Case Report

Vesical Endometriosis in a Male Patient on Treatment for Papillary Urothelial Carcinoma

Abstract

Endometriosis denotes the abnormal growth of tissue resembling endometrium in ectopic sites and has largely been studied in women of reproductive age. It is an extremely rare phenomenon in men. We came across an exceptional clinical scenario of histologically proven bladder endometriosis in a 66-year-old man in relook bladder biopsy following completion of adjuvant intravesical Bacillus Calmette-Guerin induction course for G3pTa bladder cancer. We have pencilled down pathophysiology and commonly seen predisposing factors for "endometriosis in male patients" from available case reports and applied those findings to hypothesise the disease profile of our patient in this case report.

Keywords: *Bladder endometriosis, finasteride, high circulating oestrogen level, intravesical BCG, men, steroid*

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Introduction

Although the topic of endometriosis has garnered numerous clinical studies and research mostly in women to find out the causative factor, its precise aetiology is unknown.[1] Even less is discussed about the number of men who have undiagnosed and unreported endometriosis because of the rarity of such occurrences. A total of only 16 cases were previously reported in the literature, and in majority of the cases, the disease was present in the genitourinary tract.[2] Risk stratification from previous case reports suggests that increased serum oestrogen in men with liver cirrhosis, high body mass index, or prostate cancer treated with long-term oestrogen therapy could promote endometriosis in men. As our patient did not have any of the aforementioned risk factors, we, herein, investigated his demographic feature, medical and medication history, and relevant personal history to identify "unexampled" potential risk factors to explain such orphan disease.

Case Presentation

We are presenting a 66-year-old man who was referred from the primary care centre to us with one episode of visible haematuria and lower urinary tract symptoms. Computed tomography (CT) urogram reported a clear upper renal tract. His past medical history includes chronic plaque psoriasis, panproctocolectomy and ileo and jejunal pouch formation in 1996 for ulcerative colitis. His regular medications include rivaroxaban for Atrial fibrillation and amlodipine, and doxazosin for hypertension. He started taking finasteride and tamsulosin (in addition to Doxazosin) 6 weeks before his clinic appointment with us. Following visual confirmation of 12 papillary tumours around bladder neck and trigone ranging from 0.3 to 3 cm in size by flexible cystoscopy, he underwent elective, complete, primary transurethral resection of bladder tumour (TURBT). Histopathology revealed papillary urothelial carcinoma, G3pTa. As per local policy for high-grade non-muscle invasive bladder cancer, first relook TURBT after 6 weeks of primary TURBT was performed reporting benign histology. As there was no upstaging of disease, he then had weekly induction of intravesical Bacillus Calmette-Guerin (BCG) for 6 weeks. Rigid cystoscopy after 3 weeks of the last BCG instillation revealed a 3 mm superficial, papillary urothelial lesion close to the left ureteric orifice, and biopsy was taken. Interestingly, the histopathology showed features of endometrium (both endometrial gland and stroma), which

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was confirmed with stroma), which was confirmed with immunostains—stroma was positive for CD 10 and ER immunostains, glands were positive for CK7 and ER immunostains, and no transitional epithelium was seen [Figures 1-4]. Endoscopic view of the lesion was not suspicious for endometriosis.

His surveillance CT scans and 3 monthly cystoscopies did not show any macroscopic recurrence of urothelial or endometriosis-like lesions. He continued with BCG maintenance therapy (3-weekly instillations at 3, 6, 12, 18, 24, and 30 months after initial BCG treatment) as per our local guidelines for high-grade bladder tumours. His oestradiol and testosterone levels on follow-up blood tests appeared within normal range.

Discussion

Many theories relating to the aetiology of endometriosis have been proposed. These hypotheses have been divided into four groups: transport, coelomic metaplasia, embryonic cell rests, and immunological theories.[2]

"Transportation theory" is suggestive of the implantation and growth of functional endometrial cells on the surrounding pelvic structures and peritoneum. In women, this happens due to retrograde reflux of these cells into these ectopic sites through the fallopian tubes during menstruation. This theory cannot explain the incidence of endometriosis in males because of the absence of menstruation and different anatomy.

Embryonic organogenesis states that the separation between male and female urogenital systems occurs in the embryo between the 8th week and the 4th month. The embryonic cell rests theory postulates the possibility among both sexes, to have some embryonic cell rests from the opposite sex while this division takes place. The Mullerian duct, which primarily forms female reproductive systems, usually regresses in male foetus under the influence of anti-Mulleian hormone. It is hypothesised that Mullerian cells may persist in men due to incongruous division during foetal life and appropriate unknown exogenous or endogenous biological factors can disrupt the dormancy of cell rests and initiate dedifferentiation of these cells into endometrial cells. The

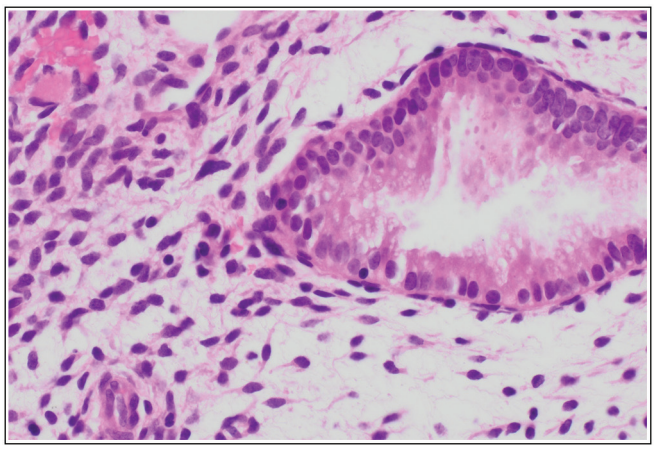

Figure 1: H&E x60: Haematoxylin & Eosin stain, magnification x600 – shows secretory activity in endometrioid gland

