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Metastatic Brenner Tumor – a Case Report

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In our report we present a case of metastatic Brenner tumor of the right ovary in a 74-year-old woman. The diagnosis was based on microscopic examination of surgical specimen and a comparison of the immunohistochemical profile of the primary and metastatic tumors. Additionally, we proved urothelial differentiation of the proliferating Brenner tumor, which is in accordance with the literature.

Introduction

Brenner tumors (BTs) are a heterogeneous group of predominantly ovarian neoplasms categorized in the WHO Classification of Ovarian Tumors in the group of transitional cell neoplasms together with transitional cell carcinomas [6]. BTs constitute approximately 1–2% of all ovarian neoplasms and are divided according to their histopathology and prognosis into three subgroups of benign, borderline and malignant types [2, 6]. In this report we present the case of a 74-year-old woman with BT (which was initially diagnosed as proliferating – borderline – BT) that metastasized to the chest wall. We also show immunohistochemical data which support recent publications proving true urothelial differentiation of these neoplasms [3, 4].

A Case Description

The patient was admitted to our hospital because of a pain in the right side of her chest and discomfort during breathing. The ultrasonography revealed a solid-cystic mass measuring 10 cm in diameter at the level of the 10th and 11th ribs. Subsequently, a thoracotomy was performed with the removal of the tumor. On gross examination one of the rib structures was replaced by a cystic poorly-demarcated tumor with papillary processes protruding into the lumen of the cyst (Fig. 1). Microscopically it presented sheets of epithelial cells with partially vacuolated cytoplasm and "coffee bean"-shaped nuclei forming solid and cystic structures (Fig. 2). Mitotic figures were quite frequent but normal

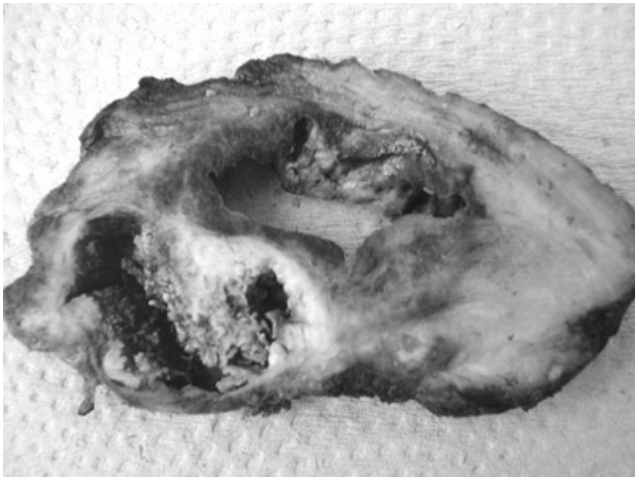

Fig.1. A cross section of the metastatic tumor – rib tissue replaced by papillary-cystic lesion.

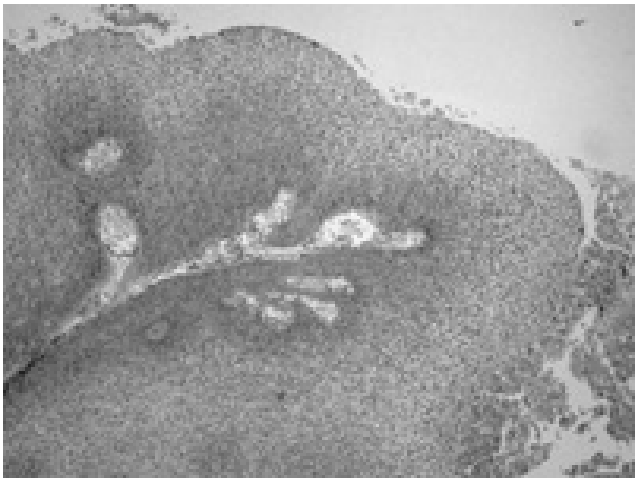

Fig. 2. A papillary formation in the metastatic tumor – note the fibrovascular core covered by transitional epithelium. HE. Magn. 100×.

(1-10/10HPF). The tumor grew in an expanded way compressing adjacent tissue.

In the patient's history we found that she had complained of ascites and abdominal pain 6 years earlier and was admitted to the Institute of Obstetrics and Gynecology where she had been operated on. The laparotomy had revealed a tumor of the right ovary, which had been intraoperatively diagnosed as a proliferating Brenner tumor (prof. H. Kędzia, M.D., Ph.D. – Institute of Obstetrics and Gynecology, Poznań). Grossly the tumor measured 7 cm in diameter and had solid and cystic appearance on cross section. Additionally, after the examination of the postoperative specimen a benign Brenner tumor of the left ovary had also been diagnosed. We should emphasize that within the former tumor a benign component had also been observed and there were no features of stromal invasion or malignant transformation of the epithelium. However, the number of samples taken from the tumor was inadequate to its size to exclude the probability of the existence of the malignant component.

We compared the morphology of the metastatic tumor with the morphology of the primary right ovary neoplasm. This revealed that both neoplasms were similar. The expression of immunomarkers, especially cytokeratins specific for urothelium, was observed. The immunoprofile of both tumors was similar with a higher proliferation rate (Ki-67) and focal expression of CK20 in the metastatic tumor.

