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Lesions of the Female Urethra: a Review

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Precis: Lesions of the female urethra are reviewed.

Key words: Female, urethral neoplasms, urethral lesions

Abstract:

Objectives:

The female urethra may become involved by a variety of conditions, which may be challenging to providers who treat women. Mass-like urethral lesions need to be distinguished from other lesions arising from the anterior(ventral) vagina.

Methods:

A literature review was conducted. A Medline search was used, using the terms urethral neoplasms, urethral diseases, and female.

Results:

Reported lesions of the urethra were reviewed. Many of these lesions can be mistaken for each other clinically.

Conclusions:

A review of the scope of urethral lesions is presented to assist in developing a differential diagnosis if a patient with a urethral lesion is encountered. For practitioners who care for women, this will encourage communication, and consultation where appropriate.

Introduction:

Numerous conditions, many of which are difficult to clinically differentiate, may affect the female urethra. Mass-like lesions of the urethra need to be distinguished from other lesions arising from the anterior(ventral) vagina(table 1). Aside from a good history and physical examination, imaging studies such as ultrasound, MRI, and voiding cystourethrogram, as well as cystourethroscopy have been utilized. Urologic consultation may be indicated in some cases. A familiarity with these lesions will be helpful if a patient with a urethral lesion is encountered, and facilitate communication and consultation as necessary(Table 2).

Anatomy and histology:

The female urethra is shorter than the male, and is about 4-6 cm long(1). It is lined by transitional epithelium proximally(vesical) while the distal(caudal) and meatal portions are comprised of nonkeratinized squamous epithelium which merges with the vestibular epithelium. Under the epithelium is a very vascular submucosa containing abundant elastic fibers. The urethral lining and submucosa are very estrogen responsive. The urethra has outer smooth muscular layers, varying from 2 distally to 3 proximally, and the distal two thirds of the urethra has a layer of skeletal muscle outside the smooth muscle(2). On either side of the urethra are the Skene's glands. The major ducts drain on either side of the urethral orifice, posterolaterally, however it is also believed that branches of the duct drain directly into the distal urethra. The Skene's glands are thought to be analogous to the male prostate, supported by immunohistochemical staining of prostatic antigens such as prostate specific antigen(PSA).

Congenital and Pediatric Lesions:

A variety of congenital lesions can affect the female urethra, including but not limited to atresia(3), duplication(4), epispadias(5), hypospadias(6), prolapsed ureterocele(7), and persistent urogenital sinus or cloaca(8,9). Some of these children may present with voiding abnormalities and urinary tract infections(6). In addition, urethral polyps, a lesion seen in children, may be congenital(10).

Urethral polyps are more common in males, but do rarely occur in females, and are thought to be congenital, although infection, irritation, obstruction and trauma have also been proposed as etiologies(10,11). A case of a giant urethral polyp in a female newborn was reported, with a large red mass protruding through the labia(10). The infant underwent a voiding cystogram and ultrasound showing normal bladder and kidneys. Subsequent cystoscopy revealed the lesion arising from the posterior(dorsal) urethra, and it was treated with excision. The polyp had a mixed squamous and transitional lining over a mesenchymal core. The authors suggest that this lesion represents a hamartoma. The differential diagnosis of a mass protruding through the labia in a neonate also includes paraurethral cyst, prolapsed ectopic ureterocele, and embryonal rhabdomyosarcoma (sarcoma botryoides)(10). Although generally a pediatric lesion, urethral polyp has been reported in adults, including in a patient with post-coital hematuria(12). Goel et al delineate three architectural patterns to a urethral polyp; polypoid with projections resembling a cloverleaf, florid cystitis cystica/glandularis, and

a polypoid lesion with finger-like projections resembling polypoid cystitis(13). The lesions are lined by transitional or glandular epithelium.

A rhabdomyoma, a benign tumor of skeletal muscle, was described in the urethra of a 7-month-old girl, whose mother noted a protruding mass. Genital rhabdomyomas are rare tumors that can occur on the vulva, vagina or cervix of middle aged women(14). The authors suggest that their case was the first such in the female urethra.

