Urothelial papilloma of the urethra: A case report and review on its histopathological mimickers

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Abstract

Urethral neoplasms are relatively rare, considering the diversity of pathological diseases in the urethral region. From the perspective of a urologist or a pathologist, benign urethral lesions may mimic cancer. However, due to the rarity of urethral neoplasms, it can be challenging to finalise the definitive diagnosis. We presented the case of a 53-year-old gentleman, a chronic smoker with a history of painless haematuria for three weeks associated with incomplete voiding and urinary frequency. Cystoscopy revealed fluffy, polypoid tissues over the prostatic urethra. Clinically, urothelial carcinoma cannot be excluded. Interestingly, the histopathological assessment revealed a case of urothelial papilloma. An illustration of the diagnostic approach based on solitary polypoid lesions and papillary neoplasms from the urethra was elaborated. The salient features of each disease spectrum were also highlighted. A pathological approach in conjunction with clinical and radiological findings may help correctly recognise urethral pathology.

Keywords

Haematuria, urethral neoplasms, papilloma, polyp
Introduction

The diversity of the disease spectrum on the urothelial pathology of the ureter, bladder, and urethra is frequently discussed collectively. In contrast, specific primary neoplasms originating from the urethra are not well elaborated in the literature due to rare incidences [1]. However, the epithelial tumours of the urinary bladder are among the ten most common neoplasms reported in the adult population. On the other hand, it is extremely rare in children [2]. Although it can affect both genders, men are more likely to be affected. The average age of diagnosis is 73 years old [1]. Depending on the nature of the disease, the presentation can range from asymptomatic to various urological symptoms such as haematuria, lower urinary tract symptoms (LUTs), abdominal pain, abdominal distension, fever, and constitutional symptoms. The disease’s rarity makes it challenging for pathologists to establish a definitive diagnosis. We presented a case of a patient with urothelial papilloma of the urethra. The diagnostic and pathological approach to the case is discussed in our report.

Case report

A 53-year-old man who was a chronic smoker with a history of infective endocarditis presented with painless haematuria, incomplete voiding, and urinary frequency for three weeks. On physical examination, there was no abdominal pain, distension, fever, or constitutional symptoms. Cystoscopy revealed fluffy polypoid tissues over the prostatic urethra. No urethral stricture or bladder abnormalities were detected. He underwent an excisional biopsy of the urethral lesion, and the tissue was sent for histopathological evaluation (HPE). Macroscopically, it consisted of three small fragments of brownish tissue measuring 0.5x0.5x0.5 mm, 1x1x1 mm, and 1x1x1 mm. Polypoid tissue with a fibrovascular core surrounded by multiple papillary projections on the surface was visualised microscopically. The papillary projections were lined by a normal thickness of urothelial cells, and the arrangement between the urothelial cells and umbrella cells was well-preserved. No mitosis, cytology atypia, or dysplasia was identified (Figure 1). Post-diagnostic excision of this polypoid-like urethral lesion was performed. The patient’s symptoms were relieved, and he was discharged well.

Written informed consent was obtained from the patient for the publication of this case report and the use of all accompanying images.

Figure 1: (A) Polypoid tissue with multiple papillary projections (H&E, 40X) (B) Fibrovascular stroma (arrowhead), lined by the normal thickness of urothelial cells (H&E, 200X).
Discussion
The discovery of solitary polypoid lesions from the urethra indicates a potential array of differential diagnoses, either non-neoplastic (fibroepithelial polyp, polypoid-papillary urethritis, or prostatic-type polyp) or neoplastic (urothelial papilloma, squamous papilloma, papillary urothelial neoplasm of low malignant potential, or non-invasive papillary carcinoma) in origin [1,3,4]. Furthermore, in this patient, his symptoms also overlapped with other pathological conditions of the genitourinary system. The cystoscopy gave an overview of the gross appearance and the site of the lesion. The microscopic findings from HPE revealed a polypoid lesion exhibiting a fibrovascular core with true papillary projections covered by an unremarkable normal appearing urothelium. The findings were suggestive of the diagnosis of urothelial papilloma. Urothelial papilloma generally manifests as a benign, small, and solitary exophytic lesion with papillary projections [5]. The urothelium overlying the lesion shows normal thickness, preserved umbrella cells, and no signs of cell atypia. Small congested capillaries are also seen within the papillae [3,4]. These salient features were all observed in this case.

