

### Clear Cell Carcinoma

Benign and borderline clear cell tumors are exceedingly rare, and clear cell carcinomas are uncommon. They are composed of large epithelial cells with abundant clear cytoplasm, an appearance that resembles hypersecretory gestational endometrium. Because these tumors sometimes occur in association with endometriosis or endometrioid carcinoma of the ovary and resemble clear cell carcinoma of the endometrium, they are now thought to be variants of endometrioid adenocarcinoma. In line with this idea, the most common genetic aberrations (*PIK3CA*, *ARID1A*, *KRAS*, *PTEN*, and *TP53*) are shared with endometrioid carcinoma, albeit at somewhat different frequencies. Clear cell tumors of the ovary can be predominantly solid or cystic. In the solid neoplasms, the clear cells are arranged in sheets or tubules, while in the cystic variety, the neoplastic cells line the spaces. Clear cell carcinoma confined to the ovaries has a 90% 5-year survival, but in advanced stage disease it appears that clear cell morphology portends a poor outcome. Clear cell carcinoma is treated like other types of ovarian carcinoma.

### Cystadenofibroma

Cystadenofibromas are uncommon variants in which there is more pronounced proliferation of the fibrous stroma that underlies the columnar lining epithelium. These benign tumors are usually small and multilocular and have simple papillary processes that do not become as complicated and branching as those found in the ordinary cystadenoma. They may contain mucinous, serous, endometrioid, and transitional (Brenner tumors) epithelium. Borderline lesions with cellular atypia and, rarely, tumors with focal areas of carcinoma occur, but metastatic spread of either is extremely uncommon.

### Transitional Cell Tumors

**Transitional cell tumors contain neoplastic epithelial cells resembling urothelium and are usually benign.** They comprise roughly 10% of ovarian epithelial tumors and are also referred to as Brenner tumors. Uncommon transitional cell carcinomas also occur in the ovary.

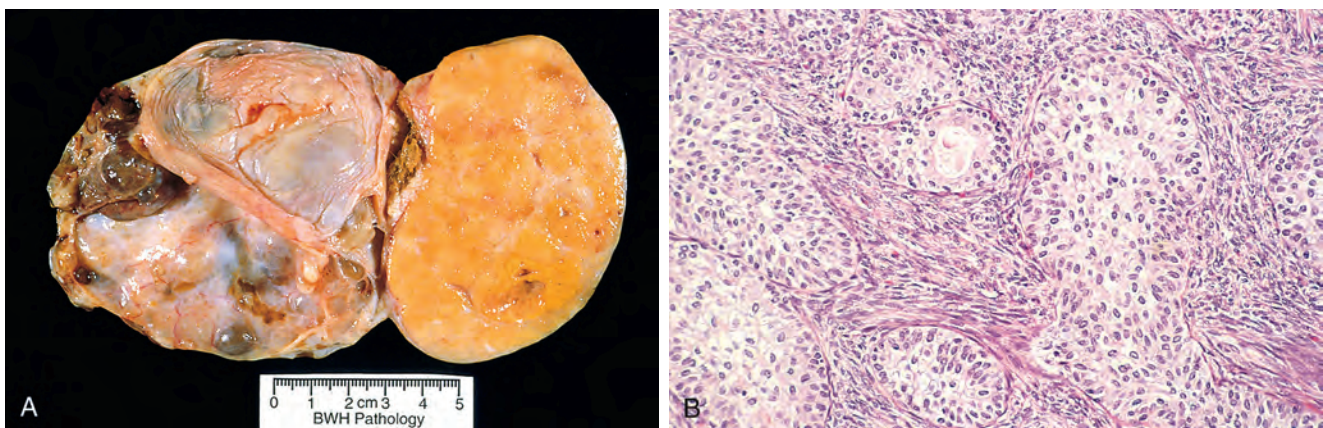
### MORPHOLOGY

These neoplasms may be solid or cystic, are usually unilateral (approximately 90%), and vary in size from small lesions less than 1 cm in diameter to massive tumors up to 20 to 30 cm in diameter (Fig. 22-36A). The fibrous stroma, resembling that of the normal ovary, is marked by sharply demarcated nests of epithelial cells resembling the epithelium of the urinary tract, often with mucinous glands in their center (Fig. 22-36B). Infrequently, the stroma is composed of somewhat plump fibroblasts resembling theca cells; such neoplasms may have hormonal activity. Most Brenner tumors are benign, but borderline (atypical proliferative Brenner tumor) and malignant counterparts have been reported. Tumors with benign Brenner nests admixed with malignant tumor cells are referred to as malignant Brenner tumors, while tumors with greater than 50% malignant transitional type epithelium are considered transitional cell carcinomas of the ovary.

Brenner tumors are often detected incidentally and even when large behave in a benign fashion. Malignant Brenner tumors generally present in stage 1 and for prognostic purposes are considered to be equivalent to low-grade (type I) carcinomas. The uncommon transitional cell carcinomas are considered to be equivalent to high-grade (type II) ovarian carcinomas; these often present at advanced stage and are treated like high-grade serous carcinomas.

### Clinical Course, Detection, and Prevention of Ovarian Epithelial Tumors

**All ovarian carcinomas produce similar clinical manifestations, most commonly lower abdominal pain and abdominal enlargement.** Gastrointestinal complaints, urinary frequency, dysuria, pelvic pressure, and many other symptoms may appear. Benign lesions are easily resected and cured. The malignant forms tend to cause progressive weakness, weight loss, and cachexia. If the carcinomas extend through the capsule of the tumor to seed the peritoneal cavity, massive ascites is common. Characteristically, the ascitic fluid is filled with exfoliated



**Figure 22-36** Brenner tumor **A**, Brenner tumor (*right*) associated with a benign cystic teratoma (*left*). **B**, Histologic detail of characteristic epithelial nests within the ovarian stroma. (Courtesy Dr. M. Nucci, Brigham and Women's Hospital, Boston, Mass.)