Case Report

Primary transitional cell carcinoma of the endometrium: Exceptional presentation of a rare tumor☆

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ABSTRACT

Transitional cell carcinoma (TCC) is an extremely rare gynecologic tumor, particularly in the endometrium. All endometrial TCC cases reported so far in the literature were diagnosed at relatively advanced stages. In the present article, we report a pure primary endometrial TCC initially revealed by an abdominal mass and classified as an International Federation of Gynecology and Obstetrics stage IA. The patient was successfully treated with surgery and adjuvant radiotherapy. This case highlights the importance of early diagnosis of gynecologic malignancies, offering satisfactory outcomes even in the rarest types for which evidence-based recommendations are lacking.

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Introduction

Transitional cell carcinoma (TCC), also known as urothelial carcinoma, is an exceptional histological type in gynecologic oncology. The cases reported in the literature are most often localized to the ovary, where they represent less than 2% of ovarian cancers [1,2]. More importantly, endometrial TCC represents a diagnostic and therapeutic challenge for clinicians, given the lack of specific recommendations for this tumor. However, it is essential to perform an entire urinary tract exploration before making the diagnosis of primary endometrial TCC to rule out a urologic origin of the tumor.

Only a few cases of endometrial TCCs have been reported in the literature, almost all of which were diagnosed at advanced stages with myometrial tumor invasion [2–16]. However, cases of invasive TCC discovered at an early stage have never been published. We report below a case of pri-
primary invasive TCC of the endometrium diagnosed at an early stage.

**Clinical presentation**

A 58-year-old White-skinned female with no previous medical history presented with an abdominal mass associated with whitish leukorrhea and intermittent vaginal bleeding lasting for 2 months. Physical examination found a large, painless subumbilical mobile mass of firm consistency. Gynecological examination found endo-uterine bleeding without noting any abnormality of the cervicovaginal tract. An abdominal-pelvic computed tomography (CT) scan showed a dual-component pelvic mass (cystic and fleshy) at the expense of the uterine body, measuring 12.96 × 15.55 cm. No deep adenomegaly was detected, and the upper and lower urinary tract and digestive structures were radiologically normal (Fig. 1).

An endometrial biopsy brought poorly differentiated carcinomatous cells. Then the patient underwent a total hysterectomy with bilateral adnexectomy, without lymph node dissection. Macroscopically, the uterus was enlarged, weighing 850 g, distended by endocavitary serous fluid dilating the uterine wall, which became thinned to less than 5 mm at the lateral and fundal areas. This fluid collection was accumulating upstream of a large friable isthmic tumor of 7 × 7 × 5 cm diameters. A microscopic study found an infiltrative malignant epithelial proliferation, affecting only the endometrium at its isthmic part, made of transitional-type cells of high-grade malignancy and assembled in infiltrative sheets and papillary structures resembling urinary tract TCC. Peri-tumoral vascular emboli were absent. The myometrium was tumor-free but highly atrophic with only 5 mm thickness. No other associated histological type was observed.

Immunohistochemical staining of the tumor cells found positive labeling for anti-CK7, anti-CK20, and anti-P63 antibodies and negative labeling for anti-P53, anti-WT1, and anti-β-catenin antibodies (Fig. 2).

Urinary panendoscopy performed postoperatively did not detect any primary tumor of the urinary tract. We concluded that the patient had a primary pure high-grade TCC of the endometrium, without myometrial invasion and without vascular emboli, corresponding to the International Federation of Gynecology and Obstetrics (FIGO) stage IA and to the European Society of Medical Oncology high-intermediate risk category.

On the advice of the multidisciplinary team meeting, the patient received adjuvant external radiotherapy to the pelvis.

**Fig. 1.** – Pelvic axial-enhanced CT image showing a large intrauterine fluid collection (black continuous arrow) thinning the uterine wall (white dotted arrow) upstream of a 7 cm posterior isthmic tumor (black asterisk).

