Case Report **OPEN ACCESS**

Bilateral proliferating Brenner tumor of the ovary associated with recurrent urothelial carcinoma of the urinary bladder

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Abstract

Context: Brenner tumors of ovary are relatively uncommon neoplasm. Most of them are benign and less than 5% are proliferating or borderline. The association between Brenner tumor of the ovary and papillary urothelial carcinoma of bladder is extremely rare. **Case report**: We describe an unusual case of proliferating bilateral Brenner tumor of the ovary with a highly recurrent low-grade papillary urothelial carcinoma of bladder. **Conclusion**: The immunohistopathological similarities of ovarian and bladder tumors and their association in the current case, may be coincidental but may reflect a common initiating event inducing similar pathogenesis changes in the epithelium of both organs. More cases are needed to be reported to better understand this association.

Keywords: Brenner tumor, ovary, urinary bladder, urothelial carcinoma.

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Introduction

Transitional cell tumors or Brenner tumors of ovary are uncommon neoplasm. Most of them are benign and less than 5% are proliferating or borderline [2, 3]. To our knowledge, the association between brenner tumor of the ovary and papillary urothelial carcinoma of bladder is extremely rare. In the present article, we report an unusual case of proliferating bilateral Brenner tumor of the ovary with a highly recurrent low-grade papillary urothelial carcinoma of bladder and discuss the clinico-pathological features and the histogenesis of this entity.

Case Report

A 30-year-old woman was admitted to the hospital in 1994 for hematuria. A papillomatous bladder tumor was diagnosed and removed during a transurethral resection. Histological examination showed a papillomatous transitional epithelium without cellular atypia. There was no evidence of infiltrative growth in the subepithelial connective tissue. This case was reviewed and graded according to the World Health Organization (OMS)/International Society of Urological Pathology (ISUP) Consensus Classification of Urothelial Neoplasms of the Urinary Bladder [1] as a low grade papillary urothelial carcinoma. During the following (12 months (1995), 48 months (1999), 72 months (2001), 108 months (2004), and in 2006) a recurrent bladder tumor was resected. Histologically, the tumor showed the similar pattern. An infiltrative growth pattern was not seen on any occasion, and increasing cellular atypia with time did not occur.

On December 2007, a right ovarian tumor and a nodule of the left ovary were discovered and surgically removed. At the same time, some small papillomas of the urinary bladder were endoscopically removed. Macroscopically, the right ovary was changed into a monolocular cyst with a diameter of 30 cm, containing a bright yellow serous fluid. The outside of the cyst was smooth but the inside was partly covered with several papillomatous vegetations

(Fig. 1). Microscopic examination (Fig. 2a, b) showed a cyst with endoluminal papillae covered by transitional epithelium, practically indistinguishable from the urinary bladder tumors (Fig. 3a, b), without stroma infiltration. These findings were similar to the proliferating Brenner tumor of ovary. The nodule of the left ovary showed close histological similarity with the previously described ovarian mass.

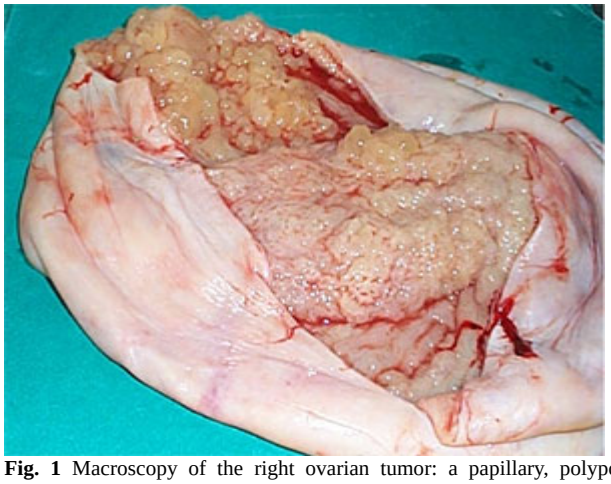

Fig. 1 Macroscopy of the right ovarian tumor: a papillary, polypoid component protrudes into a cystic space.

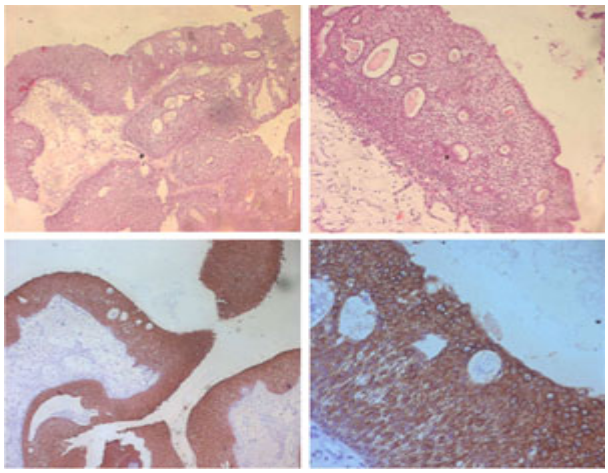

Fig. 2 Proliferating Brenner tumor of the right ovary: a and b: Hematoxylin and eosin staining showing the papillomatous, without infiltrating configuration with low grade cytological features (Magnification ×40 and ×200); c and d: Immunohistochemistry showing positivity of the tumor cells for cytokeratin 7 (Magnification ×40 and ×200).

