Urethral Carcinoma in a Urethral Diverticulum, a Rare Presentation of Post-Menopausal Bleeding: A Short Case Report and Review

Primary carcinoma of the female urethra is rare [1-3]. It accounts for 0.02% of all female malignancies [4,5]. It can occur in urethral diverticulum but only ~100 cases have been reported [1]. This case report from a regional area of Australia details just the second case occurring in Australia. It is important for both general practitioners and gynaecologists to be aware of symptoms and vigilant on examination, as best prognosis relies on early detection.

A 58-year-old woman presented to a gynaecologist with post-menopausal bleeding and abnormal ultrasound findings. Hysteroscopic examination was unsuccessful as safe cervical dilatation was not possible. Clinical examination by a second gynaecologist diagnosed urethral bleeding and she was referred for urological opinion. Initial urological examination was unremarkable, as was the subsequent CT urogram and flexible cystoscopy. On discharge back to her gynaecologist a routine elective total hysterectomy was performed. Histopathology from the procedure revealed a benign endometrial polyp and chronic follicular salpingitis.

Further cystoscopy was performed due to repeat presentation of macroscopic haematuria five months after the initial presentation, and this time a palpable mass originating from the urethra was detected. A clear cell adenocarcinoma of the urethra which appeared to lie within a wide necked urethral diverticulum was confirmed on biopsy.

MRI demonstrated a localized 2.4x2.7x2.0 cm mass, 1.5 cm distal to the bladder neck, suspicious for urethral malignancy.

The patient was given surgical management options and counselled towards a radical urethrectomy with mitrofanov bladder drainage. She declined in favour of a partial urethrectomy despite concerns over long-term continence. A partial urethrectomy and

*Corresponding author: Corrine Lu, MBBS, Resident Medical Officer, Albury Wodonga Health, Australia, E-mail: corrine.lu@trainee.ranzcog.edu.au
neomeatoplasty was performed. Final histopathology confirmed a clear cell adenocarcinoma lying within a urethral diverticulum. The tumor infiltrated to a depth of 1.5 mm into the stroma, however the resection margins were clear. The patient remains clinically and radiologically disease free at 12 months, with social continence (Figure 1).

**Discussion**

This case report details a patient presentation in a regional facility. Such a presentation at any facility is rare; even more so in a regional area. We reviewed case reports in the literature to quantify occurrence and discuss what is known on etiology and management. Using search terms of ‘clear cell adenocarcinoma in/or and urethral diverticulum’ we searched PubMed, Medline, Cochrane library, Embase, Google Scholar, Up-to-date and reference lists of articles found. We limited literature to articles from 1995 - 2015.

**Incidence**

Approximately 100 cases of carcinoma arising from a diverticulum in the urethra are described in case reports [2,6]. Hamilton and Leach first described the occurrence in 1951 [7]. Adenocarcinoma of the urethra accounts for about 10% of female urethral carcinomas [8]. The incidence of clear cell adenocarcinoma lies at about ten percent of these cases [8-12], although the true incidence may be higher according to data from the SEER database in the USA (United States Surveillance, Epidemiology and End Results database) [10]. Clear cell adenocarcinoma of the urethra occurs in women four times more commonly than in men [5]. The reported incidence amongst different ethnicities is inconsistent but likely to be higher in Afro-American and Asian population groups [1-3]. The histogenesis of carcinomas found in the lower urinary tract of women is widely debated and a consensus has not been established [8].

**Etiology**

The female urethra is lined with blind crypts; the remnants of the embryonic prostatic structure [9]. Histologically, the proximal third is lined with transitional epithelium and the distal two-thirds are lined with stratified squamous cells [10]. This differentiates the type of neoplasm forming is each location. Clear cell adenocarcinoma of the urethra is commonly found in the proximal third of the urethra [10] where transitional epithelium is located.

Urethral diverticulum development in women is reported to be an acquired phenomenon, with a likely associated history of obstructed per urethral glands and localized resultant inflammation, cystic dilatation and abscess formation [2,6]. It is thought that possible causes are linked to localized trauma from childbirth, urethral calculi, stricture formation or repetitive catheterization [2,6]. The exact histogenesis of clear cell adenocarcinoma of the lower urinary tract is unknown [11]. Origins are postulated to be: 1) mullerian 2) glandular differentiation of epithelium (urothelial carcinoma) or 3) a unique vesicular adenocarcinoma of nonmullerian origin [8,12].

Clear cell adenocarcinoma typically display three typical cell patterns: diffuse, papillary and tubocystic [12]. They may display a histological variation in cell pattern ranging from flat, cuboidal or hobnail structure with a varying degree of cytoplasmic clearance [12,13]. There may also be associated nuclear pleomorphism with necrosis and mitotic activity [12].

**Clinical features of presentation**

The classic presentation of urethral diverticulum is a symptom triad of post-void urinary dribbling, dyspareunia and dysuria [9]. The most common presentation of clear cell adenocarcinoma of the urethra, including in urethral diverticulum, is haematuria [2,3]. Other symptoms are common to that of urethral diverticulae: dysuria, frequency, incontinence, recurrent cystitis, vaginal pain and dyspareunia or the sensation of a vaginal mass [1,3,9]. Recurrent haematuria should be investigated further to exclude malignancy [9]. According to Davis, et al. [14], about 18% of adults with gross haematuria, initially found to be clear, will progress to a finding of malignancy. This underlines the importance of further investigation for persistent haematuria.

**Investigations**

Clinical investigations include: urinanalysis, urine cytology, and cystoscopy [2]. Imaging may include trans-vaginal ultrasound, urogram, voiding cysto-urethrogram, CT-intravenous pyelogram or more optimally MRI [1,2,9].

**Management**

Management of clear cell adenocarcinoma of the urethra varies in the literature. There are no large trials due to the rarity of the cancer itself. Surgery is the primary mode of management in almost all cases. This may include local excision for smaller tumours right through to anterior exenteration for larger tumours [1,6]. More proximal tumours tend not to be suitable for conservative surgery as surgery in this area has a significant impact on continence. Typically post-treatment surveillance is conducted three-six monthly for the first two years from diagnosis and treatment [8].

**Conclusion**

Urethral carcinoma is very rare. This case illustrates the importance of persistence in the investigation of recurrent haematuria and the need for caution when assuming bleeding from the vagina is of a gynecologic cause. This case was complicated by concurrent ureteral and urethral bleeding and a delayed diagnosis as no pathology was visualized at the initial cystoscopy.

**References**