Based on the WHO 2016 Genitourinary Tumours Classification, urothelial papilloma is regarded as a benign neoplastic tumour. It is extremely rare and commonly affects the proximal portion of the urethra [6]. Recurrence and malignant transformation of this tumour are relatively rare upon complete excision [5,7]. Given the rarity of urothelial papilloma, excluding other common non-neoplastic lesions should be considered during diagnosis. For instance, urethral fibroepithelial polyps are benign tumours that occur at the proximal ureter and ureteropelvic junction. In some cases, the formation of larger polyps may extend into the bladder cavity [8], thus mimicking urothelial papilloma. However, urethral fibroepithelial polyps are more common. It usually affects younger age groups in the first two decades of life, particularly neonates with a history of congenital urethral wall defect [4]. The lesion size could increase and cause torsion of the stalk and give rise to the clinical symptom of haematuria [9]. Morphologically, fibroepithelial polyps exhibit finger-like projections resembling papillae of the abundant dense stroma instead of true branching of papillary structures [4].

Another differential diagnosis of urothelial papilloma is polypoid-papillary urethritis. However, due to chronic irritation to the urethra, such as instrumentation or trauma, polypoid-papillary urethritis often manifests in significant stromal oedema or inflammatory infiltrates. These inflammatory processes may cause urothelial hyperplasia or regenerative urothelium in some cases, but true dysplasia, such as those in urothelial papilloma is typically infrequent [5].

In addition, the prostatic-type polyp differs from the urothelial papilloma in terms of the papillary fronds or irregular filiform stalk projections on the benign prostatic-type epithelium. On the other hand, the intermixture of prostatic-type epithelium with urothelium is uncommon [4]. This lesion typically affects the periurethral region.

Identifying neoplastic lesions is crucial as it affects the patient’s management and prognosis. Another benign neoplastic condition mimicking urothelial papilloma is squamous papilloma. As the name implies, squamous papilloma can manifest as a polypoid lesion with papillary architecture. However, it is lined by mature squamous cell epithelium. It is more common in females and is sometimes associated with Human Papilloma Virus (HPV) infection [4]. Contrary to the urothelial or squamous papilloma, if the papillary proliferation of squamous epithelium with hyperkeratosis and koilocytosis is observed, the condition is known as urethral condyloma. HPV 6, 11, and less frequently, 16 and 18, can be detected in these cases [9].

Other than malignant urothelium, prostatic carcinoma must also be excluded [5]. The morphological distinction between urothelial papilloma and exophytic urothelial carcinoma may not be straightforward in selected cases. In both non-invasive and infiltrating urothelial carcinomas, the features that should be present are cytologic atypia, nuclear pleomorphism, irregular nuclear membranes, mitoses, or necrosis. Additionally, areas of invasion or lymphovascular permeation could be visualised in the infiltrating type of
urothelial carcinoma \[9\]. To differentiate between urothelial papilloma, papillary urothelial neoplasm of low malignant potential (PUNLMP), low-grade papillary urothelial carcinoma, and high-grade papillary urothelial carcinoma, it is vital to delineate the pattern of papillary architecture, degree of cytologic atypia, cellular polarity, and level of mitotic activity activities within the urothelial thickness \[4,10\].

Although PUNLMPs have delicate papillary architecture and normal cellular polarity, like urothelial papilloma, they tend to have thickened urothelium and minimal cytologic atypia. These main features distinguished them from urothelial papilloma \[9,10\]. Compared to PUNLMPs, low-grade papillary urothelial carcinoma has thickened urothelium and minimal cytologic atypia but more fused papillary branching and minimal loss of polarity. The occasional mitoses are usually limited to the lower half of the urothelium as compared with PUNLMPs \[10\]. More importantly, fused papillae that show a more solid appearance of the exophytic lesion with additional loss of polarity and significant cellular atypia are more typical in high-grade papillary urothelial carcinoma \[1\]. It is crucial to identify invasive components to exclude the invasive type of urothelial carcinoma.

Currently, ancillary tests to distinguish different types of papillary urothelial neoplasms are not recommended for routine investigations as PUNLMP, low-grade papillary urothelial carcinoma, and high-grade papillary urothelial carcinoma all showed the expression of the p53 and Ki67 stains. As for CK-20, it is only helpful in highlighting the presence of the umbrella cells \[10\]. As a result, more advanced molecular studies are imperative to facilitate the exploration of various urethral pathology.

**Conclusion**

The pathology features of urothelial papilloma of the urethra are a great mimicker of other urethral lesions. Thus, recognising the different types of urethral pathology is vital to ensure optimum management for the patient. Overdiagnosis or misdiagnosis can be averted by a systematic clinical, radiological, and pathological investigation approach.

**References**