Prolapse of urethra

Urethral prolapse is in the differential diagnosis of a labial mass in a child. Urethral prolapse is more common in African-American girls(7). It is a cause of premenarchal bleeding, and because this may raise a question of abuse, familiarity with this diagnosis is important for providers. Conservative therapy involves topical estrogen and sitz baths. Surgery may be necessary, and histologically, thrombosis may be seen(figure 1). This lesion may also occur in postmenopausal women(15). A rare case was reported in a 39-year-old woman in association with the Valsalva maneuver associated with weight lifting(16). The characteristic donut shape of the protrusion is a clinical clue, helping to distinguish it from other lesions(figure 1)(15).

Urethral strictures and fistulas

Urethral strictures are uncommon in children, and when they do occur, are usually in boys. Urethral strictures in girls may occur after pelvic fracture, and in these cases may be associated with vesico-vaginal or urethrovaginal fistulas(17).

Iatrogenic Lesions:

Female genital mutilation may result in a variety of complications, including urethral injury(18)

Urethral obstruction may occur after surgical treatment for stress incontinence, and has been reported to occur in 5-20% of patients(19).

Inflammatory Lesions

Urethritis

Urethritis may be sexually transmitted. Causative organisms include *N. gonorrhoea*, *Chlamydia trachomatis*, *Ureaplasma urealyticum*, *Trichomonas vaginalis*, and *Herpes simplex*(18). Symptoms include discharge and dysuria, however patients may be asymptomatic. Short-term dysuria in the absence of significant bacteriuria is termed “acute urethral syndrome” and may be associated with gonorrheal and chlamydial infection(18). If the symptomatology of urethral syndrome persists, “chronic urethral syndrome” may

be present. This chronic condition has more recently been termed “urethral pain syndrome”(20). It is comprised of intermittent urethral pain, usually on voiding, in the absence of proven infection. Daytime frequency and nocturia are also associated. Etiology has not been established definitively, but theories include infection/inflammation, interstitial cystitis, neuropathic hypersensitivity, trauma, allergy, spasm, fibrosis or stenosis, hypoestrogenic atrophy, stress, and psychiatric disorders(18,20). Therapy is often trial and error, and has included alpha blockers, laser, acupuncture as well as antibiotics, and psychological support. A multidisciplinary approach is often needed(20).

Other infectious processes

Inflammatory processes characteristic of other locations may rarely occur in the urethra. Vulvar condyloma accuminatum may involve the urethra.

Malakoplakia, a lesion more often seen in the bladder(21) is a mass-like lesion comprised of histiocytes termed Von Hansemann cells. It is thought to be due to incomplete immune response to bacteria, which can be seen in the cells with a PAS stain. Accumulation of calcium occurs, and characteristic targetoid Michaelis-Guttman bodies may be seen in the cytoplasm(figure 2). E. coli is thought to be the most common causative organism(21). Clinically, the patient of Karaiossifidi et al(21) presented with hematuria and a lesion thought to be a caruncle.

Granulomas with central necrosis suggest tuberculosis in the differential diagnosis. Tuberculosis has occurred in the female urethra(22), presenting as a caruncle, periurethral mass, or intraurethral lesion. Necrotizing(caseating) granulomas are seen on histology,

and acid fast bacilli may be identified, often with difficulty, as this is not the most reliable way to confirm tuberculosis.

Rhinosporidiosis, a chronic granulomatous fungal lesion usually occurring in the anterior nares and seen in India and Sri Lanka has been described in the female urethra in two cases(23). Symptoms of the condition can include voiding difficulties, mass, and bleeding. The infection is thought to spread in infected water and soil, commensurate with the rural background of the patients in this series(23).

