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Case Report

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A Paraurethral Neoformation in a Patient with Uterine Fibromatosis: An Incidental Case of Paraurethral Leiomyoma and Review of the Literature

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Abstract

Leiomyomas are benign smooth muscle tumors commonly occurring in the genitourinary tract, most frequently in the myometrium. Extrauterine localization of leiomyoma is extremely rare, especially in deep soft tissues such as the female urethra. The presence of a mass near the urethra can be associated with a broad spectrum of both benign and malignant pathologies of gynecological or urological origin, and always poses a challenge for differential diagnosis. Because the signs and symptoms of these conditions often overlap, establishing an accurate clinical diagnosis can be difficult. Histological diagnosis is still essential today, however recent technological advances in Magnetic Resonance Imaging (MRI) and ultrasound (US) allow for a more detailed evaluation of urethral and periurethral anomalies, as well as for an easier diagnosis before surgery and presurgical planning. The present article describes the case of a paraurethral leiomyoma in a woman in her 40's, who complained of abnormal uterine bleeding and abdominal swelling. A review of the literature on the diagnostic and therapeutic management of this rare pathology is also treated.

Background

Extrauterine leiomyomas are very rare, and they are most frequently observed in the genitourinary tract. Leiomyomas that arise from the internal or external smooth muscle of the urethra are usually diagnosed after surgery. However, they must be treated with great care during surgery due to their unusual position and their adherence to surrounding structures. Being able to distinguish between benign and malignant pathology before surgery allows in some cases to avoid surgery, especially in asymptomatic patients in whom the finding is completely incidental.

Case Presentation

A woman in her 40's, nulliparous, arrived at our hospital complained abnormal uterine bleeding and abdominal swelling. Transvaginal US showed an enlarged, anteverted uterus, with an inhomogeneous echostructure due to fibromatosis. Particularly, a subserosal (FIGO 7) [1], large fibroid of 100 mm in size was identified on the posterior wall. In the endometrial cavity, two hyperechoic polypod lesion respectively of 10 mm and 5 mm with irregular margins were also present, with typical "feeding vessel" at the color-Doppler examination (color score 2-3). The ovaries were regular. On the anterior side of the urethra, a solid rounded and hypoechoic mass was detected. It showed diameters of

22x17x17 mm and regular margins, with an inhomogeneous echostructure, without shadows, and mild vascularized at the color-Doppler imaging **(Figure 1)**. The characterization of this paraurethral mass was not possible at only US examination.

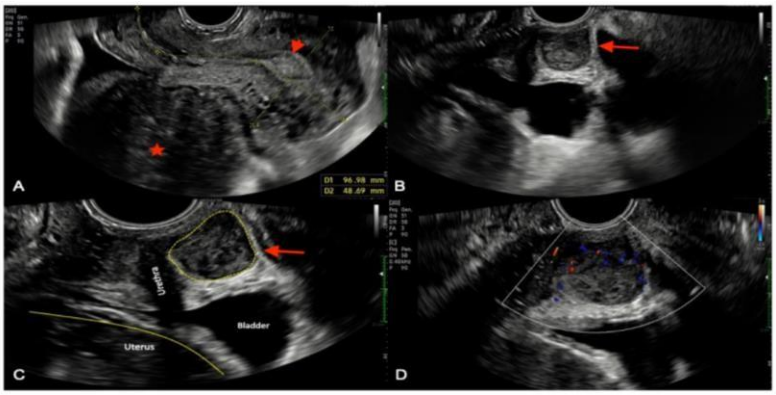

Figure 1: Sagittal transvaginal ultrasound images (A) shows an enlarged uterus with posterior large, subserosal fibroid (FIGO 7) (red star) and endometrial polyps within uterine cavity (red arrow head). Axial (B) and sagittal transvaginal ultrasound images (C) shows a solid stromal lesion anteriorly to the urethra (red arrow), with regular margins, with inhomogeneous echogenicity, without shadows, not compressible at the pressure with the transvaginal probe. The axial color-Doppler image (D) shows a moderately vascularized lesion (color score 2-3).

A pelvic MRI was performed to assess the uterine fibroids and paraurethral mass. On the anterior side of the urethra, in the retropubic area, the paraurethral mass was confirmed, located in the left antero-median area. The mass showed clear edges, with a maximum axial diameter of 28x18 mm and a cranio-caudal extension of 19 mm. This lesion displaced the urethra posterolaterally on the right side, and showed isointense signal intensity onT1-weigthed images, predominantly hypointense on T2-weigthed images, and no significant restriction of the diffusion coefficient **(Figure 2)**.

