Transitional Cell Carcinomas in the Bladder and Ovary: Unusual Primary Association or Metastatic Lesions?

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Transitional cell carcinoma (TCC) has been recognized as one of the main epithelial carcinomas of the ovary. It is a rare tumor, but its true incidence remains unknown. It is characterized by its histologic resemblance to TCC of the bladder. The coincident association of TCCs of the ovary and the bladder involves two possible diagnoses: the ovarian TCC could be a primary TCC, or it could be the result of metastasis of a bladder TCC. We present a case of TCC of the ovary in a patient who had previously suffered from high-grade superficial transitional cell urinary bladder cancer.

A 42-year-old woman was admitted to Ibn-Sina hospital with hematuria. She underwent transurethral resection of the bladder (TURB) for diagnostic and therapeutic purposes. Histopathologic analysis showed a TCC pT1b G3. Concurrent ultrasound examination and abdominal computed tomography (CT) showed no other tumors in the pelvis or abdomen. Further superficial papillary tumors involving the bladder were resected at the 24- and 36-month regular follow-ups. CT scans performed as part of the follow-up procedures failed to detect any other pelvic or abdominal tumors. TURB was performed on both occasions, but the patient refused intravesical chemotherapy.

The patient was hospitalized for abdominal pain 2 months after the last resection (38 months after the initial resection). Pelvic CT scan revealed an 11.0-cm cystic mass in the pelvis (Figure 1). The results of bladder imaging were normal. Laparoscopic resection of the ovarian tumor was performed, including a left salpingo-oophorectomy, omentectomy, and sampling of ascites fluid. The right ovary was macroscopically normal.

Pathologic examination of the monocystic lesion revealed multiple small papillary formations partly covering the external and internal surfaces of the cyst. Microscopic examination showed ovarian tissue infiltrated by malignant transitional epithelium composed of blunt papillae lined with stratified epithelium with solid nests. Periodic acid-Schiff-positive microcystic spaces were also identified (Figure 2). The cells had round or ovoid nuclei, with nucleoli or longitudinal grooves, and frequent mitosis. The tumor was extensively sampled, and no components of other ovarian epithelial tumors, such as serous or endometrioid adenocarcinomas, were found. The presence of a benign or borderline Brenner component was also excluded. The omentum was free of tumor and the cytology of the ascites fluid was negative for malignant cells. This ovarian tumor was indistinguishable from the previous TCC of the bladder, and was initially diagnosed as an ovarian metastasis from the urinary bladder carcinoma. Indeed, the TURB examination performed at 36 months demonstrated the same features, with papillary structures lined

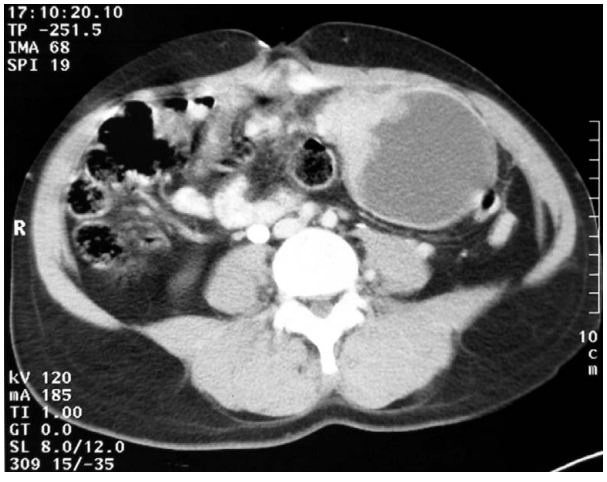

Figure 1. Pelvic computed tomography scan shows an 11.0-cm cystic mass of the pelvis.

