

## CASE REPORT

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### Declaration of ethical aspects

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# Primary transitional cell carcinoma of the fallopian tube

## Carcinoma primario de células transicionales de trompa de Falopio

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### ABSTRACT

Primary fallopian tube carcinoma is rare among primary malignant neoplasms of the genital tract. It accounts for approximately 1% of all malignant neoplasms of the female reproductive tract and is most common in menopausal women. A very rare histologic variant that may involve the fallopian tube is primary transitional cell carcinoma. It resembles epithelial ovarian cancer histologically and clinically. However, patients often have non-specific symptoms. Preoperative diagnosis is difficult due to the lack of specific diagnostic elements and the fact that it is rarely considered preoperatively. Diagnosis is usually based on histopathologic findings. In comparison to typical fallopian tube adenocarcinoma, this carcinoma is probably not as aggressive, has a better response to chemotherapy and a good prognosis compared to epithelial ovarian carcinoma. It is important to consider primary tumors of the fallopian tube in the differential diagnosis of pelvic tumors. A case of primary transitional cell carcinoma of the fallopian tube is presented.

**Key words:** Carcinoma, transitional cell, Fallopian tube carcinoma

### RESUMEN

El carcinoma primario de la trompa de Falopio es poco frecuente entre las neoplasias malignas primarias del tracto genital. Representa aproximadamente el 1% de todas las neoplasias malignas del aparato reproductor femenino y es más frecuente en las mujeres menopáusicas. Una variante histológica muy poco frecuente que puede afectar la trompa de Falopio es el carcinoma primario de células transicionales. Se parece al cáncer epitelial de ovario desde el punto de vista histológico y clínico. Sin embargo, las pacientes suelen presentar síntomas inespecíficos. El diagnóstico preoperatorio es difícil debido a la falta de elementos concretos para ello y a que rara vez se le considera en el preoperatorio. Generalmente el diagnóstico suele basarse en los hallazgos histopatológicos. En comparación con el adenocarcinoma típico de las trompas de Falopio, es probable que este carcinoma no sea tan agresivo, tenga una mejor respuesta a la quimioterapia y un buen pronóstico en comparación con el carcinoma epitelial de ovario. Es importante tener en cuenta los tumores primarios de las trompas de Falopio en el diagnóstico diferencial de las tumoraciones pélvicas. Se presenta un caso de carcinoma primario de células transicionales de la trompa de Falopio.

**Palabras clave.** Carcinoma de células transicionales, Trompa de Falopio, carcinoma

### INTRODUCTION

Primary fallopian tube carcinoma is the least common gynecologic neoplasm. It accounts for approximately 1% of malignant neoplasms of the female reproductive tract. The most common malignant histologic type is adenocarcinoma, which accounts for 90% of cases<sup>(1)</sup>. Sarcoma and clear cell, squamous cell, endometrioid, transitional and mixed cell carcinomas are other less common histologic types<sup>(2)</sup>.

Primary transitional cell carcinoma of the fallopian tube is a rare histologic variant that usually occurs in menopausal women, with approximately 25 cases documented in the literature. Its origin is a subject of research and debate among experts. Several theories have been proposed, but there is no definitive explanation<sup>(3)</sup>. Abdominal or pelvic lump, vaginal bleeding, abdominal pain and ascites are the most common clinical manifestations<sup>(4)</sup>. Because the signs and symptoms are nonspecific, it is very difficult to make a preoperative diagnosis. Most cases require surgical treatment together with adjuvant chemotherapy<sup>(3)</sup>. A case of primary transitional cell carcinoma of the fallopian tube is presented.

