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Case report

Female primary urethral carcinoma: A rare case report

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ABSTRACT

Introduction: Primary tumors of the female urethra are exceedingly rare and account for <0.02% of the malignant disease occurring in women. This disease usually presents late and, hence, has a poor outcome. Early diagnosis is necessary to prevent further metastasis and prevent urinary catheter-dependant. Tumors arising from the distal urethra tend to be early stage and cure rates are high, however lack of knowledge about this disease is notorious, the transmission of knowledge is made only by case reports.

Case presentation: A 76-years-old woman presented with the chief complaint of lower pelvic pain. The complaintas also accompanied by a burning sensation in the urethra and stranguria, urinary retention, and hematuria. Macroscopic observation revealed the lesion was whitish with vegetative aspect at the urethral meatus, involving the entire urethra. The fragile mass was palpable in distal urethra and external meatus urethra per vaginally and easily bleedings. Laboratory examination of blood chemistry results within normal limit. Urinalysis showed pyuria and hematuria. Urethrocystoscopy findings were whitish lesion with vegetative aspect also fragile mass along the urethra, abnormal bladder neck, and bladder mucous was hyperemis. The histopathological result showed metaplasia squamous cell carcinoma, clear cell carcinoma. She is planned on getting cystouretherectomy (anterior exenteration) later.

Clinical discussion: The female urethral carcinoma is a disease with low prevalence with urothelial carcinoma (transitional cell) is the most common histological type (Leão et al., 2016; Adolfsson et al., 2012). Symptoms of urethral carcinoma are varied. The carcinoma spreads initially by local invasion into the periurethral tissue, vagina, and vulva and proximally spread to the bladder neck (Leão et al., 2016; Mittal et al., 2020). Distant metastasis is uncommon (Mittal et al., 2020). The most suitable method for collecting material for biopsy is the urethrocystoscopy. MRI is commonly used for staging. For post-surgical staging, the best investigation is the excretory urography (Gourtsoyianni et al., 2011; Picozzi et al., 2012). The management in vogue are surgical such as tumor excision, radical nephro-ureterectomy or anterior pelvic exenteration with radiotherapy or chemotherapy complementary. This cancer is associated with poor outcomes. Therefore, prognostic factors are important to be known.

Conclusion: Although female urethral carcinoma is a rare disease entity, clinicians should have strong suspicion of malignancies in patients to make an exact diagnosis. Early radical surgery can achieve better outcomes, although the standard therapy remains controversial.

1. Introduction

Primary tumors of the female urethra are exceedingly rare, more prevalent among women than in men, and account for <0.02% of the malignant disease occurring in women. This disease usually presents late and, hence, has a poor outcome [1]. There are two predominant forms of female urethral adenocarcinoma: mucinous and clear cell. Mucinous adenocarcinoma is more common, can appear microscopically similar to colonic or cervical adenocarcinoma, and may produce carcinoembryonic antigen. Clear cell adenocarcinoma is microscopically similar to clear cell carcinomas of the female genital tract, can secrete prostate-specific antigen, and is more commonly found in urethral diverticula. Clear cell adenocarcinoma (CCAU) accounts for 0.003% of malignant tumors occurring in female urogenital tract, with the average age of occurrence in females being 58 years. Even in the female CCAU is very rare. Information regarding CCAU has been obtained from single case

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reports and small case series [2]. Unlike bladder cancer, urethral carcinoma shows clinical and histological dissimilarities between male and female patients [1,2]. As any cancer, early diagnosis is necessary, which would reduce the risk of metastasis so that the patient does not need a more aggressive surgical approach to control the progression of the disease [3]. Furthermore, as a result of the surgery, the patient may become dependent on the urinary catheter.

Clinical management varies depending on the clinical stage and location of the lesion. There are no prospective randomized studies on which to base treatment of this disease. Surgery and radiotherapy have been advocated as effective treatment for early urethral cancers. Tumors arising from the distal urethra tend to be early stage and cure rates are high, however lack of knowledge about this disease is notorious, the transmission of knowledge is made only by case reports [4,5].

