Cancer of the female urethra


Introduction: Primary cancer of the urethra is rare and represents about 0.02% of all neoplasia found in women and the majority of them are squamous cell carcinomas. Diagnosis is difficult due to the fact that the disease has usually reached advanced stage. Prognosis is dependent on clinical stage at the moment of diagnosis and tends to be poor.

Clinical case: This case is a 56-year-old female patient diagnosed with poorly defined primary papillary transitional cell carcinoma of the urethra with positive lymph nodes.

Discussion: Primary carcinoma of the urethra is a rare tumor with a higher incidence in women than in men (4:1). It most commonly appears in the sixth decade of the patient’s life. Chronic inflammatory processes and human papillomaviruses 16 and 18 have been associated as possible etiological factors. By 2004 one thousand two hundred cases had been described in women and 600 cases in men. Disease stage is the most important survival prognosis factor. Treatment is determined by the sex of the patient, disease stage, histological type, extension and localization.

Key words: Cancer of the urethra, papillary transitional cell carcinoma of the urethra

El cáncer primario de uretra es una rara entidad que representa cerca de 0.02% de todas las neoplasias encontradas en la mujer. La mayoría de éstas son de estirpe celular escamosa. El diagnóstico es difícil, debido al estadio avanzado en el que se suele presentar. El pronóstico de esta enfermedad es pobre, y depende del estadio clínico de la neoplasia al momento de su diagnóstico.

Caso clínico: Presentamos el caso de una paciente de 56 años de edad, con diagnóstico de carcinoma papilar transicional, poco diferenciado, primario de uretra, con ganglios positivos.

Discusión: El carcinoma primario de uretra es un tumor poco frecuente; su incidencia es mayor en mujeres que en hombres (4:1); la edad de aparición más frecuente es la sexta década de la vida. Como posibles factores etiológicos se han relacionado la inflamación crónica y el virus del papiloma humano tipos 16 y 18.

Hasta 2004 existían alrededor de 1200 casos descritos en mujeres y 600 en hombres. El estadio de la enfermedad es el factor pronóstico más importante de sobrevida. El tratamiento depende del sexo, de la estadificación, del tipo histológico, de la extensión y de la localización de la lesión.

Palabras clave: Cáncer de uretra, carcinoma papilar transicional de uretra, México.
INTRODUCTION

Primary cancer of the urethra was first described in 1833 by Boiven and Deuges in women and in 1834 by Thiaudarre in men (1). Until now, this is the only oncological urinary pathology showing a greater preference for women with a 4:1 ratio. The disease is rare and represents about 0.02% of all neoplasms found in women (2). The majority of these are classified as squamous cell neoplasms followed by adenocarcinoma and transitional cell carcinoma (2). Around 20% are adenocarcinomas of unknown origin (3). Diagnosis is difficult because the disease is usually in an advanced stage and symptomatology is dependent on localization and secondary to local irritation. Its clinical presentation varies from lower urinary irritative syndrome to microscopic or macroscopic hematuria (4). Prognosis is poor and dependent on tumor stage at the time of diagnosis. A combination of radiotherapy and surgery may result in local control of the disease and may increase the rate of survival (5) which does not surpass 20-30% at 5 years (4).

This article presents a case of papillary transitional cell carcinoma along with an extensive literature review.

CLINICAL CASE

The patient is a 56-year-old woman with a medical history of smoking 20 packs of cigarettes per year, type 2 diabetes mellitus of 10-year progression and vaginal hysterectomy for uterine myomatosis 5 years ago. She sought medical attention because of the sensation of a foreign body at the anterior wall of the vagina of 6-month progression, transvaginal bleeding accompanied by irritative urinary symptoms such as nocturia, urinary frequency, dysuria and initially intermittent hematuria. She said she had no fever, weight loss, transvaginal secretion or other accompanying symptoms. A private physician ordered kidney and bladder ultrasound and filling cystogram, all of which were normal. She was referred to the Gynecology Service because her urinary symptomatology became worse. Genital examination revealed a mass at the vaginal dome that was biopsied and sent to the Urology Service for evaluation.

The patient complained of significant dysuria as well as strangury that did not improve with analgesics. Physical examination revealed inguinal adenopathy and a hard, fixed, approximately 5 cm mass of stony consistency that was painful to the touch extending from the vaginal dome to the anterior wall of the vagina.

Laboratory tests reported Hb: 10.5g/dL, leukocytes: 11,200, platelets: 243,000, glucose: 163mg/dL, creatinine: 0.9mg/dL, liver function tests without alterations and LDH: 257. Abdominal computerized axial tomography (CAT) showed mass of approximately 5 cm at the proximal urethra level as well as bilateral inguinal adenopathy (Image 1).

The patient underwent urethrocystoscopy and the friable lesion which took up the proximal half of the urethra obstructing 80% of the urethral opening was biopsied. Excision biopsy of inguinal lymph nodes and puncture cystostomy were also carried out.

