Gastrointestinal- and Müllerian-type epithelium in ovarian mucinous cystadenoma: Immunohistochemical analysis of 139 cases

Sultan Ahmad Halimi MD, PhD[1,2], Daichi Maeda MD, PhD[2], Akiteru Goto MD, PhD[2]

1. Department of Pathology, Kabul University of Medical Science, Kabul, Afghanistan

2. Department of Cellular and Organ Pathology, Graduate School of Medicine, the University of Akita, Akita, Japan

Background

Ovarian mucinous tumors show stepwise malignant transformation from mucinous cystadenoma (MA) to mucinous borderline tumor (MBT) and to mucinous adenocarcinoma (MCa). Two subsets of MBT have been established: gastrointestinal (GI) and Müllerian (M) types. However, no such distinction is made for MAs. An association between Müllerian derivatives and M-type mucinous tumors has been reported, while the origin of GI-type mucinous epithelium is unclear. This study analyzed a series of MAs immunohistochemically using gastric, intestinal, and Müllerian markers to elucidate the direction of the differentiation of mucinous epithelium that arises in the ovary and to seek a link between GI- and M-type epithelium.

Design

We retrieved 139 cases of MA. The tumors were initially evaluated morphologically for presence or absence of GI- and Müllerian-type epithelium. Representative slides of morphologically pure GI- and M-type MAs were chosen. If a transition from M-type epithelium to GI-type epithelium was observed, slides containing such areas were sent for immunohistochemistry. The expression of the gastric marker claudin-18 (CLDN18) and intestinal (CDX2) and Müllerian (ER) markers was evaluated immunohistochemically. The epithelium that was positive for CLDN18 or CDX2

was designated as “GI type”, and the epithelium showing the CLDN18–/CDX2–/ER+ phenotype as “M type”.

Results

GI-type epithelium characterized by CLDN18 or CDX2 positivity was present in 93% (129/139) of the MAs. Of these, 14 were associated with teratomas and one with a Brenner tumor. A transition from M-type (CLDN18–/CDX2–/ER+) epithelium to GI-type epithelium was seen in 12 cases (9%). Although most GI-type epithelium was ER-negative, scattered ER positivity was observed in 19 cases (14%). A rare subset of MAs (eight cases) was purely Müllerian type, consisting of epithelium with Müllerian morphology and diffuse ER expression.

Conclusions

Ovarian MAs can be subclassified into GI and M types. In GI-type tumors, the gastric phenotype is predominant. Since the transition from M-type epithelium to GI-type epithelium is seen in some cases, we conclude that GI-type epithelium can arise not only from teratomatous lesions or Brenner tumors but also from Müllerian duct derivatives or ovarian surface epithelium via metaplastic/neoplastic processes.