2. Case presentation

A 76-years-old woman presented with the chief complaint of urinary retention. The complaint was also accompanied by a burning sensation in the urethra and stranguria, urinary retention, and hematuria. No drug history, family history of cancer, or history of smoking. Macroscopic observation revealed the lesion was whitish with vegetative aspect at the urethral meatus, involving the entire urethra. The fragile mass was palpable in distal urethra and external meatus urethra per vaginally and easily bleedings. There was no palpable inguinal lymph node (Fig. 1).

Laboratory examination of blood chemistry results within normal limit. Urinalysis showed pyuria and hematuria. Ultrasound showed thickening of her bladder wall (Fig. 2). Urethrocystoscopy findings were whitish lesion with vegetative aspect also fragile mass along the urethra, abnormal bladder neck, and bladder mucous was hyperemis (Fig. 3). In the histopathological sections, the tumor tissue showed stromal infiltrated by mucous-secreting malignant signet ring cells with moderate pleomorphism, low mitotic index, releasing large amounts of mucin into the interstitial space. There was no blood or lymphatic vascular infiltration by the tumor. No lymph nodes were identified in the surgical specimen and the surgical resection margins were free of neoplastic involvement. The histopathological microscopic appearance shows minimum fibromyxoid tissue. Some tissues show the distribution and grouping of malignant tumor cells among the fibromyxoid tissue, including cells with enlarged nuclei, pleomorphic, coarse chromatin, protruding nuclei, and some hyperchromatic. Cytoplasm was clear, N/C ratio was increased, and mitosis could be found, suggestive for metaplasia squamous cell carcinoma and clear cell carcinoma as shown in Fig. 4.

According to the previous examination, patient was planned to have a Magnetic Resonance Imaging (MRI) of her pelvic and lower abdomen region. She is planned on getting urethrocystouretherectomy (anterior exenteration) later. Histopathology of the specimen revealed metaplasia squamous clear cell carcinoma of external urethral meatus.

The urethrocystoscopy was performed by one operator. This patient was treated after surgery for approximately 5 days, and the histopathological examination carried out on 1 week post-operative. This work has been reported in line with the SCARE 2020 criteria [6].

3. Discussion

The female urethral carcinoma is a disease with low prevalence, which corresponds to 0.02% of all cases of malignant tumors in women; and accounting for 5% of cases among urological tumors in women [7]. In terms of overall prevalence, among men and women, urothelial carcinoma (transitional cell) is the most common histological type, accounting for 54%–65% of cases; the squamous cell corresponds to 16%–22% of cases; and adenocarcinoma accounts for 10%–16% of cases of urethral carcinoma [8]. Our case could be classified as squamous cell carcinoma.

Our case has the chief complaints of lower pelvic pain. The complaint was also accompanied by a burning sensation in the urethra and stranguria, urinary retention, and hematuria. Symptoms of urethral carcinoma are varied ranging from dysuria, dyspareunia, hematuria, perineal pain, urinary retention, overflow incontinence, to urethral mass, or a protruding meatal mass. It spreads initially by local invasion into the periurethral tissue, vagina, and vulva and proximally spread to the bladder neck [7,9]. Furthermore, it is possible the occurrence of purulent and malodorous discharge and secondary infections in necrotic tissue. In the asymptomatic stage of the disease, it may appear hard lumps in the labia, bladder neck, vagina and perineum, sites for which metastasis is more common [7]. Lymphatic drainage of proximal urethra goes to the obturator and internal iliac lymph nodes, while the distal urethra drains into inguinal group of lymph nodes. As many as 30% of patients have clinically palpable lymph nodes, and >90% of these are metastatic. Distant metastasis is uncommon [9].