Histopathological study reported poorly defined primary papillary transitional cell carcinoma of the urethra with positive lymph nodes, classifying it as stage T3N2M0, clinical stage IV.

The patient was treated in the Oncology Service and was given 6 sessions of Gemzar® plus cisplatin chemotherapy and 25 radiotherapy sessions. She was kept under surveillance for a year and a half and remained stable until presenting with symptoms of intestinal obstruction and was diagnosed in the General Surgery Service with peritoneal carcinoma. She later presented with frozen pelvis and underwent anterior pelvic exenteration but her condition progressed rapidly and she died.

DISCUSSION

The urethra can be the site of both benign (neurogenic adenoma, papilloma, amyloidosis, hemangioma, leiomyoma, etc.) and malignant tumors. Primary carcinoma of the urethra is a rare tumor with a higher incidence in women than in men (4:1 ratio) (6), appearing more frequently in the sixth decade of life (7) and particularly affects white women (2). Chronic inflammation and 16 and 18 human papillomavirus have been associated as possible etiological factors (8).
By 2004 one thousand two hundred cases in women and six hundred cases in men had been described (6). The majority of these tumors are squamous cell tumors, followed by transitional cell tumors. The rarest tumors are adenocarcinoma. Macrosopically tumors may appear as polypoid, hardened or as superficial tumors are adenocarcinoma. Macroscopically tumors followed by transitional cell tumors. The rarest was squamous cell carcinoma (2).

In making diagnosis, imaging studies such as retrograde urethrography that can show urethral filling defect and computerized axial tomography and nuclear magnetic resonance that can evaluate local disease extension and distance are useful, but definitive diagnosis is made with urethrocytoscoppy and biopsy (9).

In reference to prognosis, in 2005 Yuvaraja et al. reviewed 18 cases and observed that disease stage was the most important survival prognostic factor. There was a 50% survival rate at 5 years in early tumor stage. In advanced disease there was a 56% survival rate at 3 years and no survival at 5 years. Mean survival rate in stage III and IV tumors was 23 months (4). Another prognostic factor observed in the study was tumor size. Survival rate was 60% in tumors under 2 cm, 46% in tumors between 2 and 4 cm and 13% in those larger than 4 cm. Histological type is another factor that should be taken into consideration since both synchronous and metachronic lymphatic metastases are more frequent in squamous cell carcinoma and are rare in transitional cell carcinoma (2).

Treatment is dependent on the sex of the patient, disease stage, histological type and lesion extension and localization. Survival rate at 5 years for women presenting with anterior urethral neoplasm is 75% and is 10-17% in patients presenting with disease in the posterior urethra (6). It is recommendable to treat anterior lesions with radical surgery (partial or total urethrectomy). On occasion local or laser excision can be used in superficial tumors. Posterior urethral lesions in women require pelvic exenteration with urinary diversion and ilioinguinal lymph node dissection (12).

Radiotherapy can be a curative alternative for inoperable local tumors that helps preserve anatomy and function. Ir-192 brachytherapy can be used in early stage lesions and external radiotherapy in larger tumors at doses of 45 – 50 Gy over 5 weeks (7). If there is lymph node affection the dose is 60-65 Gy (6) followed by interstitial implants with a total accumulative dose not exceeding 7500cGy. Wide fields that include the groin are recommended in cases of squamous cell and adenocarcinoma as well as in tumors that affect the vulva or vagina. Radiotherapy as palliative treatment does not appear to offer benefits in this disease. A combination of brachytherapy and external radiotherapy (13) has been used in some patients. In 2001 Guido Dalbagni et al reported a series of 6 patients treated with high doses of intraoperative brachytherapy followed by external radiotherapy in locally advanced disease. It was relatively well-tolerated and the authors suggested evaluating a larger series in order to obtain more reliable results.

Chemotherapy in advanced disease has only been used in non- controlled studies due to the low incidence of the pathology. It should be used in lesions affecting pelvic or inguinal lymph nodes with a 5-year survival rate not greater than 10-30%. Cisplatin, bleomycin 5 fluorouracil and methotrexate are the most commonly used cytostatics, although monotherapy is used only as palliative treatment. Curative treatment employs a combination of any of these agents and their use together with consolidation radiotherapy is recommended (14-18).

Our case was a 56-year-old woman presenting with papillary transitional cell carcinoma with locoregional extension due to lymph node invasion (clinical stage IV). Local curative treatment was not possible and so she was given combined chemotherapy and radiotherapy treatment. Complete response was achieved with the regimen employed although it produced early disease progression. Based on this experience we conclude that the combination of chemotherapy and radiotherapy continues to be an important alternative for patients who are not candidates for local treatment.

The absence of well-structured management protocol due to the low incidence of this disease in the world, points to the need for controlled multicentric studies to be carried out so that such protocol can be established.

BIBLIOGRAPHY