Complication of treatment of carcinoma in situ of the bladder with photodynamic targeted cystodiathermy

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ABSTRACT

We report two cases of bladder contracture following photodynamic or 'blue light' detection and cystodiathermy for bladder carcinoma in situ. These patients were unsuitable for treatment with immunotherapy/chemotherapy or had disease recurrence following such treatment. Radical cystectomy was not a treatment option in either patient. Each underwent serial photodynamic cystodiathermy over a three-year period. Neither patient developed muscle invasive disease. However, treatment resulted in contracture of the bladder and incontinence of urine. Patients need to be fully aware of this potential complication in order to make informed choices about their care.

KEYWORDS

Photodynamic – Cystodiathermy – Bladder – Carcinoma in situ

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Case 1

This patient was a 75-year-old man with frank haematuria who was found to have a diagnosis of carcinoma in situ (CIS) on biopsy following suspicious urine cytology. Relevant medical history included idiopathic thrombocytopenia purpura, a prior splenectomy, three previous deep vein thromboses, and an unspecified vasculitis requiring immunosuppression with azathioprine and prednisolone. Intravesical bacillus Calmette–Guérin (BCG) or mitomycin therapies were contraindicated owing to his immunosuppressed status and history of thrombocytopenia. His premorbid state deemed him an unsuitable candidate for a radical cystectomy. Following initial resection, he underwent blue light guided cystodiathermy ablation of fluorescent areas on a six-monthly basis. Between May 2007 and March 2010, six such procedures were carried out, following which he complained of urinary incontinence. He was found to have developed a shrunken, poorly compliant bladder thought to be a consequence of repeated resections and cystodiathermy with subsequent scarring.

Case 2

This patient was a 75-year-old woman with a previous diagnosis of G2 pT1 bladder cancer who was found to have CIS on routine follow-up cystoscopy. She was treated with an initial six-dose course of BCG. Nevertheless, two years later she was found to have recurrence of CIS and was offered a radical cystectomy. She was not keen on surgical

intervention and instead opted for further treatment with a combination of intravesical BCG and interferon. Further disease recurrence was found after a two-year interval and, at this point, surveillance blue light cystoscopies with cystodiathermy were decided on as the most appropriate management strategy. Between March 2009 and March 2012, she had six such interventions. Prior to cystodiathermy, she had satisfactory bladder capacity evidenced by normal voided volumes. However, as in the previous case, she developed incontinence of urine with a poorly compliant bladder on urodynamic studies with a 150ml capacity.

Discussion

Approximately 75–85% of bladder cancers present with disease that is confined to the mucosa (stage Ta, CIS) or sub-mucosa (stage T1).¹ These categories are grouped as non-muscle invasive bladder tumours. CIS, which accounts for about 5% of these,² is a flat, high grade, non-invasive urothelial carcinoma. Histologically, CIS is an overtly malignant entity in itself that is frequently a precursor of muscle invasive disease. When found in isolation or in the presence of Ta/T1 disease, currently recommended strategies subsequent to transurethral resection include intravesical immunotherapy (eg BCG therapy), intravesical chemotherapy (eg epirubicin) or indeed radical cystectomy.²

Without any treatment, approximately 54% of patients with CIS progress to muscle invasive disease.³ This highlights the importance of early diagnosis and subsequent

treatment. A problematic issue is the often elusive nature of CIS to the observer's eye under white light cystoscopic conditions. Macroscopically, CIS can be missed at cystoscopy or it can be considered an inflammatory lesion if it is not biopsied.⁴ As such, a relatively new technique to aid the visualisation of tumours was developed: so called 'blue light' or fluorescence guided cystoscopy.⁵ Intravesical administration of 5-aminolaevulinic acid or the newer hexaminolaevulinate (commercially known as Hexvix® [Photocure, Oslo, Norway]) prior to cystoscopy aids the identification of abnormal cells, which fluoresce under blue light examination. Hexvix® is converted to the photoactive protoporphyrin IX, which is known to accumulate selectively in rapidly proliferating cells. Protoporphyrin IX fluoresces red under blue light, thereby allowing abnormal cells to be more easily identified by the surgeon.⁶

We explored the use of blue light cystoscopic treatment of patients in whom intravesical immunotherapy and chemotherapy was contraindicated or unsuccessful and in whom radical cystectomy was not an option. Our experience highlights the potential complication of bladder contracture with repeated cystodiathermy, and suggests that the role of blue light cystoscopy in long-term follow-up and treatment of CIS with cystodiathermy is not without problems. Of note, however, is the absence of disease progression in either patient.

Those patients opting electively against radical cystectomy need to be made aware of this complication if deciding on surveillance cystodiathermy. Difficulty arises when a patient is deemed unfit for a radical cystectomy on medical

grounds and has failed intravesical immunotherapy or chemotherapy. These patients have limited treatment options and surveillance photodynamic cystodiathermy may be considered a viable option. In such cases, the best patient is one fully forewarned of the potential complications and resulting impact on their quality of life.

Conclusions

Photodynamic 'blue light' cystoscopy has a key role in initial detection of CIS. The employment of surveillance photodynamic cystodiathermy where disease recurrence is apparent can be limited by the development of bladder contracture. Patients need to be fully aware of this complication in order to make informed choices about their care.

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