurethral resection of the prostate (TURP) in 1981 (7). In the study of Helpap and Vogel, they evaluated 2850 prostate specimens and reported granulomatous prostatitis in 7.1% of them (8). Granulomatous prostatitis after BCG administration can be seen when it is given intravesically or systemically (5).

With the widespread use of PSA in the field of screening in recent years, the number of prostate biopsies performed under TRUS guidance for the diagnosis of prostate cancer increases. In recent years, many researchers have reported that the incidence of granulomatous prostatitis after this procedure increases. It has been reported that

granulomatous prostatitis is seen between 0.36% and 11% in the pathologies of patients undergoing prostate biopsy under TRUS guidance due to PSA elevation (1).

Traditionally, scattered plasmacytes, intraepithelial inflammatory cells, neutrophils, lymphocytes and macrophages together with diffuse, cluster-like, and less frequently lymphocytic nodules or combination of all of them are most commonly seen pathologically in prostate infections. Neutrophils and macrophages are typically found in the lumen (9). When the histopathology of granulomatous prostatitis is evaluated, the histological appearance characterized by lobular and mixed inflammatory infiltrates containing abundant amounts of histiocytes, lymphocytes, and plasmacytes and the small and different granular structures are observed. Infiltrative formation of epithelioid histiocytes and rarely multinucleated giant cells, lymphocytes, and plasma cells may also be seen. In our case presented in this study, similar findings were observed in the histopathological examination (1).

In cases diagnosed with granulomatous prostatitis, a digital rectal examination performed before the diagnosis may be abnormal and high PSA levels may be present as in our case. Considering these two findings, granulomatous prostatitis may mimic prostate cancer clinically and histologically (10). This increase in PSA levels is often temporary. When the literature is examined, some studies have reported that high PSA levels in patients diagnosed with granulomatous prostatitis return to normal levels without any treatment (1, 2).

## CONCLUSION

In conclusion, it should be considered that PSA elevation, which occurs in a patient who receives intravesical BCG therapy due to bladder cancer and who does not have a history of PSA elevation, may be due to granulomatous prostatitis that is caused by BCG therapy and is rarely seen. It will be useful to perform TRUS guided prostate biopsy in order to determine whether this elevation in PSA levels occurs due to concurrent prostate cancer or granulomatous prostatitis.

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