We conclude our findings in diagnosing metastatic Brenner tumor.

Discussion

According to the recent WHO classification of ovarian tumors Brenner tumors (BTs) with transitional cell carcinomas constitute a group of transitional cell tumors. Within the group the former neoplasms are divided into three subgroups: benign, borderline and malignant. This distinction was made because of the specific morphology and different prognosis of each subgroup [2].

In the presented case the primary tumor was initially placed into the second category, of borderline BTs.

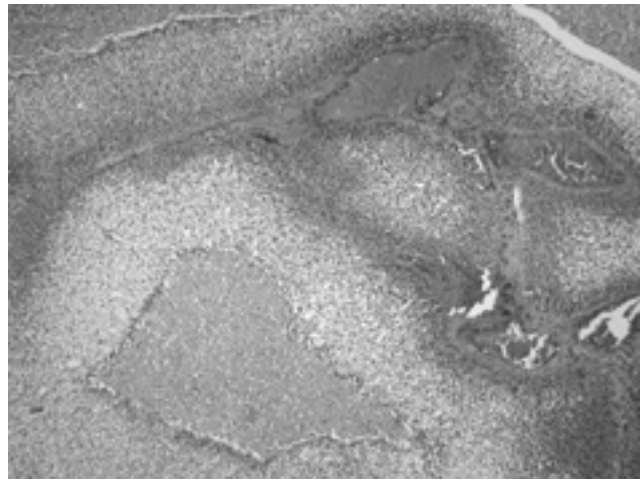

Fig. 3. Papillary structures of the primary tumor. HE. Magn. 100×.

TABLE 1

Comparison of the expression of different tumor markers in the presented case (primary and metastatic tumor) with data from the paper by Riedel et al. [4]; (+) positive reaction; (–) negative reaction; (0) not studied

MARKER	PRIMARY TU	METASTATIC TU	RIEDEL ET Al
CK7	+	+	+
CAM5.2	+	+	+ (CK8)
CK5/6	+	+	+
CK10/13	+	+	+ (CK13)
CK20	–	SINGLE CELLS	FOCALLY
CA125	SINGLE CELLS	SINGLE CELLS	FOCALLY
VIM (STROMA)	+	+	+
UPIII	0	0	+
CD68 PG-M	0	–	0
CA19-9	+	+	0
EMA	+	+	0
CEA	+	+	0
Ki 67	ca. 5%	UP TO 20%	0

These neoplasms, usually measuring 16–20 cm are in most cases unilateral, confined to the ovary, and account for 3–5% of all BTs [5, 6]. The synonyms used to describe these tumors are: Brenner tumor of low malignant potential and proliferating Brenner tumor (for cases with low grade features). On gross examination, as mentioned previously, they form papillae protruding into the cystic spaces. Microscopically the papillae consist of a fibrovascular core covered by uniform medium-sized cells with vesicular nuclei with grooves (like a coffee-bean) and glycogenated cytoplasm (Fig. 3). They resemble transitional epithelium of the urinary tract and, as has been proved in a few previously published papers, have a similar immunophenotype [3, 4]. Our immunohistochemical study has shown that the expression of cytokeratins (CK) characteristic for normal and neoplastic urothelium [1] (e.g. CK7, CK8, CK5/6, CK13 and CK20) was present in the primary and metastatic tumor in the discussed case but with differing intensity and extension (Tab. 1). Cytokeratins 10/13, 8/18 (CAM 5.2), 7 and 5/6 were markedly expressed in the superficial part of the epithelium covering papillae. CK20 was focally positive particularly in the superficial layer of the umbrella-like cells. Adversely, such markers as CA19-9, EMA and CEA were expressed in the basal part of the epithelium. The expression of CA125 was visible only in few cells. The tumors stroma showed a positive reaction with vimentin. The proliferative marker, Ki67, was expressed in both tumors but in a heterogeneous pattern. Only ca. 5% of nuclei of the primary neoplasm epithelial cells showed expression of this marker. The metastatic tumor had fields of a relatively high proliferation rate – up to 20% of nuclei and areas where Ki67 expression was on the level of ca. 5%.

However, the terminology and diagnostic criteria of borderline BT are still controversial. Some pathologists advocate placing low-grade cases from this group into the "proliferating BT" category (as we did). Others designate tumors resembling grade 2 or 3 transitional cell carcinoma of the urinary tract as "borderline with intraepithelial carcinoma". The common point is that the basic feature needed to diagnose borderline BT is the coexistence of a benign BT component and proliferative variably atypical but non-invasive transitional epithelium [2, 6].

Conclusion

The distinction of the borderline BTs was made on the ground of the differing morphology and an uncertain prognosis of these neoplasms. However, the literature does not give any example of metastasis of the proliferating BT. This fact indicates that we should take into account the possibility of the existence of a malignant BT component in the primary tumor, which has not had the representation in the obtained samples. In the conclusion, we must say that in the light of collected data we may only discuss a metastatic BT of the right ovary, which had been initially diagnosed as proliferating BT.

We should also emphasize that our further immunohistochemical investigation revealed true urothelial differentiation of the BT, which is in concordance with the published data.

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