Inflammatory conditions of non-infectious or unknown etiology

Sarcoid is a granulomatous condition of unknown etiology, usually affecting the lungs. Sarcoidosis of the urethra was described(24) presenting with decreased urinary stream. The 49-year-old patient was thought to have urethral carcinoma, having enlarged groin nodes in addition to her urethral lesion. She had recently been diagnosed with pulmonary sarcoid with characteristic hilar lymphadenopathy. The lesion is characterized by non-necrotizing granulomas negative for stains for microorganisms.

A rare case of a plasma cell granuloma, a rare polyclonal plasma cell proliferation(as opposed to the monoclonal and therefore neoplastic plasmacytoma) producing a mass was described in the urethra of a 21-year-old woman. The lung is the usual location for these lesions(25). A urethral solitary monoclonal plasmacytoma was reported in a 56-year old woman who was treated with simple excision. This is an exceptionally rare presentation of a lesion that usually presents as a bone marrow primary with dissemination, ie multiple myeloma(26).

Calculi

Calculi can occur in association with urethral diverticulum or stricture, but rarely may occur de novo in the urethra, where they can cause pain and obstruction. In the case presented by Thomas et al(27), the obstructing calculus was felt to have descended from the upper urinary tract based on its being composed of calcium oxalate.

Benign tumor-like lesions:

Urethral diverticulum

An often unsuspected lesion, the incidence of urethral diverticulum ranges from 0.6-3% in different series(18). It has been stated that a high index of suspicion is the best diagnostic tool(28). It is thought to arise secondary to rupture of infected periurethral glands into the urethra(29), and some authors feel that the distinction of paraurethral cyst and urethral diverticulum as two separate disease processes should not be made, as both may be results of a resolved paraurethral abscess(30). It is most common in mid-life perimenopausal African-American women, although congenital lesions have been described rarely. It is associated in adults with a history of persistent urinary symptomatology, and is more common with chronic genitourinary conditions such as infections(31). Symptoms include dysuria, frequency, urgency, cystitis, stress

incontinence, pain, hematuria, dyspareunia and dribbling urination(32), sometimes termed the three “d’s”(dysuria, dyspareunia, dribbling post-void)(33), however the condition may be asymptomatic. A variety of imaging studies including transvaginal and transperineal ultrasound, transurethral sonography, voiding cystourethrogram, and CT urogram with subtracted images have been used to assist diagnosis, however the diagnostic modality of choice is MRI Imaging will also help distinguish another lesion in the differential, an ectopic ureter. Diverticular lesions are located on the distal anterior(ventral) vaginal wall, and in one case that led to its being mistaken for anterior vaginal wall prolapse(cystocele)(28). Rarely the diverticulum may rupture, leading to fistulization into the vagina, or fluid in the urethrovaginal space. Stone formation due to stasis of urine occurs in 1.5-10% of women with urethral diverticuli(34). Treatment is primarily surgical, however surgical complications range from 5-46%, and include urethrovaginal fistula, stress incontinence, urethral stricture, and recurrence of diverticula and new onset urgency(31,35). Urethral diverticuli can be associated with urinary tract infections in a high percent of cases, as well as bladder outlet obstruction, stone formation and incontinence. Histologically they are comprised of fibroconnective tissue, often devoid of lining(figure3), which when present is columnar, transitional or squamous(29,30). An unusual case lined by colonic epithelium with Paneth cell metaplasia was reported(32), as well as a case of endometriosis in a urethral diverticulum(36). In addition, there is a risk of neoplasia within the diverticulum, including benign nephrogenic adenomas(37) and rare malignancies. Carcinoma arising in a diverticulum is usually adenocarcinoma, with up to 70% of cases being adenocarcinoma(38), but transitional cell carcinoma, and occasionally squamous cell

carcinoma also occur. The clear cell variant of adenocarcinoma is highly associated with diverticuli, with about a third of all urethral clear cell adenocarcinomas arising in a diverticulum(38). Squamous cell carcinoma is the most common female urethral carcinoma in the absence of a diverticulum(18,34). Risk of carcinoma is not insignificant, and about 5% of all urethral carcinomas in women arise in a diverticulum, and these tumors are often late stage at diagnosis and aggressive(34). In a series of 90 female patients with excision of urethral diverticuli, there were 5 carcinomas(1 clear cell adenocarcinoma, and 4 “invasive adenocarcinomas”)(39). These authors recommended careful clinical examination and follow-up in patients with diverticuli, as well as informed evaluation of excised specimens for dysplastic and malignant change, because of the cancer risk.

