

## Exceptional Case

# Peritoneal tuberculosis presenting as recurrent peritonitis secondary to treatment with intravesical Bacillus Calmette-Guérin in a patient receiving peritoneal dialysis

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### Abstract

Intravesical Bacillus Calmette-Guérin (BCG) is an established treatment for high-risk superficial bladder cancer [Morales A, Eidinger D, Bruce AW. Intracavitary Bacillus Calmette-Guérin in the treatment of superficial bladder tumors. *J Urol* 2002; 167: 891–893, Lamm DL, van der Meijden APM, Morales A *et al.* Incidence and treatment of complications of Bacillus Calmette-Guérin intravesical therapy in superficial bladder cancer. *J Urol* 1992; 147: 596–600]. We describe a patient receiving peritoneal dialysis (PD), who developed peritoneal tuberculosis following treatment of bladder cancer with intravesical BCG instillations. To the best of our knowledge, this is the first case of peritoneal tuberculosis following intravesical BCG treatment in which the mycobacterium has been typed and confirmed as a BCG strain with genetic analysis.

**Keywords:** intravesical BCG; peritoneal dialysis; peritoneal tuberculosis

### Introduction

Intravesical BCG is a well-recognised treatment for high-risk superficial bladder cancer [1, 2] and is generally well tolerated. However various local and systemic adverse effects are reported including cystitis [2], isolated renal tuberculosis [3] and multi-organ failure [4]. Diagnosis of peritoneal tuberculosis poses a significant challenge to clinicians especially in patients receiving peritoneal dialysis (PD) and a high degree of clinical suspicion is essential to make the diagnosis [4]. Diagnosis is challenging due to its indolent nature, variability in presentation and inconsistent pattern of sensitivity of various diagnostic tests especially in context of renal failure.

We present a case of an elderly man receiving PD for End Stage Renal Failure and a past history of bladder cancer treated by intravesical BCG instillations. He developed recurrent PD peritonitis and was treated with standard intraperitoneal antibiotics twice before a diagnosis of peritoneal tuberculosis was suspected. This was confirmed by peritoneal fluid analysis and the isolate was identified as BCG strain.

### Case

An 86-year-old male patient with a past history of muscle-invasive bladder cancer diagnosed in 2000 was treated with external beam radiotherapy and transurethral

resection of the bladder tumour. He was then followed up with 6-monthly surveillance flexible cystoscopies. A recurrence of his bladder tumour in November 2007 staged as carcinoma *in situ* and was treated with standard six instillations of intravesical BCG. The final BCG therapy was given in May 2008.

His renal function deteriorated during the course of urology follow-up to a creatinine of 310  $\mu\text{mol/L}$  and an estimated glomerular filtration rate of 17 mL/min/1.73 m<sup>2</sup> and a renal ultrasound showed moderate left hydronephrosis and severe chronic hydronephrosis of atrophic right. Left hydronephrosis was related to recurrence of bladder cancer and was not evident on previous imaging. He had bilateral ureteric stents inserted and was referred to the renal team. His renal function continued to decline and he was started on continuous ambulatory PD (CAPD) in July 2009.

In December 2010, he presented acutely with abdominal pain, fever and cloudy dialysis bags. Microscopy of his CAPD fluid showed  $400 \times 10^6/\text{L}$  of polymorphs with no lymphocytes and no growth on culture. He was treated for PD peritonitis with standard intraperitoneal vancomycin and gentamicin. Clinically, he made a recovery and was discharged home only to present again 1 month later with similar symptoms. On this occasion his CAPD fluid showed  $130 \times 10^6/\text{L}$  polymorphs,  $28 \times 10^6/\text{L}$  lymphocytes and again no growth on standard culture. He recovered after receiving a further course of intraperitoneal vancomycin and gentamicin. He re-presented a month later with septic shock and cloudy bags. Standard blood, urine and

PD fluid cultures were all negative. Due to the recurrent nature of his peritonitis, his CAPD fluid was sent for acid- and alkali-fast bacilli, which was positive. His Tenckhoff PD catheter was therefore removed and peritoneal tuberculosis was confirmed by extended culture of CAPD fluid. The isolate was later identified as BCG strain by genetic analysis (using Hain GenoQuick® technology) at the regional public health laboratory (Birmingham, UK). A cytology of PD fluid was not performed. Computed tomography scan of the chest, abdomen and pelvis did not reveal any evidence of disseminated tuberculosis or lymphadenopathy.

