Endometrial Gastric-type Carcinoma

An Aggressive and Morphologically Heterogenous New Histotype Arising From Gastric Metaplasia of the Endometrium

To the Editor:

We read with great interest the study by Wong et al,[1] which described the first case series of endometrial gastric-type carcinoma (EGC). The authors tried to define diagnostic criteria for EGC, hypothesizing that it derives from gastric-type mucinous lesions of the endometrium.[1] In congratulating them for their excellent work, we would make our contribution in this field by presenting an extraordinary case of EGC which mimicked almost all endometrial carcinoma histotypes and demonstrated a direct evolution from gastric-type mucinous metaplasia of the endometrium.

A 50-year-old woman underwent total hysterectomy with bilateral salpingo-oophorectomy due to an endometrial lesion with presumed bilateral adnexal involvement. On the preoperative biopsy, the lesion had been reported as mucinous carcinoma. At gross examination, an intracavitary lesion of 3.5 cm with the irregular surface was observed in the uterine fundus; both adnexa were largely involved by the tumor, and the Fallopian tubes could not be identified. In contrast, the uterine cervix was not involved. Histologic examination showed a carcinoma infiltrating the myometrium for less than half of its thickness; the same carcinoma infiltrated both ovaries. The lesion was highly heterogenous: the most represented pattern was composed of cells filled with intracytoplasmic eosinophilic mucin and mild-to-moderate nuclear atypia, arranged in a glandular-papillary architecture (Fig. 1A); several poorly differentiated areas composed of discohesive cells with high nuclear grade and signet-ring cell features were observed. Remarkably, the tumor displayed highly different areas which mimicked several endometrial carcinoma histotypes: endometrioid (Fig. 1B), serous (Fig. 1C), conventional mucinous (nongastric-type), clear cell (Fig. 1D). The tumor was widely in continuity with morphologically benign gastric-type glands, mostly arranged in a "lobular glandular hyperplasia" pattern (Fig. 1E). At the periphery of the tumor, the endometrial surface appeared lined by a gastric-type mucinous epithelium, which was in continuity with normal endometrial epithelium. Focally, the morphologically benign gastric-type epithelium appeared to continue into the carcinomatous component through a low-grade dysplastic component (Fig. 1E). On histology, the uterine cervix was entirely examined and appeared uninvolved. On immunohistochemistry, the tumor was negative for estrogen and progesterone receptors and WT1 and showed a p53 wild-type pattern; positivity for the gastrointestinal markers cytokeratin 20 and CDX2 was observed in the carcinoma and multifocally in the gastric-type metaplasia; the gastric marker MUC6 was positive in the gastric-type metaplasia and multifocally in the carcinoma; positivity for PAX8 confirmed the gynecologic origin.

The described features yielded a diagnosis of EGC arising in an extensive gastric-type mucinous metaplasia of the endometrium, with bilateral ovarian involvement.

We think that our case may be of value for the following reasons:

(1) This case may demonstrate that EGC arises from gastric-type mucinous metaplasia of the endometrium, as postulated by Wong and colleagues. However, in their series only one EGC showed gastric-type metaplasia in a coexistent adenomyomatous polyp. Our case showed areas of transition from morphologically benign gastric-type epithelium to carcinoma, through a putative low-grade dysplastic component, supporting that the former was the precursor of the latter.

(2) This case suggests that EGC may display a striking morphologic heterogeneity. Therefore, a diagnostic algorithm requiring a well-defined gastric/gastrointestinal differentiation (voluminous, pale eosinophilic or clear cytoplasm with distinct cell borders and/or goblet cells) might be restrictive.

(3) This case showed that EGC could mimic almost any histotype of endometrial carcinoma, including not only mucinous and clear cell (as widely discussed by Wong and colleagues), but also endometrioid and serous, which are by far more common. On this account, EGC might easily be misdiagnosed as a conventional endometrial carcinoma in the routine diagnostics, leading to underestimate its prevalence.

(4) Our case, in agreement with the series by Wong and colleagues, supports that EGC has an aggressive behavior. This may raise the question whether EGC should be considered at increased risk compared with an endometrioid carcinoma of the same grade and stage.

In the light of these observations, an accurate and extensive examination of the tumor and of adjacent areas might be crucial to raise the possibility of an EGC when the typical morphologic features are lacking. The presence of benign gastric-type epithelium adjacent to the tumor, or of unusual patterns with even few mucinous cells, especially if signet-ring, should alert the pathologist (Supplementary Figure 3). As pointed out by Wong and colleagues, immunohistochemistry should be performed to confirm the diagnosis. It appears crucial to quantify the risk of malignant progression of endometrial gastric-type metaplasia, to assess whether its presence in endometrial biopsy specimens may require hysterectomy.

We hope that further studies may help defining this new and morphologically challenging histotype of endometrial carcinoma.

