

NONSEROUS OVARIAN EPITHELIAL TUMORS

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KEYWORDS

- Ovary • Intestinal mucinous borderline tumor • Intestinal mucinous carcinoma
- Clear cell carcinoma • Endometrioid borderline tumor • Endometrioid carcinoma
- Transitional cell carcinoma • Malignant Brenner tumor • Undifferentiated carcinoma ovary
- Mixed epithelial carcinoma

ABSTRACT

This review covers the group of relatively uncommon nonserous ovarian epithelial tumors. The authors focus on the group's distinctiveness from the much more common serous tumors and show the similarities across entities. Diagnostic criteria that separate the different entities are currently being debated. Particular problems include the reproducible diagnosis of high-grade endometrioid, transitional cell, mixed epithelial and undifferentiated carcinomas. Furthermore, despite recognition that most malignant mucinous tumors involving ovary represent metastases from extraovarian primary sites, many misdiagnoses still occur. The authors discuss the rationale behind the opinions about these problematic topics.

OVERVIEW

The nonserous ovarian epithelial tumors include intestinal mucinous, Mullerian mucinous, endometrioid, clear cell, transitional cell, squamous, undifferentiated and mixed epithelial varieties (**Table 1**). Benign, nonserous ovarian epithelial tumors, such as cystadenomas, are common worldwide, but nonserous ovarian carcinomas are relatively uncommon, particularly in North America and Europe. Assembling these fascinating tumors into one article emphasizes the group's distinctiveness from the much more common serous tumors and allows emphasis of similarities across entities. Mucinous, endometrioid and some clear cell

carcinomas arise through stepwise progression from longstanding precursors such as cystadenomas and borderline tumors, and when transitional cell, undifferentiated and high stage clear cell carcinomas are excluded, the remaining tumors tend to display indolent clinical behavior.¹

A discussion of these topics is contentious, as diagnostic criteria that separate the different entities are currently being debated. Particular problems include the reproducible diagnosis of high-grade endometrioid, transitional cell, mixed epithelial and undifferentiated carcinomas. Furthermore, despite recognition that most malignant mucinous tumors involving ovary represent metastases from extraovarian primary sites, many misdiagnoses still occur. The field is also plagued with arguments about nomenclature used to describe tumors that are proliferative, but neither highly atypical nor invasive: the "borderline tumors" (see **Table 1**). The term "borderline" tumor will be used in this review, mostly because of historical precedent and familiarity. Other terms used to describe borderline tumors are "tumors of low malignant potential," "tumors of borderline malignancy," and "atypical proliferative tumors." Aside from serous and Mullerian mucinous borderline tumors, borderline tumors are benign, do not present at high stage, do not recur, do not transform to carcinoma if completely resected and do not lead to disease specific morbidity or mortality. Since "atypical proliferative tumor" accurately describes these lesions' morphologic features without placing them in a malignant category, the term appears

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Table 1
Nonserous ovarian epithelial tumors

Intestinal mucinous	} Adenoma, borderline tumor ^a and carcinoma are recognized
Mullerian mucinous ^b	
Endometrioid	
Clear cell	
Brenner	
Transitional cell	
Squamous	
Undifferentiated	

^a Synonyms include: tumor of low malignant potential and atypical proliferative tumor.

^b Closely related tumors: endocervical-type mucinous; seromucinous.

most appropriate for borderline tumors lacking a serous component.

This article focuses on the most common non-serous ovarian epithelial tumors and discusses these authors' opinions about the problematic topics mentioned above and the rationale behind those opinions.

INTESTINAL MUCINOUS TUMORS

Primary ovarian mucinous carcinomas are very uncommon; a recent publication indicates that less than 3% of all ovarian carcinomas are mucinous.^{2,3} A mucinous adenocarcinoma involving the ovary is statistically more likely to represent a metastasis from an extraovarian source than a primary ovarian tumor.

GROSS FEATURES

Intestinal Mucinous Cystadenoma and Cystadenofibroma

Mucinous cystadenomas constitute approximately 15% of benign ovarian epithelial

neoplasms. Almost all are unilateral. They are unilocular or multilocular tumors of variable size with a mean of about 10 cm. The outer surface is smooth and lacks adherent mucin in almost all cases. Cut section reveals cysts containing thick gelatinous material. There may be Brenner tumor or teratomatous components in evidence. The amount of fibromatous stroma is variable.

Intestinal Mucinous Borderline Tumor

Mucinous borderline tumors are generally unilateral, large tumors, exceeding 10 to 12 cm in greatest dimension. Like the cystadenomas, these tumors lack tumor or adherent mucin on the ovarian surface. On cut section, they are multilocular, with cysts that contain mucinous material. Rare tumors contain solid nodules within them.

Intestinal Mucinous Carcinoma


Mucinous carcinomas and mucinous borderline tumors resemble one another to a substantial degree. In fact, it has been estimated that erroneous sampling of mucinous carcinomas at the time of frozen section leads to a mistaken diagnosis of borderline tumor in as many as 15% of cases.⁴ The same generalities regarding unilaterality and large size apply. It is uncommon, but certainly not unheard of, to find tumor growth on the ovarian surface. Carcinomas usually contain more solid areas than borderline tumors and may feature necrosis (Fig. 1). Rare tumors also may contain solid, mural nodules.

MICROSCOPIC FEATURES

Intestinal mucinous tumors are composed of cells containing intracytoplasmic mucin and most feature goblet cells at least focally (Fig. 2). Extraovarian mucin by itself is not sufficient for classification as an intestinal mucinous neoplasm. A diagnosis of primary ovarian mucinous cystadenoma, borderline tumor or carcinoma should only be rendered with confidence when the tumor is unilateral and larger than 10 to 12 cm and the patient lacks a history of an extraovarian adenocarcinoma (Box 1).^{3,5} Enhanced pathologic evaluation, including immunohistochemistry, is highly recommended when any uncharacteristic clinical, gross or microscopic feature is found.

Intestinal Mucinous Cystadenoma and Cystadenofibroma

These tumors feature one or more cysts separated by variable amounts of stroma (Fig. 3). The stroma may have a fibromatous appearance or resemble non-neoplastic ovarian stroma. The cysts are lined by columnar cells with obvious intracytoplasmic

 <p>Key Features PRIMARY OVARIAN MUCINOUS CARCINOMA</p>
<ul style="list-style-type: none"> • Large, unilateral tumor with intracytoplasmic mucin • Background mucinous borderline tumor • Expansile invasion>destructive stromal invasion • CK7>CK20 • Metastatic carcinoma is excluded

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