## CASE REPORT

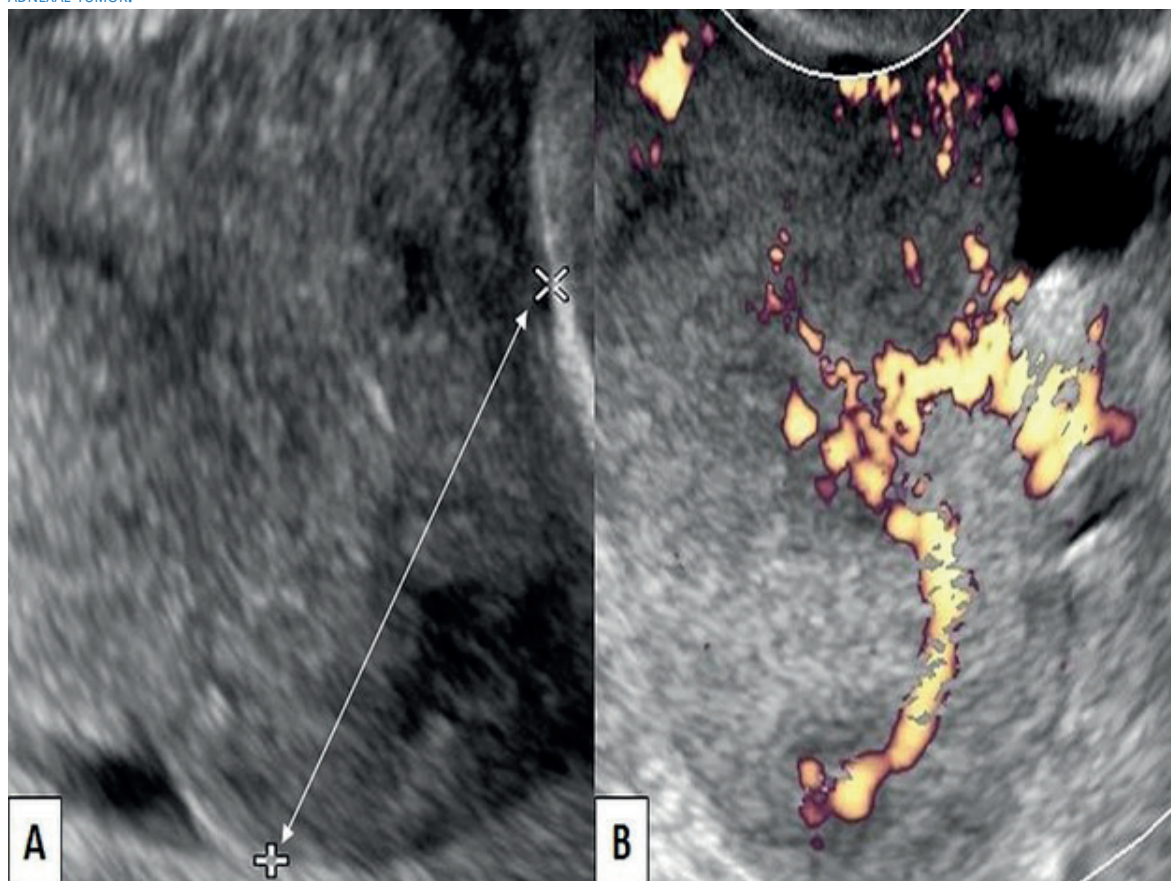
A 65-year-old nulligesta female patient came to the gynecology office for presenting adnexal lump during a routine ultrasound evaluation. She denied genital bleeding, weight loss, abdominal pain or distension, gastrointestinal problems or urinary symptoms. She reported amenorrhea since age 49 and had been diagnosed with chronic arterial hypertension 20 years ago, which was being treated with enalapril. The patient denied a history of smoking, alcohol or illicit substance use, and chronic or neoplastic diseases in her family.

On physical examination she appeared in good general condition, afebrile and hydrated. The Eastern Cooperative Oncology Group (ECOG) functional rating scale was 0. Vital signs were within normal limits. No tumors were found during abdominal examination. However, gynecological examination revealed a hypoplastic uterus with a tumor in the right adnexa of

variable consistency and limited mobility, with about 8 centimeters diameter. On digital rectal examination there was no evidence of the tumor in the cul-de-sac of Douglas. No edema or local lymphadenopathy was found.