**Fig. 2.** – Microscopic examination (hematoxylin and eosin staining, magnification ×20 on the right and ×40 on the left) of the tumor showing the malignant epithelial proliferation made of transitional cells arranged in papillary sheets, with chorion invasion, resembling TCC of the urinary tract.
Table 1. – Clinical and pathological features of previous reports of primary endometrial TCCs.

| Author (year of publication) | Patient age (years) | Histological type | Tumor size (cm) | FIGO stage | Follow-up |
|------------------------------|---------------------|-------------------|-----------------|------------|-----------|
| Chen et al. (1990) [3]       | 71                  | TCC (95%) + endometrioid + mucinous | 5.5             | III A      | NED after 5 years |
| Spiegel et al. (1996) [4]    | 75                  | TCC (75%) + endometrioid + (5%) + endometrioid + mucinous | 3              | I B        | NED after 4 months |
| Lininger et al. (1997) [5]   | 53                  | *TCC (50%) + squamous + spindle cell sarcoma | 3.2            | I B        | NED after 8 years |
|                             | 83                  | TCC (70%) + endometrioid + sero-papillary | 7              | I C        | NED after 35 months |
|                             | 64                  | TCC (75%) + endometrioid + squamous | 5              | I C        | Tumor Relapse after 1 year |
|                             | 43                  | TCC (80%) + endometrioid + squamous | 2              | I C        | Lost |
|                             | 60                  | TCC (95%) + squamous | 1.5             | I B        | Lost |
|                             | 73                  | TCC (95%) + squamous | 0.4             | I B        | Dead due to metastatic colic cancer after 13 years |
|                             | 41                  | *TCC (15%) + squamous + papillary | 0.8            | III A      | Lost |
| Fukunaga et al. (1998) [6]  | 50                  | TCC (95%) + endometrioid | 10             | I B        | NED after 7 years |
| Labonte et al. (2001) [7]   | 46                  | TCC (90%) + endometrioid | 8              | IV A       | NED after 18 months |
| Lum et al. (2005) [11]      | 77                  | NR (8.6) | 8.6            | IV A       | NED after 18 months |
| Aihuwalla et al. (2006) [12] | 78                 | TCC (95%) + endometrioid | 2              | I B        | NED after 10 months |
| Giordano et al. (2007) [8]  | 61                  | TCC (100%) | 1.5            | I B        | NR |
| Ribeiro-Silva et al. (2007) [13] | 84                | *TCC (15%) + squamous + papillary | 5              | I B        | Dead after 1 year |
| Mariño-Enriquez et al. (2008) [14] | 55              | TCC (100%) | 4              | I B        | NED after 6 months |
|                             | 76                  | TCC (80%) + endometrioid | NR             | I B        | NED after 3 months |
|                             | 63                  | TCC (50%) + endometrioid | 3.7            | I B        | NED after 16 months |
|                             | 73                  | *TCC (20%) + endometrioid | 6.5            | I B        | NED after 6 months |
|                             | 57                  | TCC (90%) + endometrioid | 5.5            | II B       | NED after 8 months |
| Tong et al. (2013) [15]     | 66                  | TCC (100%) | 3.5            | I B        | NR |
| Cuccia et al. (2018) [2]    | 65                  | TCC (100%) | 2.2            | I B        | Peritoneal relapse after 43 months |
| Cubo-Abert et al. (2018) [9] | 40                 | TCC (100%) | NR             | III C      | Stable residual disease after 7 months |
| Azzakhham et al. (2020) [16] | 62                | *TCC (15%) + squamous papillary | NR             | I B        | NR |
| Sahu et al. (2020) [17]     | 62                  | TCC (100%) | NR             | I B        | NR |
| Amjad et al. (2022) [10]    | 58                  | TCC (100%) | 0.1            | II         | NED after 5 years |
| Present case                | 58                  | TCC (100%) | 7              | I A        | NED after 5 years |

NED, no evidence of disease; NR, not reported.