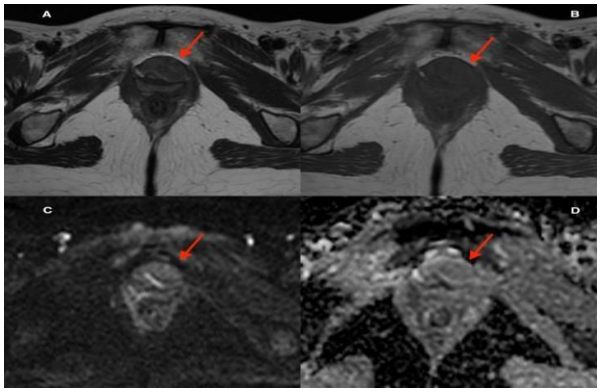

Figure 2: T2-weighted axial image (A) shows a hypointense round well-defined mass on the left anterior side of the urethra (red arrow), referring to a urethral leiomyoma. The mass appears hypointense on the T1-weighted images (B), without significant restriction of the diffusion coefficient, showing low signal on the DWI axial images (C) (b value= 1000) and high signal on the ADC map (D). Note that both on the T2-weigthed and T1-weighted images the signal intensity is very similar to that of the muscles. After paramagnetic contrast medium administration, the mass showed enhancement higher on the late phase **(Figure 3)**. The suspicion of paraurethral leiomyoma was raised.

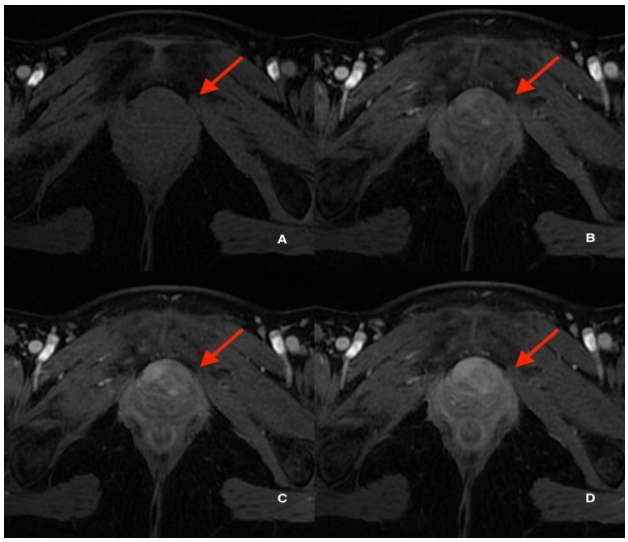

Figure 3: T1-weighted images with fat saturation in the basal (A), arterial (B), venous (C)and late (D) phase. Urethral leiomyoma appears isointense to the muscles on the basal phase (A). After Gadolinium administration, it shows poor enhancement in the arterial phase (B), showing a progressive and uniform contrast enhancement on the venous (C) and late (D) phase.

Furthermore, the MRI confirmed the presence of a voluminous subserosal myoma, with an implant base on the posterior wall of the fundus of the uterus. This lesion had maximum axial dimensions of 73x68 mm, regular margins and was iso-hypointense on T1-weighted images and predominantly hypointense in T2-weighted images, with but with some small hyperintense areas of cystic degeneration **(Figure 4)**. Additional fibroids were present on the anterior side of the fundus (maximum diameter 10 mm) and on the right posterior aspect of the body (maximum diameter 9 mm).

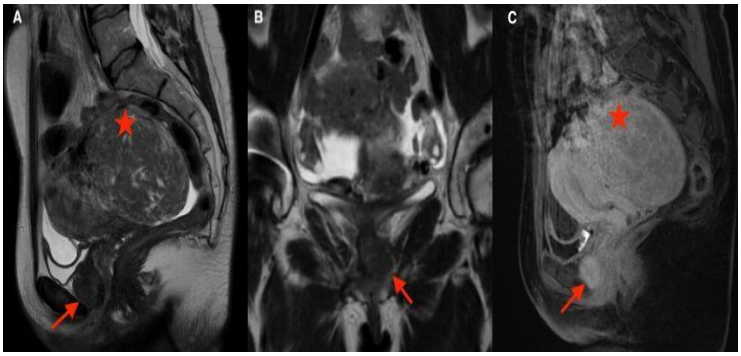

Figure 4: T2-weighted sagittal (A) and coronal (B) images reveal a well-defined round lesion (red arrow) located anteriorly to the urethra, characterized by low signal intensity; on the posterior aspect of the uterus, a voluminous subserosal myoma (red star) shows a similar signal intensity to the urethral leiomyoma, but with an inhomogeneous appearance due to the presence of hyperintense components in the context as for cystic degeneration. T1-weighted sagittal image after gadolinium administration in the late phase (C) shows the same uniform contrast enhancement of the paraurethral leiomyoma and uterine myoma.