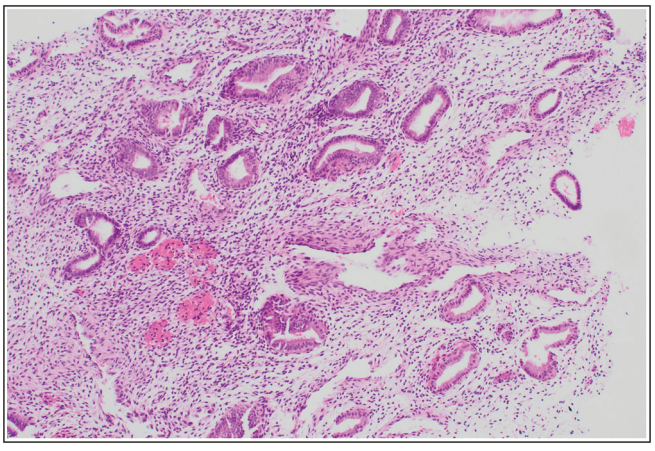

Figure 2: H&E x 10: Haematoxylin & Eosin stain, magnification x100 – shows typical features of endometrioid stroma and glands

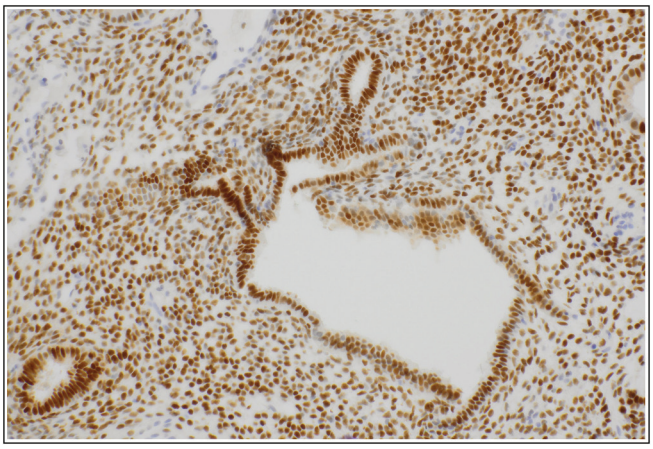

Figure 3: ER: Immunohistochemistry for ER stains the endometrioid glands and stroma (nuclear positivity)

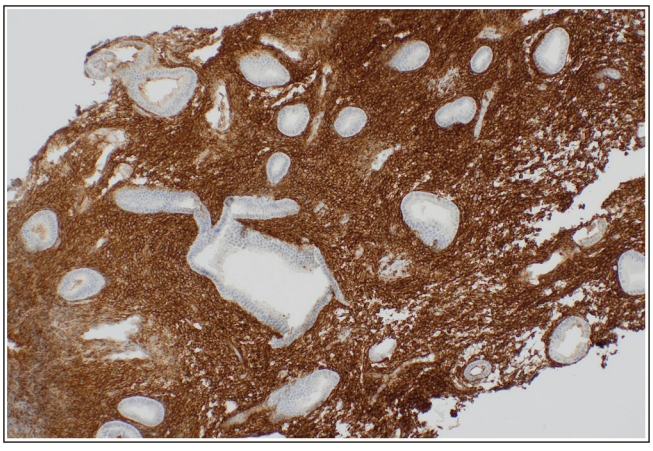

Figure 4: CD10: Immunohistochemistry for CD10 stains the endometrioid stroma

coelomic epithelium metaplasia theory states that, under the influence of inflammatory and hormonal influences, peritoneal mesothelium cellular adaptation happens, which can transform the mesothelial cells into endometrial-like tissue.[2,3]

The possibility of the development and progression of endometriosis secondary to impairment of natural internal protective mechanisms of the human body (cell-mediated and hormonal immunity) gained popularity over the past 25–30 years. Whether this immunological factor is an isolated cause or a synergistic factor to one or more of the other causes is yet to be determined.[4]

In contrast to previously observed influencing factors, our patient was very slim and neither had liver cirrhosis nor prostate cancer. Despite his being treated with steroid hormones around 20 years ago before having major bowel resection, these would have been of the inflammatory type rather than sex steroid type, therefore should have no influence. It is possible that alterations in both cell-mediated and humoral immunity due to BCG can cause defects in natural killer cells resulting in a decreased cytotoxicity to endometrial cells, which helps them to evade the normal body defence mechanisms and, as a result, implant and grow more easily in ectopic sites. However, we sordidly realise that its immunologic side effects from those few doses, within such a short time, leading to the manifestation of such a rare condition may be difficult to explain.

Another less likely but possible risk factor-Finasteride is known to cause antiandrogenic and oestrogenic effects. Oestrogen has mutagenic and carcinogenic potential and its high serum concentration in men is believed to induce malignancy (e.g., breast cancer) by causing cell proliferation.[5-7] Can finasteride induce similar metaplasia of embryonic rest cells to promote endometriosis in our patient? There is no such case in the literature and hard to expound considering the short duration of finasteride intake (5 months) before the diagnosis and normal oestradiol estimation.

Conclusion

Although we accept the fact that a robust conclusion can not be drawn based on our findings, we hope our case report will be thought-provoking and usher the window of future research for more answers.

Authors' contribution

PKS researched literature and conceived the study. MK provided histological pictures for the case report. ES was in charge for the case report. All authors reviewed and edited the manuscript and approved the final version of the manuscript.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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