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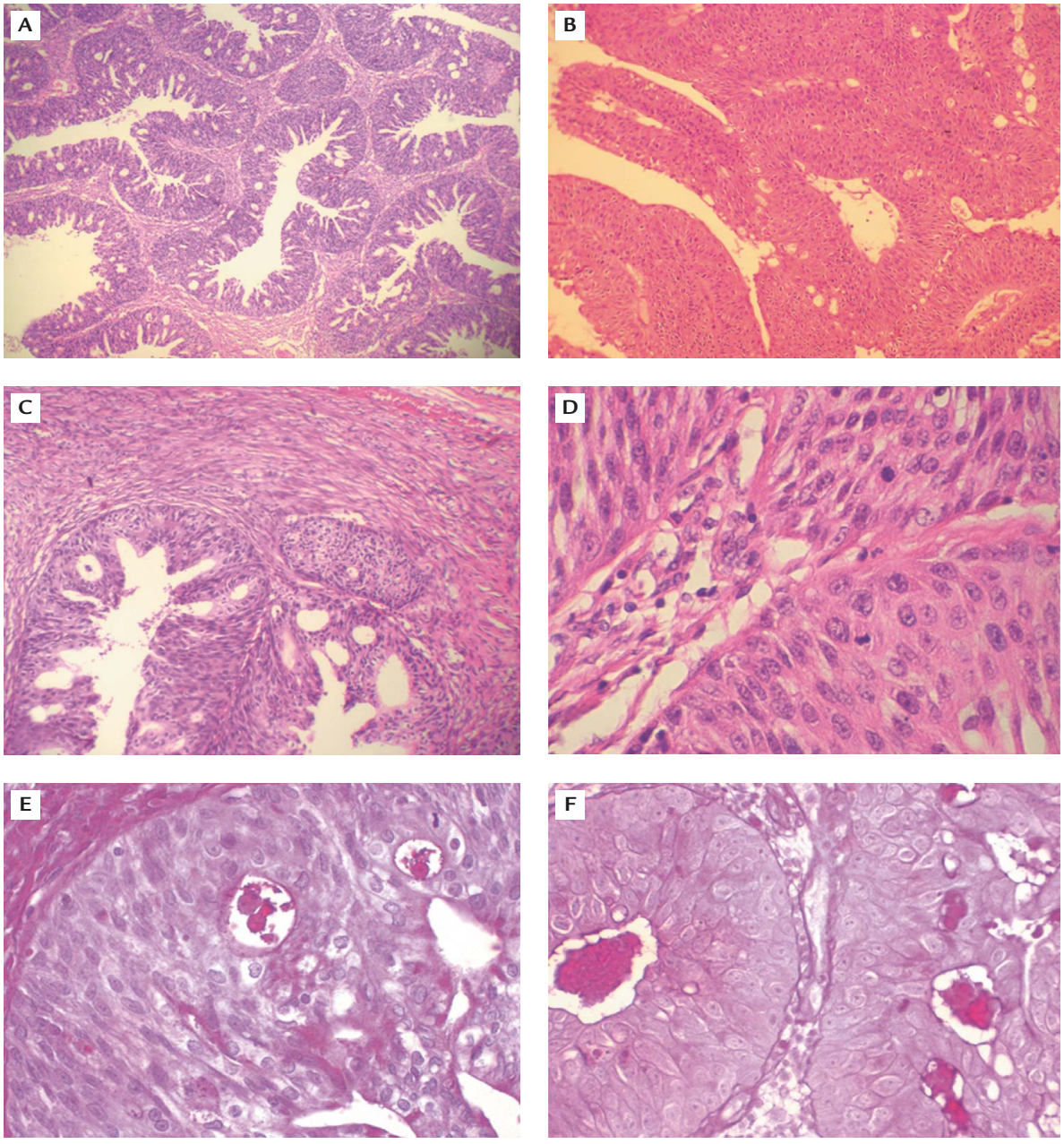

Figure 2. (A) Low-power view of the ovary tumor showing blunt papillae lined by multilayered epithelium (hematoxylin and eosin [HE]; original magnification, ×40). (B) Low-power view of the 36-month follow-up transurethral bladder biopsy showing the same pattern (HE, ×40). (C) Solid neoplastic nests invading the ovarian stroma (HE, ×200). (D) High-power view showing the ovarian tumor cells with round or ovoid nuclei, nucleoli, longitudinal grooves, and frequent mitosis (HE, ×400). Microcysts of varying sizes, strongly Periodic acid-Schiff-positive in the (E) ovarian tumour, and (F) bladder transitional cell carcinoma.

by transitional cells and mucus-containing microcysts (Figure 2).