The most suitable method for collecting material for biopsy is the urethrocystoscopy. This method, when properly performed can inform tumor extent, location and histology [3]. Magnetic resonance imaging (MRI) is the most commonly used imaging test for staging. Distance staging is recommended primarily for the detection of lesions in the liver and chest (chest and abdomen computed tomography [CT]) if there is an increased satellite nodule [10]. For post-surgical staging, the best investigation is the excretory urography [11]. In this case, patient underwent urethrocystoscopy and planned for abdominal and pelvic ultrasonography also MRI. Urethrocystourethroscopy and biopsy are integrant to confirm the diagnosis, establish the histology and grade, determine the local extent of cancer, the precise location within the urethra, and whether a concomitant bladder cancer may be present

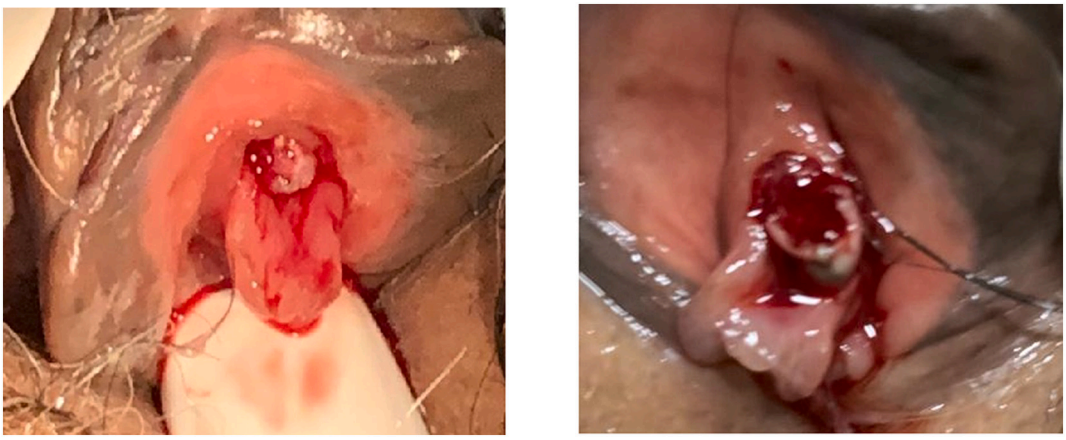

Fig. 1. Macroscopic observation of external urethral meatus per vaginal.