His renal replacement therapy was changed to in-centre haemodialysis and he was started on anti-tuberculosis medications. He was commenced on Rifater (rifampicin 120 mg, isoniazid 50 mg and pyrazinamide 300 mg) five tablets and ethambutol 300 mg daily for 6 weeks before switching to Rifinah (rifampicin 300 mg and isoniazid 150 mg) two tablets daily prescribed for a further 11 months. He received pyridoxine throughout his treatment. He had no further episodes of peritonitis during his treatment but died from withdrawal of haemodialysis 4.5 months after presentation with tuberculous (TB) peritonitis.

## Discussion

Intravesical use of BCG to treat high-risk superficial bladder cancer was introduced by Morales *et al.* in 1976 [1] and has widely been used since. BCG is thought to produce an anti-tumour effect via modulation of T-cell immunity and at the same time exerts a local inflammatory response. BCG is associated with both local and systemic side effects. Local side effects are common and are usually a result of BCG-induced local inflammation or contamination of urinary tract and include visible haematuria, cystitis, granulomatous prostatitis and isolated renal abscess. Systemic side effects vary from malaise and flu-like symptoms to life-threatening sepsis and include fever >38°C, pneumonitis, granulomatous hepatitis, mycotic aneurysm and peritonitis consistent with development of pulmonary or extra-pulmonary tuberculosis [3].

Peritoneal tuberculosis is an uncommon site of extra-pulmonary infection. The risk is increased in patients who are immunosuppressed and in patients undergoing CAPD. An HIV test was not performed in our patient, as his risk was deemed low. In our patient, the mechanism of infection is unclear; however, it has previously been theorized that PD may increase the risk of peritonitis due to direct inoculation or bacterial translocation [3].

The majority of patients will have lymphocytic ascites; however, in patients on CAPD there tends to be a neutrophilic response as seen in our patient. The protein content of the fluid is usually >30 g/L and the serum ascites albumin gradient is <11 g/L. Although normochromic normocytic anaemia and raised C-reactive protein are common, routine laboratory and radiologic investigations are non-specific and do not help in confirmation of diagnosis [4, 5].

The gold standard for diagnosis is growth of mycobacterium on ascitic fluid or peritoneal biopsy but peritoneal fluid culture may take several weeks. Microbiological analysis and Ziehl-Neelsen staining of the ascitic fluid for acid fast bacilli is positive in only ~0–6% of cases with proven peritoneal tuberculosis [4].

Mycobacterium tuberculosis DNA detection in peritoneal fluid by nucleic acid amplification using real-time polymerase chain reaction testing can provide rapid results with sensitivity reaching up to 95% in smear-positive patients; however, sensitivity falls to 48% in smear-negative patients. Various studies recommend laparoscopy as a diagnostic tool of choice for visual and histological diagnosis and confirmation of abdominal and peritoneal tuberculosis [5].

The best treatment option for peritoneal tuberculosis following BCG therapy is not known. Therefore, the treatment regimens are based upon the same principles as pulmonary tuberculosis. The prognosis is variable and mortality ranges from 8 to 50%. Factors predicting poor prognosis include older age, a delay in treatment and comorbidities [4].

## Conclusions

TB peritonitis should be considered as a differential diagnosis in any patient presenting with several weeks of abdominal pain, ascites, fever and weight loss [3]. Renal physicians and urological surgeons providing care for patients receiving CAPD and concurrent bladder cancer should discuss potential risks of TB peritonitis associated with intravesical BCG treatment. Where possible an alternative treatment for bladder cancer should be sought.

*Conflict of interest statement.* None declared. This clinical report has not been presented or published previously in either an abstract format or in whole or part.

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*Received for publication: 5.6.14; Accepted in revised form: 8.12.14*