Pelvic ultrasound showed a heterogeneous, mostly solid tumor with irregular borders near the right ovary and on the right posterolateral aspect of the uterus, measuring 24 x 22 x 20 millimeters. Its origin was difficult to determine because the adnexa and uterus presented atrophic changes associated with age. The bladder also appeared normal, without calculi. The presence of blood flow was evident on color Doppler ultrasound (Figure 1). No evidence of ascites or metastases was found. Pelvic MRI revealed a well-defined round solid-cystic lesion measuring 3 x 2 x 2 centimeters in the right adnexa and minimal free fluid in the cul-de-sac of Douglas. Chest radiography showed no alterations. Vaginal cytology findings were compatible with atrophic changes and negative for malignancy.

FIGURE 1. ULTRASOUND IMAGE OF RIGHT ADNEXA. A) GLOBULAR AND HETEROGENEOUS SOLID-CYSTIC ADNEXAL TUMOR. B) VASCULARIZATION OF THE RIGHT ADNEXAL TUMOR.





The results of complete hematology, renal and hepatic functionalism, urine tests and electrolytes were all within normal limits. The tumor marker panel showed CA-125 values of 119 IU/mL (normal value less than 35 U/mL). Alpha-feto-protein, human chorionic gonadotropin, CA19-9 and carcinoembryonic antigen concentrations were within normal limits. The results led to the decision to perform an exploratory laparotomy for the possibility of ovarian malignancy.

During the surgical procedure, the right fallopian tube was found to be enlarged, elongated, irregular in shape, with a predominance of solid areas and cystic areas and fragile in consistency. It was partially adhered to the uterine wall without evidence of infiltration. No morphological alterations were found in the right ovary. The left ovary, the left tube and the uterus showed no macroscopic alterations. There were no enlarged pelvic or para-aortic nodes. No obvious deposits were found on the peritoneal surfaces of the cul-de-sac, liver, omentum or diaphragm. No ascitic fluid was found in the abdominopelvic cavity. Intraoperative frozen section of the tumor was reported as malignant epithelial tumor, so tumor resection, total abdominal hysterectomy, bilateral oophorosalingectomy, appendectomy, infracolic omentectomy, bilateral pelvic and para-aortic lymphadenectomy, multiple peritoneal biopsies and peritoneal lavage were performed.