Subsequently, the patient underwent surgery for the removal of uterine fibroids, which were then confirmed to be benign on histological examination. During the same surgery, the paraurethral formation was initially visualized, appearing whitish and with fibromuscular appearance, but poorly cleaved from the surrounding planes. In consideration of the absence of a clear cleavage plan and of the lack of patient's symptoms, only a paraurethral biopsy was performed and further surgery was postponed. The histological examination of the biopsy fragment described the presence of fibromuscular and scleroconnective tissue, in the absence of atypia and mitosis. The diagnosis of paraurethral leiomyoma was confirmed. To date, the patient is still asymptomatic and has decided in agreement with the treating staff not to perform further surgery for the removal of the paraurethral leiomyoma.

Differential Diagnosis

Neoplasms involving the urethra can arise from any of its histological elements, particularly the transitional epithelium, stratified squamous epithelium, glandular epithelium, and smooth and striated muscles [2]. Differential diagnoses of urethral masses may include malignant causes such as leiomyosarcoma, lymphoma, transitional cell carcinoma, squamous cell carcinoma, clear cell adenocarcinoma and metastases [3]. They typically occur in postmenopausal women and significant risk factors for primary urethral cancer include chronic irritation, recurrent urinary tract infections, urethral diverticulum and HPV chronic infection [4]. Leiomyosarcomas and other vaginal neoplasms have typically a high signal intensity on T2-weighted sequences, and result irregular and heterogeneous with areas of necrosis or haemorrhage [5]. Secondary features such as rapid growth, infiltration of surrounding anatomical structures and the presence of metastases help to distinguishing leiomyosarcoma from benign entities. By contrast, smooth muscle tumors located elsewhere in the body show typically a low to intermediate signal intensity on T2-weighted images [6]. Among the benign lesions, caruncles are the most common urethral masses (96%). Urethral caruncles are seen on the posterior margin of external urethra in post-menopausal females caused by mucosal prolapse and are usually small in size [2]. Urethral caruncles, frequent in postmenopausal women and in those suffering from hypoestrogenism, are small benign lesions of the posterior border of the external urethral meatus caused by distal urethral prolapse [6]. At MRI, caruncles may manifest as a T2- hyperintense tissue surrounding the external urethral meatus, a finding that correlates with the presence of a soft exophytic lesion at the meatus at physical examination [7]. Other benign paraurethral masses are urethral diverticulum, urethral fistula, paraurethral cyst, polyps, papillomas, hemangiomas, leiomyomas, fibromas, neurinomas and adenomas [8]. The urethral diverticulum is the most common cystic lesion of the urethra and is usually found between the third and fifth decade of life [9]. They are "horseshoe shaped" protrusions or hernias that protrude between the periurethral fibromuscular layer and the anterior vaginal wall [10] and are continuous with the urethral lumen through a single or multiple ostium [11]. Urethral diverticula may be secondary to infection, rupture of a blocked periurethral gland, obstetric trauma, previous surgery, repetitive trauma or be congenital [9]. The urethral diverticula are hyperintense compared to the surrounding soft tissues on T2-weighted images because the cystic cavity contains fluid. However, diverticula with haemorrhagic or protein content are seen as hyperintense on T1-weighted images and hypointense on T2-weighted images [4]. Urethral fistulas may be found in patients with Crohn's disease, Behçet's disease or in patients undergoing urethral diverticulectomy or vaginal surgery [12,13]. On T2-weighted and gadolinium-enhanced T1-weighted MR imaging, urethral fistulas manifest as hyperintense tracts extending from the urethra to the vagina, rectum, or perineum [3]. Additional periurethral cystic lesions are Gartner's duct cysts, Bartholin's gland cyst, Skene's ductus cyst, Müllerian's cyst, epidermal inclusion cyst, perineal-vulvovaginal endometriomas, and injected collagen. These lesions, unlike urethral diverticula, do not communicate with the urethra [4].

