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Genitourinary

Multiparametric ultrasound findings of tuberculous orchitis following bacillus Calmette-Guérin therapy

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ABSTRACT

Granulomatous bacillus Calmette-Guérin (BCG) infection, both localized and disseminated, as a complication of intravesical therapy for transitional cell carcinoma of the bladder is a recognized but highly unusual phenomenon. We report the case of an 89-year-old gentleman with a history of bladder transitional cell carcinoma and subsequent intravesical BCG instillation of the bladder who presented to his general practitioner with a non-tender lump in his left testis. Histopathologic and microbiological evaluation of the subsequent orchidectomy specimen revealed granuloma formation secondary to BCG infection. The use of bubble contrast agents and elastography in ultrasound to evaluate focal testicular lesions is a relatively novel concept, and we aim to highlight the imaging features of testicular BCG infection using these techniques.

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Case report

An 89-year-old gentleman with a history of abdominal aortic aneurysm (AAA) repair in 2003 had a papillary bladder wall lesion incidentally identified on a routine surveillance scan for his AAA in September 2013. In addition to his AAA, he had a history of ulcerative colitis, hypertension, and hiatus hernia. The bladder wall lesion was confirmed on flexible cystoscopy, and the patient went on to have a transurethral resection of bladder tumor. Histology demonstrated papillary tumor without deep muscle involvement (T2a N0 M0).

Following discussion at the multidisciplinary meeting, the patient was treated with once-weekly intravesical BCG instillation for 6 weeks starting in December 2013, with maintenance treatment every 6 months. A further 3 instillations were given

Competing Interests: None.

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in June 2014. Surveillance cystoscopy 6 months following this did not reveal any evidence of recurrent disease, and the patient was discharged with routine clinic follow-up.

In September 2015, the patient was referred back to urology via his general practitioner to whom he presented with a hard, non-tender testicular lump. He complained of some initial discomfort, although this later disappeared. He denied any urinary symptoms.

A scrotal ultrasound demonstrated a hypoechoic mass in the lower pole of the right testis, measuring 3.0 × 2.6 × 2.2 cm (Figs. 1 and 2) with mildly increased peripheral vascularity on color Doppler imaging but no internal Doppler flow (Fig. 3). No hydroceles or epididymal abnormality was seen, and the left testis was normal. A further ultrasound study 4 weeks later was arranged using a LOGIQ E9 (General Electric) ultrasound machine with dedicated strain elastography software and IV sulfur hexafluoride microbubble for dynamic contrast assessment (4.8 cc of Sonovue).

Strain elastography showed uniformly increased dark-blue color corresponding to increased stiffness in relation to the adjacent normal testicular parenchyma seen in areas of green and red (Fig. 4). A ratio of stiffness was also calculated after regions of interest were drawn, showing the target lesion to be approximately 6 times stiffer than the adjacent normal testicular parenchyma (Fig. 5).

Contrast sonography reflected the increased peripheral vascularity seen on Doppler images to a greater degree and provided additional information with regard to enhancement dynamics, showing early and sustained peripheral contrast uptake but almost no appreciable internal vascularity (Fig. 6).

These initial findings were thought to be in keeping with a necrotic testicular tumor. It was explained to the patient that a testicular tumor at his advanced age would be unusual but could represent lymphoma, and as he was suitable for surgery an orchidectomy was recommended.

Histopathologic examination following surgery revealed prominent granulomatous reaction with caseous necrosis

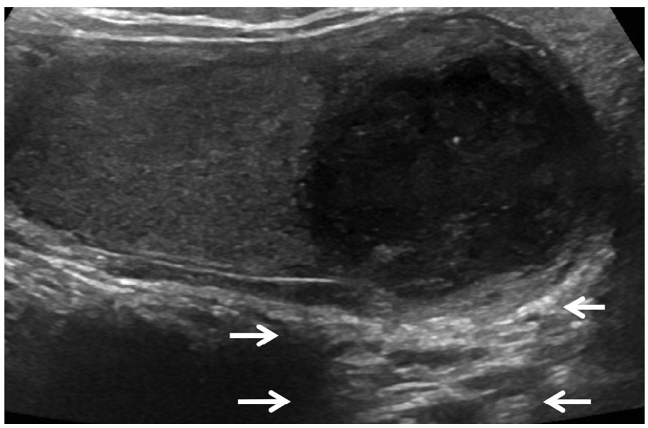

Fig. 1 – Grayscale B-mode ultrasound (sagittal section). Sagittal B-mode image shows a well-defined 3.0 × 2.6 × 2.2 cm hypoechoic lesion in the lower pole of the right testis with posterior acoustic enhancement in keeping with a necrotic center (arrows). The remainder of the right testis is unremarkable.

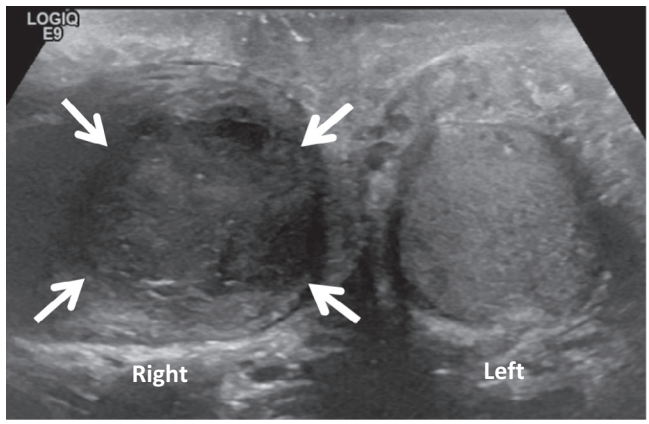

Fig. 2 – Grayscale B-mode ultrasound (transverse section). Transverse B-mode image showing the lower poles of both testes. The abnormal right testis is asymmetrically expanded by the lesion, which is hypoechoic compared with the normal testicular parenchyma seen in the contralateral testis.

(Fig. 7). Langerhans-type multinucleated giant cells were present focally. No evidence of malignancy was seen. Ziehl-Neelsen stains showed acid fast bacilli (Fig. 8) and periodic acid-Schiff stain was negative. The findings were consistent with tuberculous (TB) orchitis. It is important to note that although orchitis was confirmed, there was no imaging or histologic evidence of active concomitant epididymitis.

There was no history of TB contact or exposure, and the patient did not have any clinical symptoms of TB infection. In particular, no respiratory symptoms were present, and chest radiograph was clear. In addition, interferon gamma release assay was negative, suggesting that a diagnosis of latent TB was highly unlikely. All inflammatory markers including erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were within normal limits. The patient was started on a 6-month course of anti-TB therapy with isoniazid, rifampicin, and pyrazinamide under the care of a respiratory physician, following which he has remained symptom free with regard to TB.

Discussion

BCG (attenuated *Mycobacterium bovis*) therapy has been used to treat bladder cancer since the late 1970s [1]. Although the mechanism of action is uncertain, it is thought that BCG attaches to tumor cells via the glycoprotein fibronectin. The infected urothelial cells induce an immune response through a host of immune mediators including granulocytes, interleukins, macrophages, and tumor necrosis factor. This leads to local inflammation with subsequent host response directed at the affected tissue and eventual tumor eradication [2].

In immunosuppressed patients, BCG can cause infection and induce a granulomatous reaction in affected tissues similar to non-attenuated TB [1]. Although we are not aware of any concomitant acute illness or specific immunosuppressant in his

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