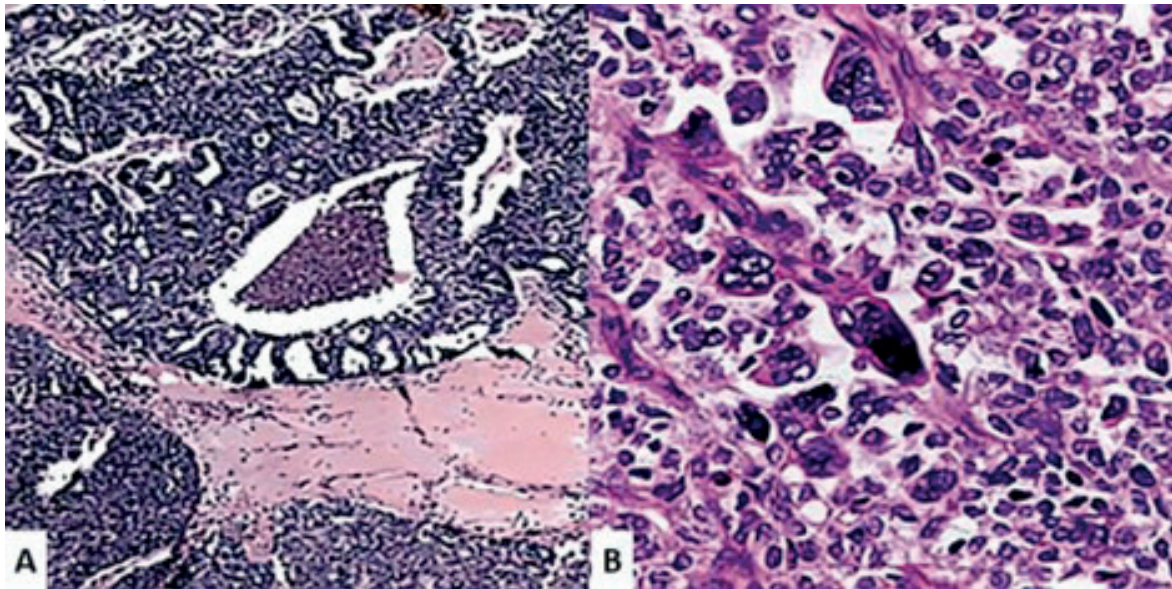
The anatomopathological study revealed that the right fallopian tube presented a mainly solid tumor with a surface area of 7 x 5 x 4 cm between the ampulla and the isthmus. Several thin-walled cysts of 0.5-20 millimeters covered its surface (Figure 2). The fimbria had a soft to rubbery consistency with lumen occluded by a grayish-bluish area, without the presence of tumors. On microscopic examination, the tumor showed a broad papillary growth pattern with fibrous septa, nests and atypical polygonal cell papillae, as well as perforated microcystic spaces and patchy areas of necrosis (Figure 3). In addition, the nuclei of the tumor cells had prominent nuclear grooves with more than 20 mitoses per 10 high-power fields. There was no evidence of tumor cells in the peritoneal lavage fluid. Immunohistochemical staining showed a positive signal for CK7 and epithelial membrane antigen, while staining was negative for p53, CK20, and p63. Histological findings confirmed the diagnosis of primary transitional cell carcinoma of the fallopian tube.

The patient was discharged four days after surgery, without complications. She received six cycles of adjuvant chemotherapy with paclitaxel and carboplatin. At the end of the treatment, CA-125 concentrations were less than 35 IU/L. No evidence of disease was found on abdomino-pelvic CT imaging. She is currently being monitored by the medical oncology service.

FIGURE 2. TUMOR IN RIGHT TUBE SHOWING HETEROGENEOUS LESION, MAINLY SOLID.



FIGURE 3. PATHOLOGIC ANATOMIC IMAGES OF TRANSITIONAL CELL CARCINOMA OF THE FALLOPIAN TUBE. A) NEOPLASTIC CELLS FORMING LAMELLAE AND TRABECULAE AND AREAS OF PATCHY NECROSIS (HEMATOXYLIN-EOSIN STAIN, 40X). B) ATYPICAL POLYGONAL CELLS FORMING NESTS AND PAPILLAE (HEMATOXYLIN-EOSIN STAIN, 400X).



## DISCUSSION

Due to a number of factors, primary fallopian tube carcinoma is often misdiagnosed as ovarian carcinoma preoperatively. These difficulties are caused by the low frequency of the condition and nonspecific clinical features. The only recognized risk factor is the germline BRCA mutation<sup>(4)</sup>. Most patients with fallopian tube carcinoma are menopausal. Tubal carcinoma is more common in nulliparous women<sup>(2,5)</sup>.

Because of its better prognosis and response to chemotherapy, transitional cell carcinoma of the fallopian tube is a rare histologic subtype that must be distinguished from the other subtypes. The form is similar to that of urothelial tumors<sup>(6)</sup>. This tumor could be a consequence of transitional cell metaplasia of the tubal serosa or mucosal epithelium. Possible causes include paratubal cyst metaplasia or Walthard cell nests<sup>(5)</sup>. Patients with these tumors have a median age of 56 years (range 41-79 years)<sup>(3)</sup>.

The diagnosis of adnexal tumors is complex and involves clinical features, ultrasound findings and tumor markers. Each individual parameter is non-specific and may be absent<sup>(7)</sup>. Because of the nonspecific symptoms and low index of suspicion due to their rarity, preoperative diagnosis of tubal tumors is often a difficult task, with a reported preoperative diagnosis rate of 2%<sup>(1)</sup>.

