Letter to the Editor

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Tuberculosis as a complication of BCG immunotherapy in bladder cancer

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Bacillus Calmette-Guérin (BCG) immunotherapy has been widely used for the treatment of bladder cancer. However, tuberculosis-like symptoms have been observed in some patients undergoing this treatment.[1-7] We read the recent manuscript by Hameed et al., describing two cases of tuberculous cystitis developed after the fourth and sixth doses of Bacillus Calmette-Guérin (BCG), and one case of genitourinary miliary tuberculosis after the fifth dose. The patients were 55-, 60- and 68-years old, diagnosed with transitional bladder cell carcinoma (TBCC), and underwent treatment with rifampicin, isoniazid, pyrazinamide, and ethambutol, with good responses obtained within the initial four months of therapy. The authors highlighted intravesical BCG instillation as an adjuvant for bladder cancer treatment and focused on the possibility of local or distant complications, such as orchitis, prostatitis, pneumonitis, hepatitis, sepsis, and hypersensitivity in less than 5% of cases. They commented on recent trans-urethral resections, traumatic bladder catheterizations, macroscopic hematuria, and urinary infections as contraindications for the use of BCG. Moreover, the screening by QuantiFERON TB test, before a BCG vaccine was recommended.[1] In this scenario, some additional data might interest health-care workers on the role of BCG immunotherapy for TBCC and the eventual adverse effects.[2–7]

Berneri *et al*. reported the case of a 74-year-old immunocompetent male with confirmed T11/12 discitis and osteomyelitis, besides an epidural abscess, due to the intravesical instillation of BCG therapy for a recurrent TBCC.[2] The management of BCG infection by treatment with rifampicin, isoniazid, pyrazinamide, ethambutol, and prednisolone, besides surgical decompression and washout with spinal fusion/bone graft were successful.[2] Gözüküçük *et al*. described a 73-year-old man, who had a bladder tumor treated by transurethral resection plus intravesical instillations of BCG and developed bilateral miliary lung lesions controlled by rifampicin, isoniazid, ethambutol and streptomycin. The authors highlighted the rarity of miliary tuberculosis following BCG immunotherapy, which may constitute a challenging condition, easily misdiagnosed or under detected.[3] Okafor *et al*. emphasized the role of single doses of intravesical BCG immunotherapy to delay and prevent the progression of non-invasive cases of bladder cancer.[4] Shibutani *et al*. reported two cases of BCG urinary tract infections: a 77-year-old male, who had the affected bladder and prostate unsuccessfully treated with rifampicin, isoniazid, and ethambutol, leading to resection of both organs; and an 84-year-old male with ureteral and bladder infections improved by isoniazid, ethambutol, and rifabutin. The authors stressed the rarity both of complications and the need for surgery.[5]

Tominaga *et al*. described a 73-year-old male who had in situ BCG immunotherapy for carcinoma of the bladder and developed a local BCG infection 17 months later. He was treated with rifampicin, isoniazid, and ethambutol with complete cure of the bladder infection; however, bilateral hydronephrosis and a voiding dysfunction persisted. The authors emphasized the finding of this bladder infection a long time after the BCG immunotherapy.[6] Yao *et al*. reported a 64-year-old male who had BCG instillations to treat bladder cancer. This individual temporarily presented with elevated prostate-specific antigen levels associated with the BCG-induced granulomatous prostatitis that developed three months after restarting BCG therapy. After treatment with isoniazid, ethambutol, rifapentine, levofloxacin, and intravesical epirubicin, he became asymptomatic, without tumor recurrence ten months after the diagnosis.[7]

As developing tuberculosis seems to be a possible effect of BCG immunotherapy in bladder cancer, healthcare providers need to make informed decisions by carefully analyzing the risk–benefit ratio of the treatment. Moreover, careful, continuous, and large-scale monitoring of patients with bladder cancer undergoing BCG immunotherapy is further required before generalizing the effects of this therapy.

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