* Not classified as endometrial TCC primaries as the TCC component represented less than 50% of the tumor

† Substages IA, IB, or IC not reported.

40 days after surgery using the 3D conformal technique. A total dose of 45 Gy in 1.8 Gy/fraction was delivered to the tumor bed and pelvic lymphatic chains by 6 photon beams of 18 MV energy in 25 fractions and 35 days. Five years after the end of radiotherapy, the patient remained tumor-free, without any side effects affecting her daily life.

Discussion

Because of its rarity, knowledge about primary endometrial TCC has been exclusively limited to clinical case reports. To date, only 27 cases have been published, almost all about tumors discovered at relatively advanced stages (Table 1) [2-17]. Only one publication reported by Lininger et al. in 1997 did not specify the presence or absence of myometrial involvement for 2 FIGO stage I cases [5]. Thus, our observation is the first in the English literature to report a case of pure endometrial TCC, specifying the absence of myometrial invasion (FIGO stage IA).

There are no specific features to recognize primary endometrial TCC on imaging. However, we note the uncommon presentation of our case where CT showed an enlarged uterine cavity (15.5 cm) above the large isthmic tumor of 7 cm in size, which is among the largest sizes reported so far.

TCC originating from the ovary or the urinary tract should always be ruled out before making the diagnosis of primary endometrial TCC. In addition to imaging, both immunohistochemical study and urinary tract endoscopy are essential diagnostic tools to rule out other primaries and confirm the endometrial origin of the tumor.
Pathological examination is the cornerstone of diagnosis process. Endometrial carcinoma is classified as primary TCC when the transitional component represents more than 50% of the tumor; otherwise, pathology response would be endometrial carcinoma with transitional cell differentiation [10]. Among the 27 published cases of endometrial TCC, 5 had less than 50% of the TCC component, thus failing to comply with the definition of primary endometrial TCC [5,13,14,16]. Only 7 cases were pure TCCs (TCC representing 100% of the tumor), whereas the remaining 15 cases had a mixed histology where TCC was associated with either endometrioid, mucinous, papillary serous, squamous cell carcinoma, or spindle cell sarcoma (Table 1). Our case was a pure endometrial TCC, with the particular presentation at an early FIGO stage IA despite the large tumor size.

Based on the limited literature data, adding radiation therapy after complete surgical removal is a reasonable adjuvant option to maximize control of primary endometrial TCC. The few published cases have also reported the use of adjuvant radiotherapy, either external radiotherapy or brachytherapy [2–5,7]. In our case, the tumor was classified in the high-intermediate risk category of the European Society of Medical Oncology, with propositions of adjuvant treatment ranging between external-beam radiotherapy and local vaginal brachytherapy. Given that the 7 cm tumor was entirely endouterine without cervical involvement and that the vaginal margins were negative, adjuvant external-beam radiotherapy seemed more appropriate than vaginal brachytherapy, especially when considering the low probability of pelvic postradiation toxicity (urinary and digestive) ensured by the conformal technique at the dose of 45 Gy in 25 fractions.

Our patient remained in good tumor control after 5 years of follow-up. Most published cases of primary endometrial TCC had good control at the time of publication; only 2 cases of relapse were noted during follow-up [2,5]. Nevertheless, it should be noted that the majority of cases had less than 1 year of follow-up, and only 5 cases had prolonged follow-up of 5 years or more.

Conclusion

The present case is the first in the literature to report a pure primary invasive endometrial TCC diagnosed at FIGO stage IA, with excellent long-term oncological outcomes. It highlights the major role of early diagnosis in gynecologic malignancies by facilitating patients’ access to early screening facilities. Early diagnosis increases the chances of therapeutic success, even in rare tumors lacking evidence-based recommendations.

Patient consent

Written consent was obtained from the patient for publication of this article.

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