Between 50%-60% of patients with primary malignant fallopian tube neoplasms experience vaginal bleeding or hemorrhage, abdominal and/or pelvic lumpiness and abdominal pain 30%-40%. Latzke's triad of symptoms, consisting of intermittent profuse serosanguinolent vaginal discharge, abdominal tumor and abdominal or pelvic pain has been described in only 15% of cases<sup>(4)</sup>.

Ultrasonography is useful for detecting tubal tumors. However, when detected, other imaging modalities such as computed tomography and magnetic resonance imaging are not useful in establishing the diagnosis<sup>(8)</sup>. In patients with primary fallopian tube carcinomas, pretreatment CA-125 concentrations are an independent predictor of disease-free survival and overall survival. Moreover, current evidence suggests that it could be useful for monitoring response to treatment and detecting recurrences. However, its value as an independent prognostic factor is still unclear. Further research with larger samples and good design is needed to better understand the relationship of CA-125 with prognosis of fallopian tube carcinoma<sup>(8)</sup>.

Cases of primary fallopian tube carcinomas may present with abnormal cervical cytology indicating adenocarcinoma between 0% and 23%<sup>(9)</sup>. However, a single case of diagnosis of transitional cell carcinoma of the fallopian tubes from cervical cytology has been reported<sup>(10)</sup>.



To establish the clinical course, predict the prognosis and possibly improve treatment, it is essential to make an accurate diagnosis and differentiate primary fallopian tube carcinoma from lesions arising from the ipsilateral ovary by direct extension or from the contralateral ovary by transcellular route. The definitive diagnosis is made by histologic findings. The criteria to differentiate them from ovarian tumors include: the tumor arises from the endosalpinx with a histological pattern that reproduces the epithelium of the tubal mucosa, they present transition from benign to malignant epithelium and the ovary does not present invasion or has a smaller tumor than that of the fallopian tube<sup>(11)</sup>.

The treatment for primary transitional cell carcinoma of the fallopian tube is surgery with subsequent adjuvant chemotherapy. Staging laparotomy is the recommended type of intervention. Pelvic and para-aortic lymphadenectomy is necessary in patients with primary fallopian tube carcinoma because it has been shown that, compared to epithelial ovarian cancer, they have higher rates of retroperitoneal and distant lymph node metastases<sup>(12)</sup>.

Transitional cell carcinoma is among the subtypes with good response to adjuvant chemotherapy<sup>(13)</sup>. Cases with stage I tumors without risk factors have 100% survival at 5 years and do not require additional chemotherapy. In contrast, adjuvant chemotherapy is required for stage I patients with risk factors (such as muscle layer invasion or tumor in the fimbria) and higher stages<sup>(12,14)</sup>. At two years, cases with primary transitional cell carcinoma of the fallopian tube have a better overall survival prognosis. Furthermore, compared to other primary fallopian tube carcinomas, their relapse rate is later<sup>(15)</sup>.

Primary fallopian tube carcinoma is increasingly being treated with a combination of adjuvant chemotherapy, consisting of carboplatin and paclitaxel, used in epithelial ovarian carcinoma<sup>(16)</sup>. Patients with stage I tumors without risk factors have 100% survival at 5 years and do not require additional chemotherapy. In contrast, additional chemotherapy is required for patients with risk factors (such as invasion of the muscular layer or tumor in the fimbria) and higher stages<sup>(12,14)</sup>.

In conclusion, primary fallopian tube carcinoma accounts for less than 1% of all cancers of the

female genital tract. Primary transitional cell carcinoma of the fallopian tube is a rare and malignant tumor, whose preoperative classification is difficult and definitive diagnosis depends on pathologic findings. However, it has better response to chemotherapy and good prognosis compared to epithelial ovarian carcinoma. This tumor should be considered among the differential diagnoses of adnexal tumors.

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