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Different staining patterns of ovarian Brenner tumor and the associated mucinous tumor☆,☆☆

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ABSTRACT

The association of ovarian Brenner tumors and adjacent mucinous tumors is well known but not completely understood. In this study, we analyzed immunohistochemical markers on Brenner tumors and their associated mucinous tumor to explore Mullerian as well as Wolffian and germ cell derivation and determine if the mucinous component is independent or related to the Brenner tumor. Of 32 consecutive cases of Brenner tumors, 8 were identified with significant mucinous component, and 7 additional cases included foci of mucinous epithelium within the Brenner transitional nests. All Brenner tumors were diffusely positive for GATA3 and negative for Paired box gene 8, PAX2, and Sal-like protein 4. Interestingly, the areas of mucinous epithelium as well as mucinous tumors, intermixed and adjacent to the Brenner tumor, were negative for all 4 markers; however, occasional basal-like cells retained expression of GATA3. The immunoprofile of mucinous tumors associated with Brenner tumors shares the lack of Mullerian markers PAX2 and Paired box gene 8 with the Brenner tumor but differs in the expression of GATA3 only in the Brenner tumor component.

1. Introduction

The association of ovarian Brenner tumors and adjacent mucinous cysts is well known but not completely understood. Brenner tumors with mucinous epithelium have been previously reported also as metaplastic Brenner tumor and included rare cases with a striking microcystic change [1,2]. Although literature data proposed derivation of Brenner tumors from the ovarian surface epithelium through transitional cell metaplasia [3,4], this theory has been recently challenged, and other sites of origin such as Walthard nests, teratomas, and fallopian tube epithelium have been suggested [5,6].

In this study, we analyze several immunohistochemical markers in Brenner tumors with a mucinous component or associated mucinous tumors including Paired box gene 8 (PAX8) and PAX2 (markers of Mullerian as well as Wolffian derivation), Sal-like protein 4 (SALL4) (marker of germ cell origin) and GATA3 (multispecific marker reported in Brener tumor but that also stains mesonephric lesions [7]) to analyze the immunoprofile of these 2 commonly associated tumors.

2. Materials and methods

This retrospective study was approved by our institutional review board. A cohort of 32 consecutive Brenner tumors was studied from a database search from July 2008 until June 2013. Histologic slides were rereviewed in all cases, and the diagnosis of Brenner tumor was confirmed. In addition, the presence of concurrent ovarian mucinous tumors was documented. Some Brenner tumors contained cysts lined purely by mucinous epithelium. If the size of the mucinous component was larger than 1 cm, they were classified as mucinous cystadenoma, borderline tumor, or carcinoma based on the degree of atypia. If the size was smaller than 1 cm, they were considered Brenner tumors with mucinous component. This later group also included Brenner tumors with cysts or glands lined only in part by mucinous epithelium, whereas the residual lining of the cyst/gland was composed of transitional epithelium.

Formalin-fixed, paraffin-embedded tissue blocks from the most representative histologic sections were retrieved from the archives. A postcut hematoxylin and eosin (H&E) slide was obtained for each case after obtaining unstained slides for immunostains to confirm the presence of lesional cells.

Immunohistochemical staining for PAX8 (rabbit polyclonal, 1:200 dilution; Protein Tech Group, Chicago, IL), PAX2 (clone 6E3, 1:400 dilution; Sigma-Aldrich, St Louis, MO), SALL4 (rabbit monoclonal, Ep3251, 1:50 dilution; Epitomics, Burlingame, CA), and GATA3 (L2-823 clone, mouse monoclonal, 1:100 dilution; Biocare, Concord, CA) was performed. Positive and negative controls were included with each run. Nuclear labeling was considered as positive stain. The immunostaining

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pattern was recorded as negative or positive, with distribution of staining as diffuse (>80%), or focal (percentage documented).

3. Results

3.1. Clinical and histologic features of study cases

Thirty-two consecutive cases of Brenner tumors from 30 patients were identified. Fifteen (47%) cases contained at least a small component of mucinous epithelium within the tumor. Eight (27%) Brenner tumors were associated with mucinous cystadenoma [4], borderline tumor [3], or carcinoma [1]. Age of the patients harboring Brenner as well as mucinous tumor ranged from 52 to 79 years old; mean, 63.4 years; median, 63 years. The mucinous tumor in 6 of the 8 cases was located in the right ovary. These tumors ranged in size from 2.5 cm to 32 cm (mean, 16.9 cm; median, 17.25 cm), with 5 larger than 14 cm and were significantly larger than those not associated with mucinous tumors (range, 0.2-29 cm; mean, 4.3 cm; median, 2.15 cm; only 1 case larger than 14 cm) ($P < .001$). Six of these cases showed nests of Brenner tumor intermixed with mucinous tumors, whereas the remaining 2 appeared to be located adjacent to one another with no intermingling of the 2 components (both cystadenomas) (Figure A and B).

