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CASE REPORT

Intravesical Bacillus Calmette–Guérin Therapy for Bladder Carcinoma causing Bilateral Ocular Inflammation

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ABSTRACT

We report two cases of patients, who developed ocular inflammation following intravesical Bacillus Calmette–Guérin (BCG) therapy. This is the first report of such a complication from India. The first patient developed bilateral conjunctivitis and the other developed bilateral conjunctivitis, anterior uveitis, and asymmetric bilateral arthralgia. Both the patients were treated with topical steroid eye drops to which they responded well. The increasing use of intravesical BCG may increase the number of cases of BCG-induced adverse events. The incidence of immune-mediated side effects due to intravesical BCG is very low due to genetic predispositions, such as presence of certain human leukocyte antigen (HLA). The specific associations are not clear and need to be further evaluated. Patients must be warned about this rare, but serious complication. Prompt treatment with local steroids should be started.

Keywords: Bacillus Calmette–Guérin therapy, Bladder carcinoma, Immunotherapy, Reiter syndrome.

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INTRODUCTION

Reactive arthritis (ReA) or Reiter syndrome refers to acute nonpurulent arthritis or tendinitis complicating genitourinary or gastrointestinal infections. The sites of extra-articular involvement are the eyes, mucous membranes, skin, nails, and genitalia. Ocular disease is common, ranging from transient, asymptomatic conjunctivitis to aggressive anterior uveitis.

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Intravesical BCG therapy has been used for the treatment and prophylaxis of carcinoma *in situ* of the urinary bladder and prophylaxis of primary or recurrent papillary tumors. The BCG immunotherapy has been reported to precipitate ReA in 0.5% cases[1] associated with bilateral conjunctivitis with or without anterior uveitis. We report two cases of such rare occurrence of bilateral ocular inflammation post-BCG immunotherapy. This is the first report of such cases from India.

CASE REPORTS

Case 1

A 34-year-old woman with a history of high-grade papillary urothelial carcinoma presented to us with bilateral redness and irritation in both the eyes. She also complained of mild knee joint pain on both sides. Slit lamp examination revealed bilateral conjunctivitis with no uveitis. Rest of the eye examination was normal. Patient had received intravesical BCG therapy 2 days earlier for bladder tumor. This dose was the third dose of the weekly intravesical BCG. About 6 months earlier, the patient had had six courses of weekly intravesical BCG therapy. After that, transurethral resection of the bladder tumor (TURBT) was done. Patient recollected having had an episode of mild redness of both eyes after the fifth cycle, for which she took no treatment, and it resolved completely within a few days.

The patient was given 1-hourly topical steroid eye drops. Two days later, the conjunctivitis was resolving and topical steroids were tapered. The patient received the remaining three cycles of intravesical BCG without any recurrence.

Case 2

A 72-year-old male with a history of high-grade urothelial carcinoma presented to us with bilateral diffuse redness and irritation in both the eyes. He had bilateral asymmetric knee pain. On slit lamp examination, patient had conjunctivitis and nongranulomatous anterior uveitis with grade II cells and flare in both the eyes. Patient had history of undergoing TURBT twice earlier. He was on a 6-week course of weekly intravesical BCG injections. Patient presented to us one day after the fourth dose of intravesical BCG.

The patient was given 1-hourly topical steroid eye drops and oral nonsteroidal anti-inflammatory drugs. The patient showed clinical improvement and topical steroids were tapered. The patient recovered in a few days and completed the remaining two cycles of intravesical BCG immunotherapy without any further complications.

DISCUSSION

Local instillation of BCG, a nonpathogenic strain of *Mycobacterium bovis*, is used for the treatment and prophylaxis of noninvasive bladder cancer.[2] Side effects, including fever, prostatitis, hepatitis, pneumonitis, epididymo orchitis, sepsis, arthritis, and uveitis, have been observed.[3] Endophthalmitis, autoimmune retinopathy, bilateral panuveitis with optic neuritis, after BCG immunotherapy have also been reported. The immune-mediated side effects of intravescical BCG are postulated to be due to antigenic mimicry. T cells recognize mycobacterial antigens and ocular proteins, causing cross-reaction against host ocular antigens and, hence, uveitis.[4,5] This is the most likely explanation in the two reported cases. Systemic dissemination of the microbe causing the arthritis and uveitis in our cases is unlikely because both responded to anti-inflammatory medications.

The incidences of these immune-mediated side effects are very few due to genetic predispositions, such as presence of certain HLAs. Some studies show correlation of a septic arthritis, conjunctivitis, uveitis with HLA-B-27,[6] but, in other studies,[7,8] this correlation was not clear. The role of HLA-B8[2] and HLA-DR4[1] has also been reported. These genetic tests were not done in our patients. The exact role of these HLAs should be studied in the future.

Isoniazid prophylaxis in all patients receiving BCG immunotherapy is not useful due to the low incidence of these side effects, the possible reduction in the antitumor effect, and the lack of evidence that uveitis in these cases is due to systemic dissemination of the microbe.[3] Topical anti-inflammatory drugs are the mainstay of treatment in these cases. Ophthalmologists must be aware of this rare possibility and warn patients of this serious complication. This is possibly the first such reported case from India.

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