Specimens from the bladder and ovary were stained with monoclonal antibodies for CK7, CK20, and CA125. Both tumors were diffusely and homogeneously positive for CK7. However, the bladder TCC showed focal and heterogeneous CK20 expression, while the ovarian tumor was negative for CK20. The Mullerian marker CA125 was strongly expressed in the ovarian cells, while this marker was negative in the bladder TCC (Figure 3). The immunohistochemical results are summarized in the Table. These data support the diagnosis of a primary ovarian tumor. Additional laparotomy to complete surgical resection and adjuvant chemotherapy were planned.

TCC of the ovary is a subtype of ovarian carcinoma, characterized by a histologic resemblance to TCC of the bladder [1]. The World Health Organization classification defines ovarian TCC as a carcinoma that presents with morphologic urothelial features but, in contrast to malignant Brenner tumor, lacks the elements of benign or borderline Brenner tumors. It is characterized

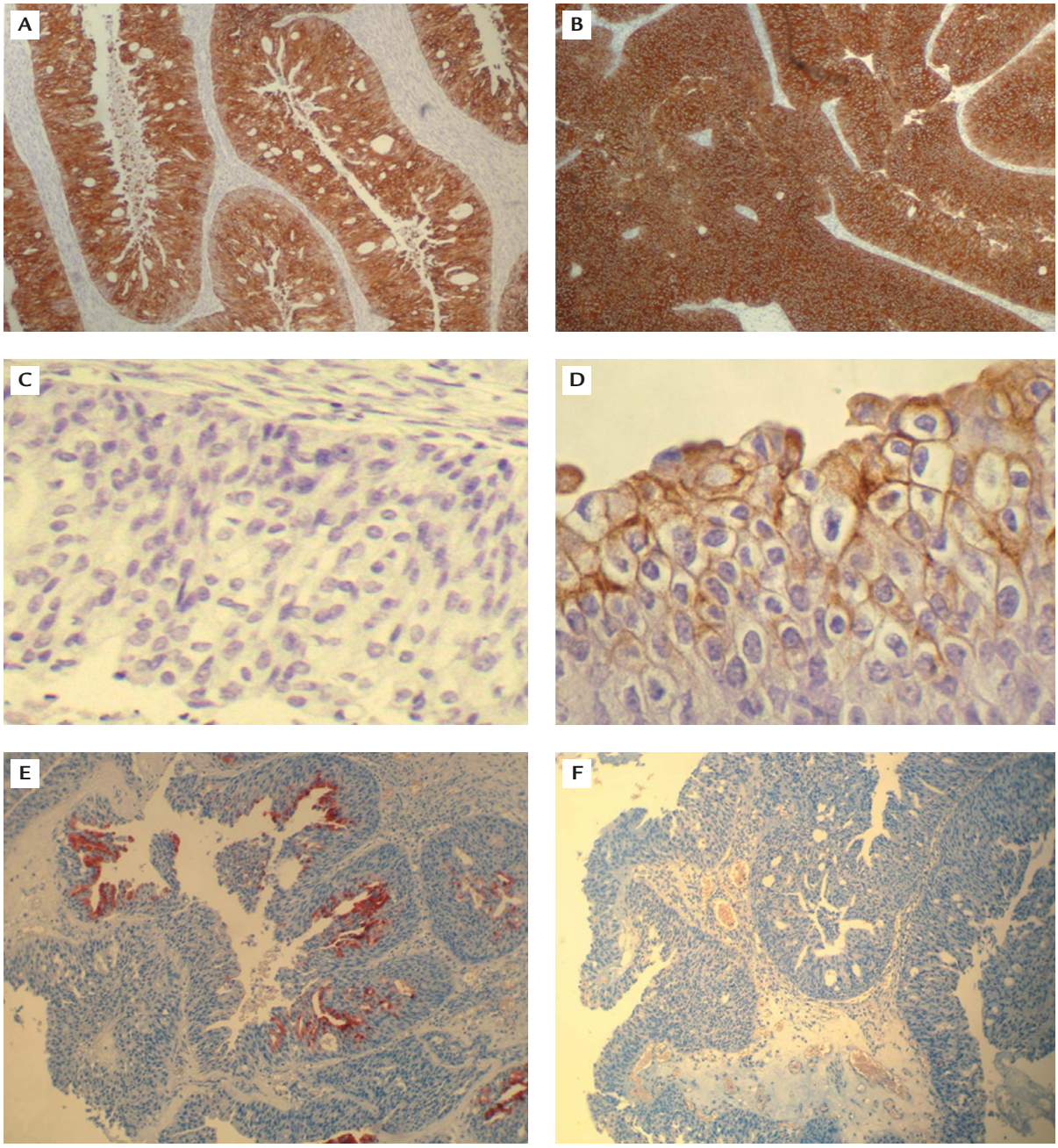

Figure 3. Immunohistochemical staining. CK7 expressed in a diffuse membrane pattern in both (A) ovarian and (B) bladder tumors (original magnification, ×200). (D) CK20 was focally expressed in a heterogeneous membrane pattern in the bladder transitional cell carcinoma (original magnification, ×400), but not in the ovary transitional cell carcinoma (C; original magnification, ×200). (E) CA125 was strongly and heterogeneously expressed in the ovarian proliferation, (F) but not in the bladder (original magnification, ×40).

Table. Summary of immunohistochemical results

Markers	Source	Clone	Dilution	Ovarian tumor	Bladder tumor
CK7	DAKO	OV-TL 12/30	1:30	Positive (membranous pattern)	Positive (membranous pattern)
CK20	DAKO	Ks20.8	1:300	Negative	Focal and heterogeneous positivity (membranous pattern)
CA125	Immunotech, Westbrook, ME	OC125	Prediluted preparation	Positive	Negative

by the presence of papillae lined by malignant cells of transitional cell type, and sometimes by mucin-producing glands [1,2]. This neoplasm can occur in a pure form, but is frequently associated with other cell types (serous, endometrioid, or undifferentiated components) [3].