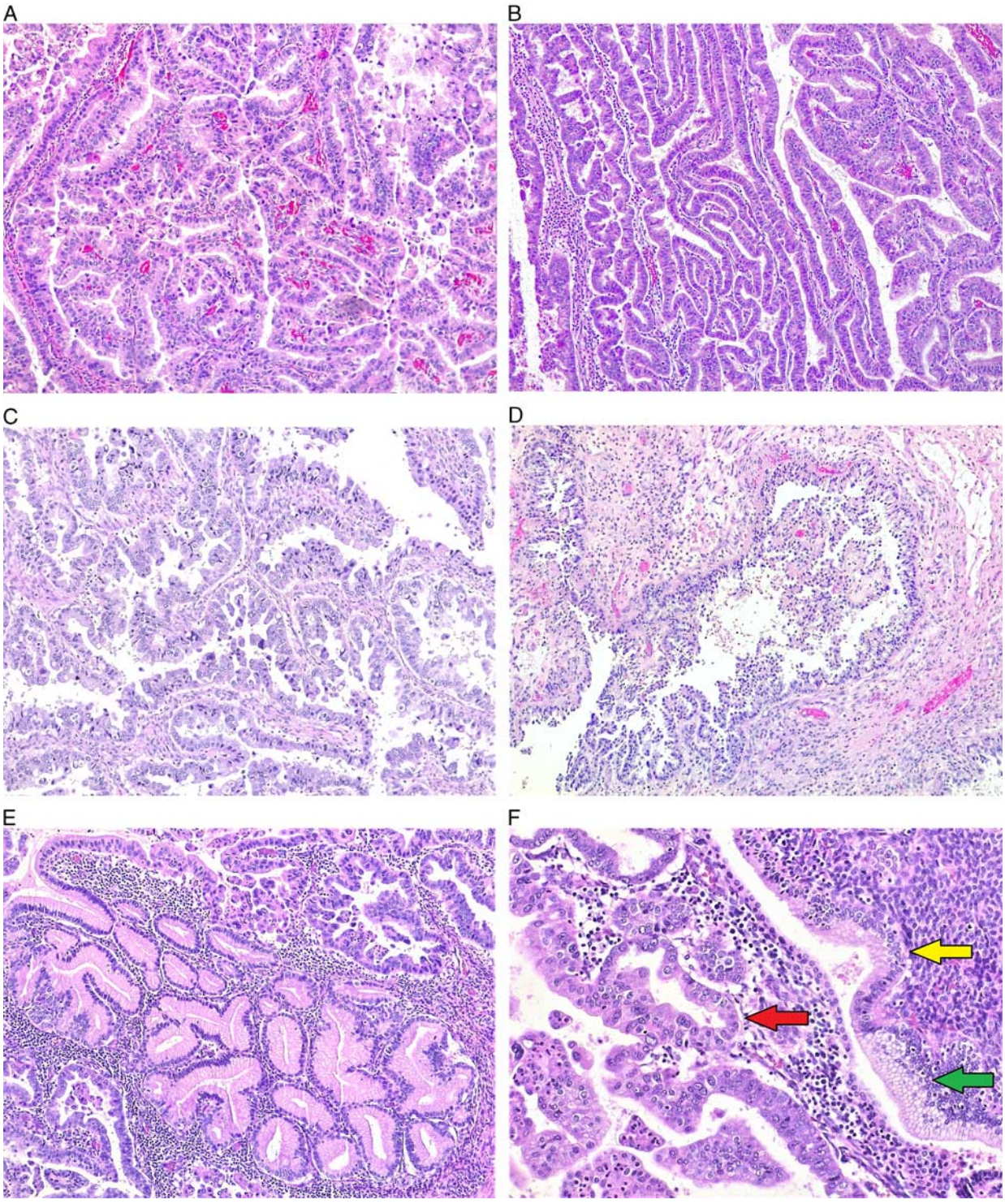

FIGURE 1. A, Cells filled with intracytoplasmic eosinophilic mucin and low-to-moderate nuclear atypia, arranged in a glandular-papillary architecture. B, Columnar cells devoid of mucin and with low nuclear grade arranged in well-formed glands, mimicking low-grade endometrioid carcinoma. C, Hobnail cells with high nuclear grade arranged in a papillary architecture, mimicking serous carcinoma. D, Hobnail cells with low nuclear grade and clear cytoplasm mimicking clear cell carcinoma. E, Detail on gastric-type metaplasia highlighting eosinophilic mucin and well-defined cell borders. F, Apparent transition from benign gastric-type epithelium (green arrow) to carcinoma (red arrow) through a putative low-grade dysplastic component (yellow arrow).

Antonio Travaglino, MD*
Antonio Raffone, MD†
Annarita Gencarelli, MD*
Antonio Mollo, MD, PhD†
Fulvio Zullo, MD, PhD†
Luigi Insabato, MD, PhD*
*Pathology Unit, Department of Advanced Biomedical Sciences
†Gynecology and Obstetrics Unit Department of Neurosciences Reproductive Sciences and Dentistry University of Naples "Federico II" Naples, Italy

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1. Wong RW, Ralte A, Grondin K, et al. Endometrial gastric (gastrointestinal)-type mucinous lesions: report of a series illustrating the spectrum of benign and malignant lesions. *Am J Surg Pathol*. 2019;44:406–419.