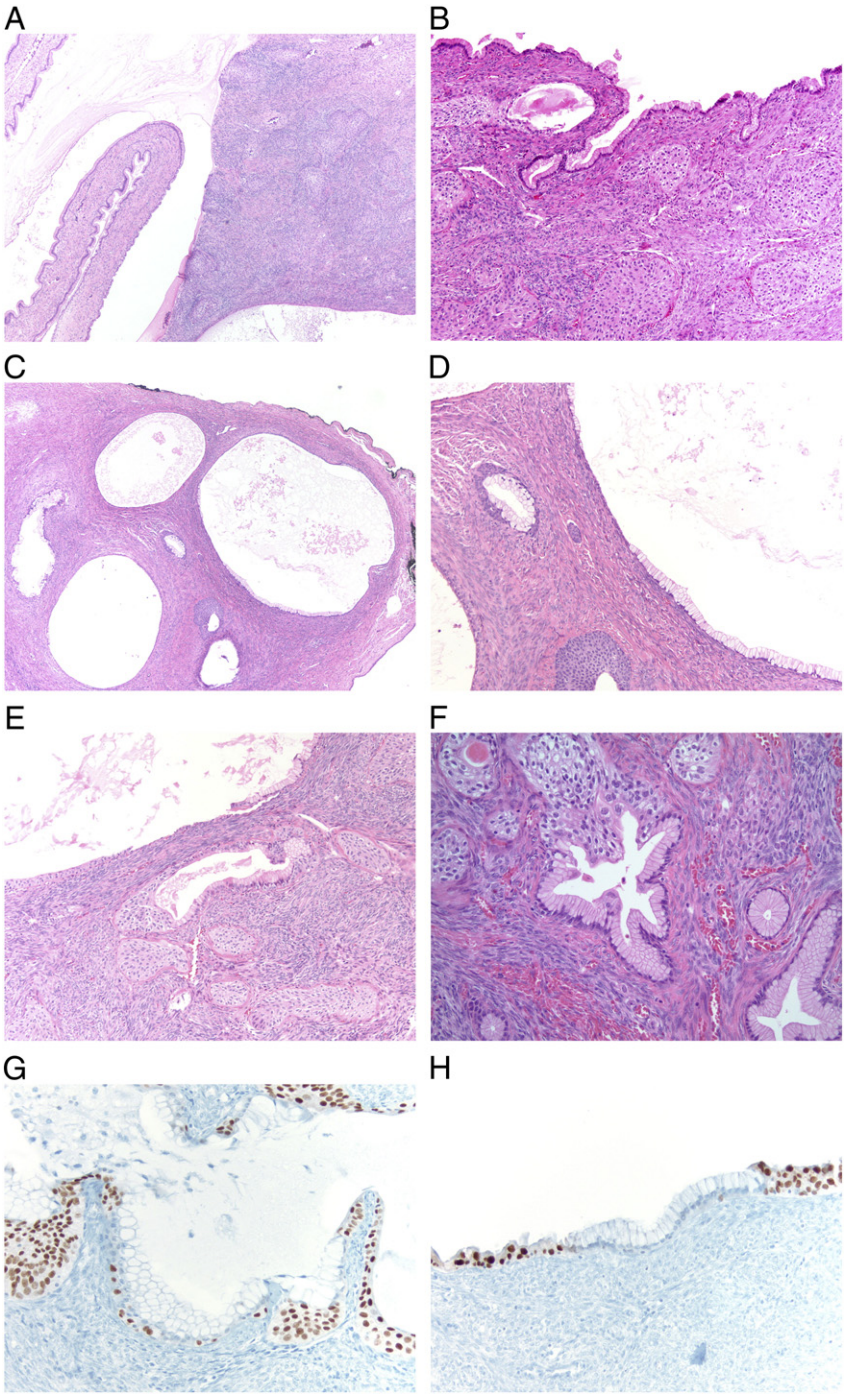

Figure. Brenner tumor with adjacent mucinous cystadenomas (HE ×40 [A]; HE ×100 [B]). Brenner tumor with intermixed mucinous cysts; the same cyst contained both transitional and mucinous epithelium (HE ×40 [C]; HE ×100 [D]; HE ×100 [E]; HE ×200 [F]). Although the transitional epithelium expressed GATA3, the mucinous epithelium within the same cyst was negative. Note occasional basal-like cells under mucinous epithelium expressing GATA3 (HE ×200 [G]; HE ×200 [H]).