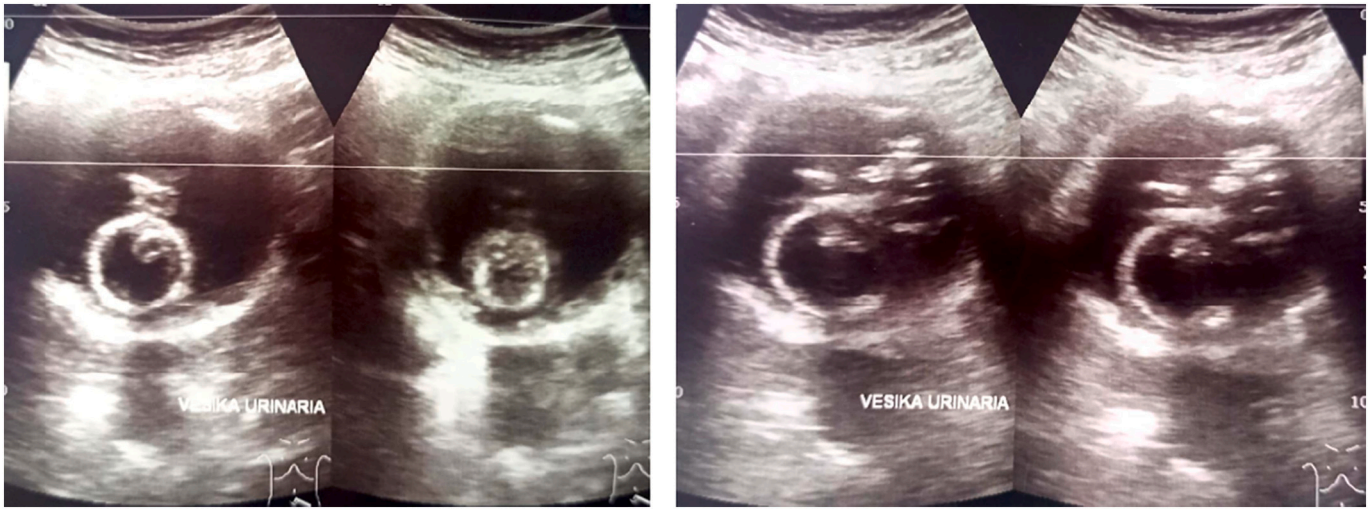

Fig. 2. Ultrasonography of the bladder.

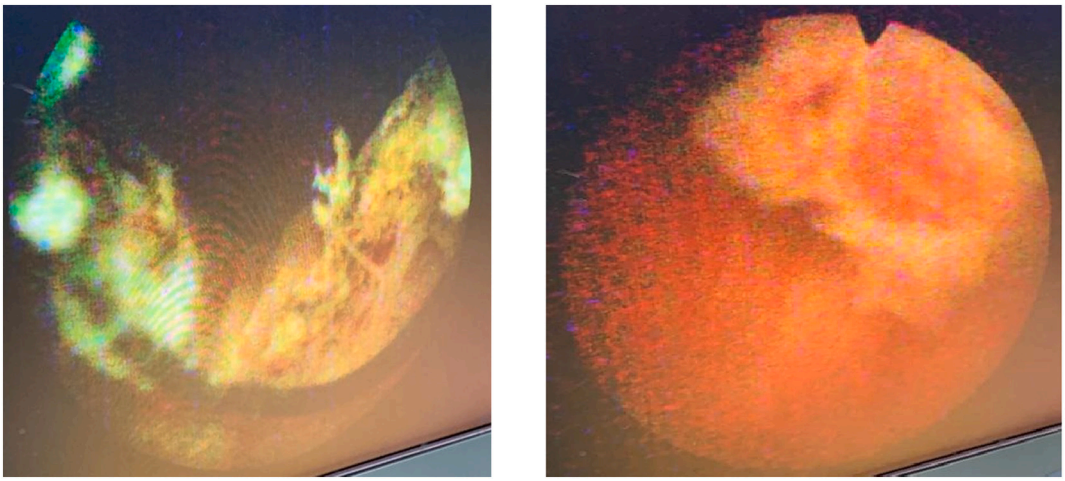

Fig. 3. Urethrocystoscopy findings.

