LETTERS

Bacillus Calmette-Guerin cystitis after intravesical therapy

Dear Editor,

Since 1976 Bacillus Calmette-Guerin (an attenuated form of wild type *Mycobacterium bovis*; BCG) has been extensively used for the treatment of superficial bladder cancer. It is a safe and well tolerated treatment with rare adverse events including allergic reactions, granoulomatous prostitidis or epididymo-orchitis, disseminated infection and BCG sepsis[1]. Although cystitis is not an uncommon adverse effect, isolation and identification of *Mycobacterium bovis* BCG as its causative agent is very rare, requiring molecular techniques[2,3].

A 61-yr-old male patient presented at our hospital with a fever of 39 ^{o}C and dysuria lasting for 5 days. All routine baseline examinations including urine culture for common bacteria were negative. By the time of admission the patient had not AIDS or any other immune deficiency. The patient had been treated fourteen months ago with intravesical BCG instillation following bladder cancer resection. He had received 4 rounds of treatment each one consisting of a weekly intravesical BCG injection for six weeks. No prophylactic isoniazid had been given during his BCG instillation treatment. The last round was 8 months prior to his admission to our hospital. Urine sample for acid-fast staining and mycobacterial cultures was obtained. It was treated according to standard procedures[4]. A Lowenstein–Jensen slant (bioMérieux, Marcy l' Etoile, France) was used for solid culture and the BACTET MGIT 960 Automated System (Becton Dickinson Biosciences, Sparks, Md.) was used for liquid culture and susceptibility testing at 37^{o}C. Acid-fast staining was negative. The liquid culture turned positive 8 days later [and the solid culture 12 days]. The isolate was identified as member of the *M. tuberculosis* complex with gene probes [AccuProbe (GenProbe, San-Diego, USA)]. Identification to the species level was achieved with GenoType MTBC (Hain Lifescience, Nehren, Germany), which is a DNA-strip assay for differentiating *Mycobacterium tuberculosis* complex strains. The procedure involves isolation of DNA from cultured material, multiplex amplification with biotinylated primers and reverse hybridization of the single-stranded, biotin-labeled amplicons to membrane-bound probes[5]. The assay was performed according to the manufacturer's instructions, using the reagents provided and Taq DNA polymerase (Qiagen, Hilden, Germany). The isolate was identified as *Mycobacterium bovis* BCG. The isolate was sensitive to isoniazid, rifampin, streptomycin and ethambutol and resistant to pyrazinamide.

The patient was treated with cessation of BCG and triple anti-mycobacterial therapy consisting of rifampin, isoniazid, and ethambutol, for the first three months followed by isoniazid and rifampin for seven months. The patient had clinical improvement on this regimen, supporting the diagnosis. Urine cultures obtained after the second month of anti-mycobacterial therapy were negative for *Mycobacterium bovis*.

Disseminated BCG infections after intravesical instillations are presenting as granulomatous hepatitis or pneumonitis and are very rare[6]. Rarer is the identification of *M. bovis* as the causative agent of these disseminated infections, feasible only with molecular techniques[3]. Cystitis due to *M. bovis* can occur after intravesical BCG instillations. Upon clinical suspicion the BCG therapy should be ceased and appropriate anti-mycobacterial regimen should be administered as soon as possible.

References

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Keywords: BCG, intravesical, urinary bladder cancer, cyctitis, *mycobacterium bovis*, dysuria

Conflict of interest

There is no conflict of interest.

Gerogianni I[1], Neonakis I[2], Petinaki E[2]

[1] Department of Respiratory Medicine
[2] Department of Microbiology, University Hospital of Larissa, Larissa, Greece

Corresponding author: Efi Petinaki, MD, PhD, Associate Professor of Microbiology, Medical School, University of Thessaly, Larissa, Greece, tel: +302413502508, +302413502517, fax: +302413501570, e-mail: petinaki@med.uth.gr