Treatment

Due to the rarity of this condition, there is no clear protocol for management and treatment. In asymptomatic patients, since leiomyoma has not been reported to develop into a malignant disease [14], regular US or MRI follow-up may be sufficient. Taking into consideration leiomyomas from other sites as well as in the case of bladder leiomyomas, Cornella et al. [15] reported that in asymptomatic patients without obstructive or other complications, no surgery is required and follow-up observations with US, cystoscopic examination, MRI and histopathological confirmatory examination can be

performed. Hormonal treatment with gonadotropin-releasing hormone analogue has been described [16], while surgical resection is often necessary because severe symptoms may occur even with smallurethral leiomyoma [17]. The distinction between urethral and paraurethral masses is fundamental for planning the surgery. In the case of leiomyomas located in the anterior urethra, near or protruding through the meatus and in the case of paraurethral leiomyomas, a complete surgical excision of the tumor through a vaginal approach is mainly used. Transurethral excision is used instead for urethral leiomyomas attached to the middle or posterior urethra [14,18]. During surgical excision care should be taken not to damage the urethra and adjacent anatomical structures such as the bladder. To prevent complications such as stenosis, fistula or stress urinary incontinence, it is important to leave an indwelling urinary catheter in place for an extended period of time [19]. During the surgical procedure it is important to suture layer by layer and look for any leaks or defective areas, in order to avoid a complication such as fistula [17]. In the study by Ozel et al. [20] it is argued that if the urethra is damaged during excision, the most likely diagnosis is a urethral leiomyoma and the alternative diagnosis of paraurethral leiomyoma can be ruled out.

Outcome and Follow-Up

Postoperative follow-up may include clinical examination, MRI at 6 months and 2 years, residual post-void volume, and uroflowmetry at 1, 6 and 12 months; in cases of urinary incontinence a urodynamic investigation can be carried out [21]. Cases of relapse after surgical excision are generally very rare and only few cases are reported in the literature. In cases of relapse, a repeated excision is usually carried out. Cases of recurrence are likely due to incomplete excision of the tumor to avoid damage to the urethra. In fact, very often at the second operation, in order to obtain a complete resection, the urethra is damaged [8]. Merrell and Brown reported a case of recurrent urethral leiomyoma that required three operations in 10 years [22]. In cases of urinary incontinence, it is suggested to proceed with the anti-incontinence surgery 6 months after the first operation. Before the anti-incontinence surgery, MRI examination should be performed to exclude a recurrence of leiomyoma, and the urodynamic investigation should confirm the stressful component of the incontinence [21].

Discussion

Leiomyomas are benign tumors of smooth muscle origin and in fertile age females are the most common uterine masses. However, any smooth muscle tissue can be involved, so leiomyomas of the genito-urinary tract can affect vulva, ovaries, urethra and urinary bladder [23]. Even more rare but possible is the involvement of the gastrointestinal tract. Urethral leiomyomas are rare, benign tumors of the urethra and the first case was described by Buttner in 1894. Several authors dispute that the definition of urethral leiomyoma is not very correct since these tumors do not seem to originate from the intraurethral muscular layer. They usually develop from the smooth muscle component around the urethra so the correct definition is paraurethral leiomyomas [21]. However, it is not easy to distinguish between vaginal, urethral and paraurethral leiomyoma due to their close anatomical relationship. They are three times more common in women and the mean age at presentation is 39.8 years (most commonly between 3rd to 4th decade) [24]. However, it is possible that the reported incidence is higher in women as they do more US and pelvic examinations during reproductive age. Leiomyomas of the urethra are rare before puberty, tend to grow and enlarge during pregnancy, and regress after delivery. For this reason, it has been suggested that these masses may express estrogen receptors and have estrogen-dependent growth [25]. Since some cases also occur in post-menopausal women, other authors exclude the hormonal origin of urethral leiomyomas [26]. These masses may develop along any part of the urethra, but the majority of