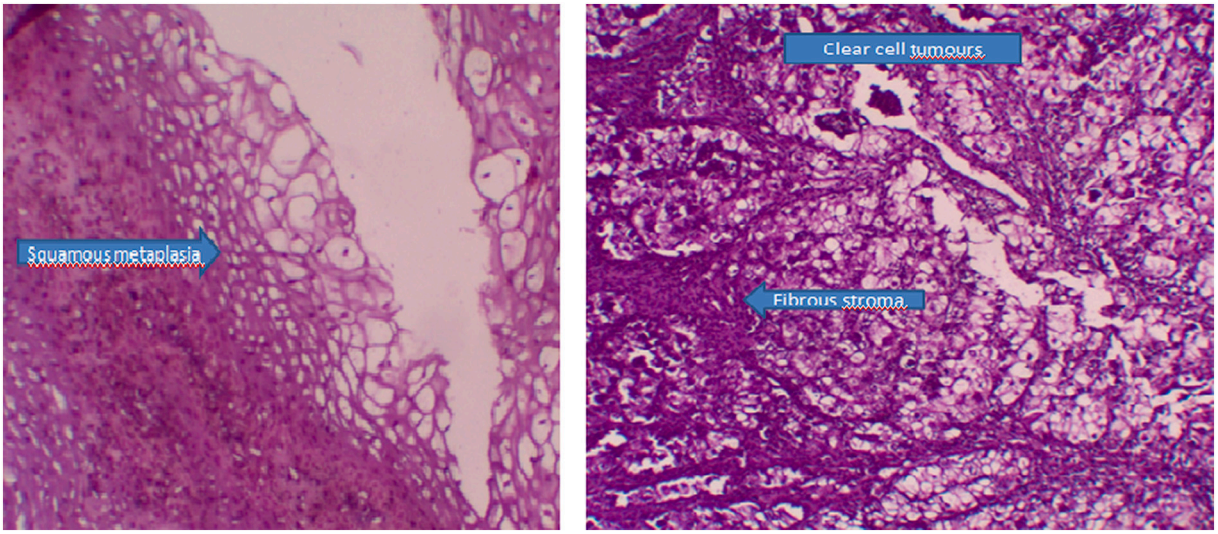

Fig. 4. Histopathological microscopic appearance.

[12].

The rarity of the disease entity made it difficult to have a definitive treatment strategy. The management in vogue is surgical such as tumor excision, radical nephro-ureterectomy or anterior pelvic exenteration with radiotherapy or chemotherapy complementary. The radical nephro-ureterectomy with the excision of the entire adjacent bulbocavernosus muscle is the only medical conduct that also presents evidence satisfactory to control he disease in T1 and T2 stages, with absence of local spread [3,5].

Urethral carcinomas are malignant cancers and are associated with poor outcomes, even in the setting of early-stage disease. Given the short urethra found in women, an already aggressive disease has considerable chance of local extension and major complications. In the case of female urethral carcinoma, local extension may mimic a primary clear cell adenocarcinoma of the vagina and differentiation is important for proper treatment. Although the rarity of FUA and the paucity of well-powered studies, several risk factors for decreased survival have been explained: age and race, tumor histology, clinical stage, nodal involvement, metastases, treatment modality, and response to treatment.

However, the most important prognostic factors are the clinical stage, the local extension of the primary cancer and the presence of nodal metastasis. Bracken et al. observed 81 cases of female urethral carcinoma and found that patients with large tumors (>4 cm) had a lower 5-year survival rate (13%) compared to patients with small tumor (<2 cm, 60%). Proximal tumors that involve the whole urethra have commonly been shown to be associated with poor oncological outcomes compared to distal tumors. Clinically, palpable lymph nodes are found in about a third of patients and more than 90% are metastatic at diagnosis. Among these patients the median 5- and 10-year overall survival is 44% and 29%, respectively. Instead, the disease free survival rate for patients with local advanced cancer is reported between 33% and 45%, but they have favourable prognosis with a 5-year survival rate of 73% when treated with anterior exenteration alone. While the treatment itself has been slow to change, mortality from the operation itself has dropped from an initial 23% to 0–5.3% as surgical technique and patient selection have drastically improved. However, 55% of urethral carcinoma recurs despite treatment and 10-year survival remains at only 60% [12].

4. Conclusion

Although female urethral carcinoma is a rare disease entity, clinicians should have strong suspicion of malignancies in patients to make an exact diagnosis. Careful clinical and image studies are helpful for making the correct diagnosis. Early radical surgery can achieve better outcomes, although the standard therapy remains controversial.

Consent

Written informed consent has been provided by the patient to have the case details and any accompanying images published, as stated by Committee on Publication Ethics (COPE) Guidelines, for the benefit of developing educational sciences. Institutional Approval is not required to publish this case. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Ethical approval

We hereby state that we have the approval from our Hospital Ethical Committee and the patient herself.

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Guarantor

Jufriadi Ismy, MD.

Research registration number

Our case report did not involve any human trials or studies, nor involving new knowledge, new device or surgical technique performed. This is a case report to enrich our knowledge more about female primary urethral carcinoma which is an exceedingly rare case.

CRediT authorship contribution statement

Study conception and design: Ismy, Pratama
Acquisition of data: Ismy, Pratama
Analysis and interpretation of Data: Ismy, Pratama
Drafting of manuscript: Ismy, Pratama
Critical revision: Ismy, Pratama.

Declaration of competing interest

None declared.

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