In the current case, the ovarian tumor was morphologically similar to urinary bladder TCC, showing the same structural features as papillae and microcysts filled with periodic acid-Schiff-positive mucus. The lack of benign or borderline Brenner elements and the absence of other cell types of ovarian origin (serous or endometrioid zones), suggested the possibility of a rare primary ovarian tumor, in contrast to a metastatic lesion derived from the bladder TCC [4]. Conventional histologic staining was unable to clarify the tumor origin.

Immunohistochemistry may be helpful for distinguishing TCC of the ovary from TCCs of urothelial origin. CK20 represents a useful marker for differentiating between these two entities, because it is commonly expressed in bladder TCC, but is negative in TCC of the ovary [5–8]. Additionally, the Mullerian marker CA125 is often strongly expressed in ovarian tumors, but is absent from bladder TCC. Some authors [5–8] have reported that the immunophenotype of ovarian TCC closely resembles that of ovarian surface epithelial-stromal tumors. This profile differs from that of bladder TCC, despite the morphologic similarities. These findings are in accord with the results of a study indicating that the genetic mutation patterns in ovarian TCC differ from those found in bladder TCC [9].

In the current case, the expression of CA125 and lack of expression of CK20 supported the hypothesis of primary ovarian differentiation, favoring independent origins for the two tumors, rather than ovarian metastasis of the bladder TCC. TCCs of the bladder and ovary have different treatments and prognoses, and it is therefore important to distinguish between these two lesions in terms of diagnostic tests and treatments.

This case emphasizes the difficulties associated with relying on morphologic analysis alone to distinguish between a primary origin for TCC of the ovary, and its metastatic derivation from a bladder TCC. We therefore conclude that immunohistochemistry should be performed in cases of coincident ovary and bladder carcinomas with transitional cell histologies.

Acknowledgments

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