Case Report

Bacillus Calmette-Guerin Granuloma in Seminal Vesicle: Report of the First Case in the English Literature

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Abstract: A 64-year-old man underwent a radical cystoprostatectomy for intravesical bacillus Calmette-Guerin (BCG) therapy-resistant, recurrent muscle invasive transitional cell carcinoma (TCC) of the urinary bladder. He had a history of left radical nephroureterectomy for a papillary TCC of the left ureter 10 months ago. On microscopic examination, not only multifocal residual papillary TCCs in the urinary bladder but also multiple small granulomas in the urinary bladder and prostate were noted. Interestingly, unusually severe granulomatous inflammation accompanying focal central caseating necrosis was identified in the subepithelial tissue of the left seminal vesicle and vas deferens. Neither prostatic adenocarcinoma nor TCC involvement was identified in the prostate and seminal vesicles. A few acid–fast bacilli were identified by the Ziehl-Neelsen staining in the seminal vesicle granulomas, confirming the BCG-induced inflammation. To the best of our knowledge, this is the first case of BCG-induced granuloma involving the seminal vesicle. It is uncertain why only the left seminal vesicle was involved with BCG granulomas and the incidence and mechanism of seminal vesicle BCG granuloma await more cases.

Key Words: Bacillus Calmette-Guerin, BCG, seminal vesicles, granuloma

Introduction

Bacillus Calmette-Guerin (BCG), a live attenuated strain of Mycobacterium bovis, was originally developed as an immunization for tuberculosis. Since the first report of BCG immunotherapy in the patients with superficial bladder cancer in 1976 by Morales et al. [1], BCG has been used as the most effective intravesical treatment for high grade superficial transitional cell carcinoma (TCC) [1]. While the granulomatous prostatitis is one of the common side effects of BCG intravesical instillation, to the best of our knowledge BCG granulomas in the seminal vesicle have not been reported in the English literature [2, 3]. Herein, we report the first case of BCG-induced granuloma involving a unilateral seminal vesicle after intravesical BCG therapy for the BCG-resistant recurrent muscle invasive TCC of the bladder.

Case Report

A 64-year-old man was referred to Asan Medical Center for further evaluation of a left ureteral mass, which has been detected during a workup for gross hematuria. A biopsy of left ureteral mass revealed TCC. A subsequent left radical nephroureterectomy was performed and a papillary TCC, grade 3/3, invading the proper muscle was identified in the left ureter. After 10 months, gross hematuria recurred. Transurethral resection of the bladder tumor (TURBT) demonstrated multifocal papillary TCCs, grade 3/3, stage T1 in the urinary bladder. Despite repeated TURBT and intravesical BCG instillation therapy, the tumor progressed and invaded the proper muscle layer of urinary bladder. On computerized tomography (CT) images, diffuse wall thickening of urinary bladder with regional lymphadenopathy was noted. The left seminal vesicle showed lower enhancement than right one, however, no definite mass lesion was noted (Figure 1). The magnetic resonance imaging (MRI) was not performed. The serum prostate specific antigen (PSA) was slightly elevated after the BCG immunotherapy from 2.9 ng/ml at the first admission to 3.1 ng/ml. A radical cystoprostatectomy was performed.

An ill-defined ulcero-infiltrative firm lesion (1.5 x 1 x 0.1 cm) was present in the dome of urinary bladder and the remaining mucosa was slightly eroded. No definite mass was identified in the prostate and seminal vesicles, and representative sections from the bladder tumors, random bladder mucosa, prostate and seminal vesicles were submitted for microscopic evaluation after careful
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Figure 1 The computerized tomographic image. The left seminal vesicle (arrow) shows less enhancement than right one without a definite massive lesion.

gross examination.

The microscopic examination revealed multifocal residual papillary TCCs with muscle proper invasion in the urinary bladder as well as multiple small granulomas in the urinary bladder and prostate. Lymph nodes were negative for tumor metastasis, although there was lymphadenopathy by CT scan. Interestingly, multiple granulomas with occasional caseating necrosis were located in the subepithelial tissue of the left seminal vesicle and vas deferens, consistent with BCG-induced granulomas (Figure 2). The right seminal vesicle showed only slightly dilated lumen with eosinophilic luminal secretion without granulomatous inflammation. To differentiate from other granulomatous conditions, Ziehl-Neelsen and Gomori methenamine silver (GMS) special stains for AFB bacilli and fungal organisms were performed. A few acid–fast bacilli were identified in the left seminal vesicle, confirming the BCG-induced granuloma. GMS stain was negative. The patient was closely followed without adjuvant chemotherapy or antimycobacterial treatment. The patient is alive and well without evidence of recurrence or metastasis of TCC, or other BCG side effects at 2 months after radical cystoprostatectomy.

Figure 2 BCG granulomas in the left seminal vesicle (a-c, H&E stain). The relatively well-defined subepithelial cellular infiltration is present in the seminal vesicle (a), which consists of numerous caseating granulomas (b). Epithelioid histiocytic aggregates with a small focus of central caseating necrosis are present (c, *). An acid-fast bacillus is demonstrated by Ziehl-Neelsen stain (d, arrow).
Discussion

Granulomatous inflammation of the seminal vesicles can occur with various infectious conditions. Tuberculosis of seminal vesicle has been reported as a cause of infertility like tuberculosis of other genitourinary tract organs [4]. A case of seminal vesiculitis caused by Mycobacterium gastri infection leading infertility has also been reported [5]. Yamamoto et al have presented a case of right intrascrotal and seminal vesicular granuloma probably by Propionibacterium acnes infection [6] and Perez-Guillermo et al have reported that infection, trauma or previous surgery related spermatic-cord granulomas may also present as tumor-like lesions adjacent to the testis or seminal vesicle [7].

The histogenesis and incidence of BCG granulomas in seminal vesicle await further case studies. However, it is assumed that BCG involvement of seminal vesicle may be a part of BCG granuloma of the prostate, which is one of the most frequent side effects besides BCG cystitis and fever after intravesical immunotherapy with BCG for urothelial cancer [2, 3]. According to the authors’ experience (unpublished data), BCG granulomas have been commonly seen in the prostate and urinary bladder, but BCG granulomas of the seminal vesicles have never been seen before, indirectly indicating an extremely uncommon event. The granulomatous prostatitis has a reported incidence with a wide range of 1.2-100% of men underwent intravesical BCG instillation [2, 3]. The average interval from initiation of BCG therapy to the diagnosis of granulomatous prostatitis has been reported to be approximately 1 year (range 3 to 25 months) [3]. The granulomatous prostatitis presents not only as focal or diffuse induration on physical examination but also hypoechoic nodule most frequently at the peripheral zone on ultrasonography, simulating prostatic carcinoma [8].

The fate of BCG-induced granulomas is not yet established. The caseating granulomas after BCG instillations may undergo spontaneous fibrosis as a natural healing process [2, 3]. We also believe that BCG granulomas in the seminal vesicles have a similar natural process with BCG granulomas in the prostate. The current case did not have specific symptoms related to BCG granulomas of the seminal vesicle or definite image abnormalities except for insignificant lower enhancement of the affected seminal vesicles, clinicopathologic significance remains to be investigated.

In conclusion, the BCG granulomas can involve seminal vesicles after intravesical BCG instillation and these granulomas should be distinguished from granulomatous inflammation resulted from other microorganisms, based on a careful clinicopathologic correlation.

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