Urethral Caruncle:

Urethral caruncles were first described by the English surgeon Samuel Sharp in 1750(40). Urethral caruncles are seen in postmenopausal women, and are thought to be due to ectropion of urethral mucosa in associated with hypoestrogenism(41). A subset of patients was found to have increased numbers of IgG4-positive plasma cells in one study, raising the theory that a subset may be related to the autoimmune phenomena associated with IgG4-associated sclerosing disease(41). Clinically, caruncles present as beefy red polypoid lesions seen protruding through the meatus(figure 4). In a series of 41 patients, 10% were initially thought to have a malignancy(42). Symptoms may be absent, or there

may be discomfort or bleeding. Histologically, a fibrovascular core is lined by squamous or transitional epithelium(figure4). Topical estrogen therapy resolved the vast majority of caruncles, and surgery is to be avoided if at all possible. Excision is usually reserved for persistently symptomatic lesions or to rule out a malignancy(29). A rare case of myeloid metaplasia(extramedullary hematopoiesis) presenting as a caruncle in a patient with a history of a myeloproliferative disorder with myelofibrosis was described(43).

Young et al(44) describe a distinctive pseudoneoplastic lesion, urethral caruncle with atypical stromal cells, which can histologically simulate a lymphoma or sarcoma, and describes the distinction. Although caruncles are not thought to be of significant malignant potential, rare squamous carcinomas have been reported to arise in caruncles, both in situ(45) and invasive(40,46).

Endometriosis

Wu et al(47) report a suburethral endometrioma in a 27-year-old woman with no prior surgical history. It did not communicate with the urethral lumen. The authors stated that the only prior history, pregnancy termination, did not explain the lesion by the implantation theory, but did not offer a theory for their case.

Localized amyloidosis

Amyloid involving the urethra can occur, usually as a secondary accumulation.

Primary localized urethral amyloidosis forming a tumoral mass is very rare, and most reported cases are in men. Kageyama et al(48) report a case in a 39-year-old woman who presented with urethral pain and bleeding and was initially thought to have a caruncle.

Amyloid can be diagnosed on tissue specimens by the characteristic apple-green birefringence seen on polarized light examination of a Congo-red stain.(figure 5).

Urethrocele

Urethroceles and cystourethroceles due to pelvic floor relaxation may present as anterior vaginal protrusions, and be associated with urethral dysfunction(49)

Benign Neoplasms

Nephrogenic adenoma

Nephrogenic adenomas are thought to be derived from misplaced renal tubular cells and can occur anywhere in the urinary tract, including urethra, more commonly in males, but in females as well, where they may arise in urethral diverticuli(50,51). The lesions stain for antibodies to EMA and PAX-8(50). Although not felt to be premalignant or malignant, there is some association with urothelial carcinoma, and the adenoma may coexist with carcinoma, or be seen subsequent to urothelial carcinoma. The lesion should not be confused with urothelial carcinoma(or prostatic carcinoma in men). Histologically, the lesion is composed of tubulocystic, papillary or flat architectural patterns lined by a

histologically benign cuboidal epithelium (figure 6). Medeiros et al describe five cases arising in urethral diverticula, and caution misdiagnosing the lesions as clear cell adenocarcinoma due to the clear cells or hobnail cells that may line the lesion, as well as the disproportionate clear cell histology of carcinomas arising in urethral diverticuli as opposed to the urethra without a diverticulum (51). The cause of nephrogenic adenoma has been considered to be secondary to irritation, however the existence in children makes this theory less plausible (50). The lesions have a recurrence potential (37).