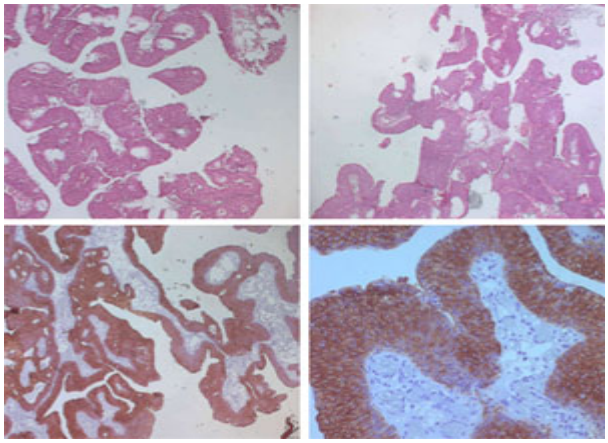

Fig. 3 Urothelial carcinoma of the bladder: a and b: Hematoxylin and eosin staining showing a papillomatous urothelial cell proliferation with low grade cytological features (Magnification ×40); c and d: Immunohistochemistry showing positivity of the tumor cells for cytokeratin 7 (Magnification ×40 and ×200).

The uterus was normal. Immunohistochemical studies demonstrated that the ovarian Brenner tumor and the multiple recurrent urothelial carcinoma of bladder stained diffusely positive for cytokeratin 7, but both of these tumors were negative for cytokeratin 20 (Fig. 2c,d and Fig. 3c,d). The patient's post-operative course has been free of recurrence of the bladder tumor for 7 months.

Discussion

Transitional cell tumors or Brenner tumors of ovary are uncommon neoplasm and less than 5% of them are borderline [2, 3]. This tumor group shows a great number of branching fibro-vascular papillae covered by transitional epithelium that manifests the same spectrum of architectural and cytological features encountered in urothelial lesions of urinary tract. The terminology applied to the intermediate group of transitional cell tumors of the ovary was controversial. Some have categorized tumors with low grade features as proliferating rather than borderline [4]. In the present case, the gross and microscopic findings are similar to the proliferating Brenner tumor of ovary.

In most cases Brenner tumors are associated with other ovarian tumors sharing, therefore, a common origin from the coelomic epithelium and all are estrogen dependent. Only, a very few of these tumors have associations with other extra-ovarian tumors [5, 6]. Simultaneous urothelial tumors of the bladder and transitional cell neoplasms, including Brenner tumors in the ovary have been described in the past [7-8]. In these cases it is usually very difficult and sometimes even impossible to establish whether the ovarian tumors are metastatic or independent primary tumors. In our current case, it appears from the data that the urothelial bladder tumor and the ovarian Brenner tumor, which only appeared 13 years after the bladder tumor, are most likely independent primary neoplasm.

The histogenesis of Brenner tumor is discussed. It is generally accepted that Brenner tumors are derived directly from ovarian surface epithelium, which undergoes metaplasia to form the typical urothelial-like components [9, 10]. However, several studies demonstrated that ovarian transitional cell lesions differ in their immunoprofile from urothelium and from tumors of the urinary bladder in spite of morphologic similarities. Therefore, many immunohistochemical studies of transitional cell proliferation of the ovary showed cytokeratin 7 positivity and cytokeratin 20 negativity, which was consistent, but not specific, with a müllerian derivation [11]. Cytokeratin 20 has been considered to represent a very useful marker for normal or neoplastic urothelium [12, 13]. However, in our case, both Brenner cells and bladder urothelial carcinoma cells showed a

müllerian immunoprofile (cytokeratin 7 positive, cytokeratin 20 negative) and not an urothelial immunophenotype. This müllerian immunoprofile can suggest, but not prove, that the multi-recurrent low-grade papillary urothelial carcinoma in our case arises from vestigial müllerian elements in the bladder or from müllerian metaplasia [14, 15].

The association of these two tumors in the current case may be coincidental but may reflect a common initiating event inducing similar pathogenesis changes in the epithelium of both organs. More cases are needed to be reported to better understand this association.

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