Case Snippets

Granulomatous hepatitis after intravesical BCG treatment for bladder cancer

Osman Ersoy, Rasit Aran,* Musa Aydinli, Ozlem Yonem, Ozgur Harmanci, Bulent Akdogan,** Ahmet Pinar,* Cenk Sokmensuer,** Yusuf Bayraktar

Departments of Gastroenterology, *Internal Medicine, **Urology, *Clinical Microbiology and **Pathology, Hacettepe University Faculty of Medicine, Ankara, Turkey

Intravesical bacillus Calmette-Guerin (BCG) is used in patients with urinary bladder carcinoma. Although it is generally well tolerated, granulomatous hepatitis is a rare but serious complication. We report a 42-year-old man and a 56-year-old man who developed granulomatous hepatitis following intravesical BCG. One of them was treated successfully with antitubercular therapy; the other died because of BCG sepsis and multi-organ failure. [Indian J Gastroenterol 2006;25:258-259]

The usefulness of intravesical bacillus Calmette-Guerin (BCG) instillation for superficial transitional cell carcinoma has been established in the treatment of carcinoma in situ and in the prevention of recurrence of high-risk superficial tumor. The mechanism by which BCG acts is unknown, but a local granulomatous inflammation, centered on a T-cell-mediated immunity response, is thought to play a role. While the majority of patients tolerate this treatment well, serious complications such as granulomatous prostatitis and pneumonitis have been reported.

Case 1: A 42-year-old man was hospitalized for fever and jaundice. He had undergone transurethral resection for a T1G3 transitional-cell bladder carcinoma one month earlier. Twenty-one days after the resection, the first BCG dose (81 mg) was given intravesically. Hematuria persisted after this treatment. After four days of treatment fever, jaundice and weakness developed. Investigations showed thrombocytopenia and moderate elevation of liver enzymes; abdominal ultrasonography was normal.

On admission his physical examination revealed jaundice, fever (39.5°C), tachycardia, tachypnea, hepatomegaly and splenomegaly. Laboratory findings included pancytopenia and elevated liver enzymes. Viral and autoimmune hepatitis markers were negative. The levels of α1-antitrypsin, ceruloplasmin, serum copper and urinary excretion of copper were normal. Bacterial cultures and viral serology (hepatitis A, B, C, cytomegalovirus, herpes simplex virus, and HIV) were negative. Chest X-ray was normal. Acid-fast bacilli were not seen in urine and sputum; polymerase chain reaction (PCR) of serum for tuberculosis complex that includes both Mycobacterium tuberculosis and M. bovis were also negative.

Liver biopsy histology showed noncaseating granulomatous hepatitis with Langhans’ giant cells (Fig); acid-fast bacilli stain was negative. PCR for M. bovis was negative in the liver tissue. Antitubercular treatment (isoniazid 300 mg/d, rifampin 600 mg/d, ethambutol 1500 mg/d) was started. The clinical and laboratory findings improved; after three weeks, laboratory tests were normal. Antitubercular therapy was completed in six months.

Case 2: A 56-year-old man was admitted with fever and jaundice. He had carcinoma in situ in the urinary bladder since three months. Weekly intravesical instillation of BCG had been performed twice. The day after the second instillation the patient complained of high fever and had been hospitalized. Physical examination revealed hepatomegaly and splenomegaly. Moderately elevated liver enzymes, hyperbilirubinemia, anemia and thrombocytopenia were noted on laboratory results. Cultures for bacterial infection and serologic tests for viral etiology were negative. Abdominal ultrasonography showed hepatomegaly.

The patient’s clinical condition deteriorated progressively and high fever persisted despite empiric antibiotic treatment. Disseminated BCG was suggested and antitubercular therapy with isoniazid (300 mg/d) and rifampin (600 mg/d) was started. Liver histology showed noncaseating granulomas with Langhans’ giant cells. Although acid-fast bacilli were not seen, ethambutol (1200 mg/d) was added to the therapy. PCR for M. bovis was negative in the liver tissue. No clinical improvement was seen. Hypotension developed, high fever (39°C) persisted, liver enzymes remained elevated, and renal function tests deteriorated. Sepsis and multi-organ failure developed, and the patient died 3 weeks following admission.

BCG is a live, attenuated strain of M. bovis that has been used for treatment and prophylaxis of superficial transitional cell carcinoma of the bladder. Intravesical BCG instillation is usually well tolerated. Side-effects may be BCG-specific or of non-specific origin. The specific risks usually occur because the virulence is attenuated but the bacillus is still viable and possesses allergic properties. Systemic side-effects include fever, influenza-like symptoms, malaise and chills, pneumonitis, hepatitis, rash, arthralgia and arthritis, renal abscess, urethral obstruction, cytope-
nia and sepsis. Non-specific risks are those related to retrograde urethral catheterization.

Hematogenous spread of BCG and immunological reactions are the two main mechanisms behind the development of systemic complications.\(^4\) Hematogenous spread through inflamed and/or disrupted urothelium is most frequently caused by traumatic catheterization, bladder perforation, or by extensive tumor resection. These patients respond well to antitubercular regimens. One of our patients developed hematuria during transurethral insertion of the catheter. A hypersensitivity response to \(M. \) \(bovis\) is also important in the pathogenesis of this disease.\(^5\) These patients respond well when corticosteroids are added to the antitubercular treatment. In our patients, peripheral blood cultures were negative for common bacteria and acid-fast bacilli. PCR for tuberculosis complex was negative in serum.

In acutely ill patients triple antituberculous therapy is recommended for 6 months.\(^3\) The use of corticosteroids has risks but the demonstrated absence of organisms in many patients with diffuse granulomas suggests that features may be the result of type IV hypersensitivity reactions.

References


Celiac crisis with hypokalemic paralysis in a young lady

Tarun Gupta, Ameet Mandot, Devendra Desai, Philip Abraham, Anand Joshi

Division of Gastroenterology, P D Hinduja Hospital and Medical Research Center, Mumbai 400 016

Celiac crisis presents as severe acute diarrhea with life-threatening metabolic derangement in a patient with celiac disease. We report a 30-year-old lady who was admitted with one-month history of worsening small bowel-type diarrhea. She developed acute quadriapresis due to refractory hypokalemia. Celiac disease was diagnosed on the basis of positive serology and histological features. She improved with aggressive correction of hypokalemia and gluten-free diet. Celiac crisis is a rare presentation of this heterogeneous disease in adulthood. [\textit{Indian J Gastroenterol} 2006;25:259-260]