Villous adenoma

Villous adenomas are common in the colon, but extremely rare in the female urethra, where there may be significant malignant potential (52,53,54). The case described by Morgan et al showed dysplastic colonic-type epithelium in the villous adenoma merging with native transitional epithelium (52). Noel et al (54) reviewed the literature, discussed the scattered case reports of a villous adenoma of the female urethra, and found one additional report of an associated adenocarcinoma in addition to the adenosquamous carcinoma they reported.

Leiomyoma

Urethral leiomyomas are rare, and usually arise from the proximal (vesical) urethra (34). They are more common in women (55). Symptomatology varies with location, with anterior (ventral) lesions more likely to present with urinary tract infection and mass, and posterior (dorsal) lesions more often presenting with dyspareunia (34). In a series of four

urethral leiomyomas, Bai et al found that if the lesion was small and lateral, there were no symptoms, if it was large and lateral it was irritative, whereas if the lesion was midline it was more likely to be obstructive. Other potential symptoms are pressure, dyspareunia, voiding dysfunction, and urinary tract infection. Surgery is the treatment of choice, but may result in fistula formation(55).

Hemangioma

This exceptionally rare tumor of the female urethra was described by Uchida et al(56). The patient was a 59-year-old woman, who, not surprisingly, presented with bleeding as well as frequency and urgency. There was concern for malignancy, however the lesion at the meatus was found to be a cavernous hemangioma. Aside from malignancy, urethral prolapse and caruncle are in the differential.

A Masson tumor(papillary endothelial hyperplasia), which histologically mimics a hemangioma, but is likely a form of recanalization of a thrombus, has been reported in the urethra(57). The 67-year-old patient developed vaginal bleeding and hematuria and was found to have an exophytic urethral mass(57) Familiarity with the histology of this lesion will help in avoiding a misdiagnosis of angiosarcoma.

Inverted papilloma

Inverted papilloma, a benign transitional cell lesion was reported in a 53-year-old woman in the Spanish literature(58). A second case in a female urethra was reported(59) in a series where there was a 9:1 male predominance. Although benign, inverted

papillomas have a recurrence risk, as well as an association with transitional cell carcinoma, and hence must be followed(59).

Superficial angiomyxoma

A rare superficial angiomyoma of the urethra was reported in a 51-year-old woman. The lesion was notable for recurrence of the mass 3 weeks after the first excision(60).

Carcinoid

Carcinoid is a neuroendocrine neoplasm that may behave in either a benign or malignant fashion. They are usually found in the respiratory and gastrointestinal tract(61). Katayama et al(61) reported the first female case of urethral carcinoid in a 57-year-old woman with five years of benign follow-up after excision. This is in distinction to the aggressive behavior in a male case(62).

Other rare benign neoplasms

A clear cell “sugar” tumor of the urethra, a variant of the PEComa family of neoplasms(perivascular epithelioid cell tumor) was reported in a 15-year-old female.(63). PEComas are notable for staining for HMB45.

Malignant tumors

Unfortunately, the presenting symptomatology of malignancies of the female urethra are nonspecific and non-diagnostic, and hence an index of suspicion must be present. Diagnosis is often late for these uncommon neoplasms. In one series, the most common presenting symptom was persistent bleeding(64).

Carcinoma

Primary urethral carcinomas are rare in women, representing about 0.02% of female cancers(34). However, they are three to four times more common in women than men, in distinction to other malignancies of the genitourinary tract(65). Most urethral carcinomas are distal(caudal), and hence squamous cell carcinoma was the most common in one series(70%)(65). Proximal(vesical) urethral carcinomas may be transitional, which was the second most common histology(20%) or adenocarcinoma, the third most common(10%) in Amin's review(65). However a more recent paper found a predominance of transitional cell carcinoma, with squamous the least common(66). Clear cell adenocarcinoma and small cell carcinoma also occur, with an association between clear cell adenocarcinoma and urethral diverticulum, and with nephrogenic adenoma(34,65). One series of adenocarcinomas showed a slight predominance in African-American women, but in general there is no racial predominance(65). Most cases are in women over 65 years of age(66). Diagnosis tends to be late, with stage and histologic type significant prognosticators. Adenocarcinoma had a worse prognosis than squamous or transitional cell carcinomas in Derksen's series, perhaps due to a greater