paraurethral leiomyomas occurs in the posterior wall of the proximal segment [15]. Paraurethral leiomyoma are usually sessile and small but rarely could be also large tumors, pedunculated and located in the distal part of the urethra protruding through the urethral meatus [27]. Leiomyomas of the proximal part of the urethra can be detected at physical examination as a mass of the anterior vaginal wall (depending upon the size) [21]. Macroscopically, the tumor is usually a hard, round, smooth, pink lesion [19]. These tumors, when enlarged, may present a radiological similarity to prostatic hyperplasia in the male patient [28]. The symptoms and the patient's clinic pattern depend on the position and size of the tumor, which can reach up to 40 cm [29] although 20-50% of patient are completely asymptomatic [15,20]. The most common symptoms include urinary tract infection (64.3%), palpable mass (50%), dyspareunia, urinary retention, and irritative lower urinary tract symptoms [2]. Patients may also present vaginal bleeding or haematuria [30]. Acute urinary retention with bilaterally hydroureteronephrosis can develop in case of complete stenosis of urethra [14]. Migliari et al. [21] noted that neoplasms located along the anterior or posterior wall of the urethra can cause symptoms of obstructive urination more frequently, whereas laterally displaced leiomyomas are more likely to cause irritation. Since such symptoms are also seen in other periurethral lesions, it is difficult to diagnose leiomyoma based on clinical features, and radiological imaging can be helpful. For this purpose, different methods can be used including voiding cystourethrography, transvaginal US, pelvic MRI and Computed Tomography (CT). Voiding cystourethrography is only useful in showing signs of extrinsic compression and urethral dislocation, associated in large masses with an elevation of the bladder base [31]. Therefore, since it is not helpful for the final diagnosis, it is rarely used today. The use of CT should be avoided in women of reproductive age to reduce radiation exposure. US and MRI are the most suitable methods for the diagnosis of pelvic masses due to the accuracy in identifying the exact location of the lesions, the relationships with the surrounding organs and the infiltration of the urethral tissue. All these informations are all useful for surgical planning [21]. On transvaginal or transperineal US, urethral leiomyomas appear as smooth-walled well-defined solid masses with iso- to hypo- echoic homogenous internal echoes. In the case of large masses, they may have a non-homogeneous echostructure with signs of cystic or necrotic degeneration, and usually exhibit significant internal vascularity on color-Doppler imaging [2]. Anyway, one of the main roles of US is to exclude the infiltrating nature of the lesion and to differentiate it from urethral diverticula, which are recognized by their relationship with the urethral lumen and by their internal fluid structure [32]. MRI is considered as a second level imaging and gold standard. It is useful to identify the urethral origin of the tumor and for planning surgical removal. It has been reported that MRI findings have a high correlation with the histological findings, including degeneration [33]. On MRI, a paraurethral leiomyoma is a well-defined mass appearing hypointense or isointense to muscle on T1-weighted images, hyperintense or isointense to muscle on T2-weighted images and with uniform contrast enhancement on T1-weighted images, as in our case. In general, most leiomyomas appear as homogeneous, well-circumscribed masses with low signal intensity on T2-weighted images, due to the presence of densely arranged muscles cells with intermediate collagen [34]. Leiomyomas can undergo either hyaline degeneration and have a more hypointense signal on T2-weighted images or have a combination of edematous swelling of the muscle cells from ischemia, cystic alteration and myxoid degeneration, which correspond to the presence of high signal intensity foci within the lesion [34]. These cellular changes explain the signal variability onT2-weighted images of leiomyomas. However, benign solid tumors in the pelvis show high signal intensity on DWI images and no restricted diffusion on the ADC map [35]. Final diagnosis, also because of the variability of MRI findings, is made only by histopathological examination through US-guided transvaginal biopsy or surgical removal. The muscular origin of the tumor cells is confirmed by the immunohistochemistry positivity for

smooth muscle actin and desmin [36]. Differentiating leiomyomas from low-grade leiomyosarcomas can be extremely difficult, especially if the sample is small. For this reason, some authors prefer surgical excision as the treatment of choice, since this provides a comprehensive pathological examination that excludes possible foci of malignant degeneration [32].

Learning Points

- Paraurethral leiomyoma is a rare benign tumor and it should be considered in the broad spectrum of differential diagnoses of urethral and paraurethral diseases, especially in women of reproductive age who present with dysuria, dyspareunia, perineal mass and other non-specific genitourinary clinical symptoms.
- MRI and real-time ultrasound are essential to help identify paraurethral leiomyoma among the complex disorders affecting the urethra and periurethral tissues and is a valid diagnostic tool in preoperative planning. However, the biopsy or surgical removal remains necessary to have a diagnosis of certainty.
- Since malignant transformation has not been reported for leiomyoma, follow-up with regular MRI examinations may be sufficient in asymptomatic patient.
- In symptomatic patients, surgical removal is the treatment of choice; the surgeon should be very careful not to damage the urethra and to leave an indwelling urinary catheter for an extended period to prevent complications such as strictures or fistulas.

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