number of cases diagnosed at a later stage(66). Proximal(vesical) lesions have a worse prognosis, possibly due to later detection and different lymphatic drainage(66). In any case, urethral carcinomas must be regarded as potentially aggressive neoplasms. In one case of transitional cell carcinoma, the patient presented with both lung and bone metastases, and developed brain metastases a year later(67). Symptoms of urethral carcinoma include bleeding, frequency, incontinence, dysuria, obstruction, mass, and infection. The lesion may be misdiagnosed as a caruncle or prolapse, given the postmenopausal demographic. Etiology is unknown, but irritation and HPV have been suggested. However, since these last two are common, and urethral carcinoma is rare, the association is weak(65).

Amin et al classify urethral carcinomas as primary, comprised of squamous, transitional, adenocarcinoma, adenosquamous carcinoma and undifferentiated carcinoma, and secondary carcinoma, such as Skene's tumors presenting as a urethral mass(65). Among the adenocarcinomas, there is clear cell adenocarcinoma. Non-clear cell adenocarcinomas may be colloid(mucinous), signet ring cell, or not otherwise specified(NOS). Overall, urethral carcinomas tend to be aggressive, although clear cell adenocarcinoma may be less so(65). A subset of urethral adenocarcinomas may actually be of periurethral(Skene's) duct origin, and stain for prostatic markers such as prostate specific antigen(PSA)(68)

As discussed previously, a subset of urethral carcinomas arise in urethral diverticuli, with an increased prevalence of the clear cell type. However, these are rare lesions, representing only 0.002% of female malignancies, with approximately 5% of female urethral carcinomas arising in a diverticulum(69). Squamous cell carcinoma in

situ has also arisen in a urethral diverticulum, in what the authors believed was the first reported case(70). Because of the rarity of these lesions, there are no consensus protocols for therapy. Ahmed et al reviewed the literature on urethral diverticular carcinoma, cataloged the cases, and suggested the creation of a registry(71). This is echoed by Grivas et al(72), who review possible therapeutic options while confirming the lack of evidence-based treatment strategies.

Rare sporadic reports of unusual histologic subtypes have appeared in the literature. Flynn et al reported two cases of high grade serous carcinomas, one arising in the urethra of a 68-year-old woman with no recurrence at 6 month follow-up after extensive excision. Their second case was in an 81-year-old woman who underwent urethrectomy and excision of her urethral diverticulum containing a mass which proved to be serous carcinoma. This patient was also tumor free at 6 months(69). A case of adenosquamous carcinoma arising in a villous adenoma in a 49-year-old woman has been reported(54). The lesion presented as a rapidly growing painful mass, with hematuria. The authors postulated possible origins of the tumor as cloacogenic remnants, totipotential urothelial stem cells, or periurethral glandular structures(54). Cloacogenic carcinoma has also been reported(73)

Melanoma

Melanoma of the urethra is extremely rare, representing about 4% of urethral neoplasms, with a female predominance(34). The lesions are usually distal(meatal) and polypoid, and so may be initially thought to be a polyp, caruncle, prolapse, or

carcinoma(34). Symptomatology is commensurate with location, and may include bleeding, dysuria or voiding difficulty. While usually aggressive, there is one report of ten year survival(74). Urethral melanomas fall in the category of mucosal melanomas which differ from cutaneous melanoma. They are not associated with sun exposure, are more likely to be diagnosed late, more likely to be amelanotic, and up to 20% exhibit c-Kit mutation(74). There is no standardized therapy, however in a literature review, the 5 year survival was only about 10%(75).

Other rare malignant tumors of the urethra

Other sporadic reports of urethral neoplasms have included small cell neuroendocrine carcinoma(76), glassy cell carcinoma(77), signet ring cell carcinoma(78), carcinosarcoma(79), lymphoma(80,81,82), and leiomyosarcoma(82).

Metastases

Metastases to the urethra are exceptionally rare (82).

Summary:

A variety of lesions may present in the female urethra. Symptomatology may include mass, pain, hematuria, infection, and disturbances in urination. Urinary retention is much less common in women than men(83), however may occasionally be the presenting sign of urethral stricture, thrombosed urethral caruncle, diverticulum or urethral tumor(84). These lesions are more familiar to the urologist and urogynecologist

than other practitioners caring for women. A familiarity with these lesions will include them in the differential diagnoses of patients presenting with their symptomatology, and facilitate treatment and consultation as appropriate.

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Table 1-Anterior(ventral) vaginal lesions that may be mistaken for a urethral lesion

- Ectopic prolapsed ureterocele**
- Ectopic ureter**
- Skene's duct cyst**
- Gartner's duct cyst**
- Müllerian cyst**
- Anteriorly placed Bartholin's cyst**
- Condyloma accuminatum**
- Endometriosis**
- Vaginal leiomyoma**
- Vaginal malignancies**

Table 2- Reported Lesions of the Female Urethra

Congenital & Pediatric Lesions

- Prolapse of urethra**
- Prolapsed ureterocele**
- Hypospadias**
- Epispadias**
- Urethral duplication**
- Urethral atresia**
- Persistent urogenital sinus or cloaca**
- Polyp**
- Embryonal rhabdomyosarcoma(sarcoma botryoides)**

Strictures & Fistulas

Inflammatory Lesions

- Urethritis(acute and chronic)**
- Condyloma accuminatum**
- Sarcoid**
- Malakoplakia**
- Calculi**
- Tuberculosis**
- Rhinosporidiosis**
- Plasma cell granuloma**

Benign tumors and tumor-like lesions

- Polyp**
- Diverticuli**
- Caruncle**
- Amyloidosis**
- Sarcoid**
- Urethrocele**
- Varix**
- Myeloid metaplasia**
- Endometriosis**
- Rhabdomyoma**

Leiomyoma
Hemangioma
Masson's tumor
Nephrogenic adenoma
Villous adenoma
Paranglioma
Benign fibrous histiocyoma

Potentially Recurrent or Malignant Tumors

Superficial angiomyxoma
Carcinoid
"Sugar tumor"(PEComa)
Inverted papilloma

Malignant tumors

Epithelial tumors

Invasive and in situ squamous cell carcinoma
Adenocarcinoma, including clear cell adenocarcinoma
Adenosquamous carcinoma
Serous carcinoma
Transitional cell carcinoma
Small Cell Neuroendocrine carcinoma
Carcinoid
Glassy cell carcinoma
Signet ring cell carcinoma
Cloacogenic carcinoma
Carcinosarcoma

Other Malignancies

Leiomyosarcoma
Lymphoma
Melanoma
Metastatic disease to urethra

Legends:

Figure 1-Prolapse of urethra- The lesion is characterized by a central dimple, giving a donut configuration (1A) Copyright Libby Edwards MD. Used with permission. All permission requests for this image should be made to the copyright holder.

Note thrombosed vessel lower right(1B)

Figure 2-Malacoplakia showing a lesion composed of epithelioid histiocytes, containing scattered Michaelis-Guttman bodies(right, arrow), which are highlighted on Von Kassa stain for calcium(lower left). The upper left shows a PAS stain highlighted incompletely digested bacteria in the cells.

Figure 3-Diverticulum. There is no epithelial lining, only a “lining” of granulation tissue

Figure 4-Caruncle-The lesion appears as granulation type tissue, without the central umbilication of prolapse(4A)(Courtesy L. Edwards, MD). Marked inflammation is seen in this transitional epithelial-lined caruncle(4B)

Figure 5-Amyloid-Amyloid stains apple green on polarization of a congo red stain

Figure 6-Nephrogenic adenoma-note the papillary architecture.