Intestinal-type mucinous ovarian carcinoma arising from a seromucinous precursor lesion

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Abstract. – OBJECTIVE: Mucinous ovarian carcinoma is a tumor with gastrointestinal differentiation, which is not associated with endometrial-type (endometriotic or seromucinous) precursors. Here, we describe a peculiar case of mucinous ovarian tumor with intestinal differentiation arising in a seromucinous lesion, which may represent a distinct entity.

CASE PRESENTATION: A 58-year-old woman underwent surgery due to a 14.5-cm ovarian mass with lymph nodal, peritoneal, omental and colorectal involvement. Histological examination with ancillary immunohistochemical analysis has been performed. Histologically, the mass was a carcinoma with intestinal differentiation and expansile growth pattern, arising in a seromucinous lesion, which may represent a distinct entity. The carcinoma and the metaplasia showed loss of Müllerian markers (estrogen and progesterone receptors, PAX8) and positivity for intestinal-type markers (cytokeratin 20, CDX2).

CONCLUSIONS: Our case may represent the ovarian counterpart of endometrial gastrointestinal-type carcinoma, which is an aggressive entity developing from gastrointestinal metaplasia of the endometrial epithelium. Acknowledging the existence of such entity might be relevant in terms of diagnosis and patient management.

Key Words: Ovarian carcinoma, Mucinous ovarian tumor, Seromucinous lesion, Gastrointestinal differentiation, Endometrioid carcinoma.

Introduction

Ovarian carcinomas constitute a heterogeneous group of neoplasms. They differ regarding etiopathogenesis, tissue of origin, clinicopathological prognostic factors, molecular pathways and biological behavior. In this scenario, the pathogenesis of mucinous ovarian carcinoma (MOC) is poorly understood. MOC is characterized by a gastrointestinal (GI)-type morphology and immunophenotype. It may be associated with ovarian teratoma or Brenner tumor. Endometrioid ovarian carcinoma (EOC) may also show mucinous features, which show a Müllerian rather than a GI phenotype. Moreover, EOC originates from ectopic endometrial cells, like those observed in endometriosis or seromucinous lesions. On this account, MOC and EOC are regarded as two completely different entities, which follow separate etiopathogenetic pathways¹⁻⁴.

Herein, we describe the clinical, morphological and immunophenotypical features of a case of MOC arising from an endometriotic/seromucinous precursor.

Case Presentation

A 58-year-old woman underwent total hysterectomy with bilateral salpingo-oophorectomy due to a 14.5 cm ovarian mass accompanied by increase of CA125 and CA19.9 levels. On intraoperative pathological examination, the lesion...
showed solid and cystic areas with mucinous secretion; on frozen sections, the tumor was diagnosed as MOC. The tumor also involved pelvic and para-aortic lymph nodes, pelvic peritoneum, omentum and intestinal wall at the colorectal junction.

Histological examination of formalin-fixed, paraffin-embedded neoplastic tissue showed well-differentiated, intestinal-type mucinous features with goblet cells and an expansile growth pattern (Figure 1). Immunohistochemistry showed positivity for CDX2, cytokeratins 7 and 20 and MUC5AC and negativity for estrogen and progesterone receptors, PAX8 and vimentin, consistently with intestinal differentiation (Figure 2); p53 was wild-type and mismatch repair was proficient.

Surprisingly, the carcinoma appeared to arise in a seromucinous cystadenofibroma, which displayed several types of Müllerian epithelia (endometrioid, tubal, mucinous, squamous) and an area of intestinal-type mucinous metaplasia adjacent to the carcinoma (Figure 1). Such area showed loss of Müllerian markers and acquisition of gastrointestinal markers on immunohistochemistry (Figure 2). Multiple endometriotic foci were observed in the ovary and in the homolateral Fallopian tube.

Although the tumor morphologically resembled a MOC, we made a diagnosis of EOC with prominent intestinal-type mucinous differentiation. Such decision was based on the association with endometriosis and a seromucinous precursor. Moreover, the biological behavior of the tumor was aggressive regardless of the expansile pattern.

Discussion

Ovarian carcinomas are subdivided into “type I” and “type II” according to Kurman1. However, each histotype shows different etiopathogenesis, tissue of origin, clinicopathological prognostic factors, molecular pathways and biological behavior5-11. MOC is an uncommon “type I” ovarian carcinoma, which had been previously categorized as “endocervical-type” or “intestinal-type”.

Figure 1. a, A seromucinous cystadenofibroma, which displayed several types of Müllerian epithelia (endometrioid, tubal, mucinous, squamous) and an area of intestinal-type mucinous metaplasia (top) and invasive mucinous carcinoma with expansile pattern (bottom) (20x). b, Intestinal-type mucinous carcinoma (right) arising in a seromucinous cystadenofibroma (left) (40x). c, Detail of the seromucinous epithelium, with intestinal-type metaplasia on the right (200x). d, Detail of the invasive carcinoma (100x).
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Figure 2. The immunophenotype of the mucinous carcinoma showed positivity for intestinal markers and negativity for Müllerian markers (4 panels on the top). The immunophenotype of the seromucinous cystadenofibroma showed loss of Müllerian markers and acquisition of intestinal markers in the area of intestinal-type metaplasia (4 panels on the bottom).
Subsequent studies have shown that the so-called “endocervical-type” MOC actually represents endometrioid carcinoma with mucinous differentiation. To date, MOC only includes tumors with GI differentiation, which range from “gastric” (i.e., mucinous cells with pale eosinophilic cytoplasm) to “intestinal” (i.e., with goblet cells). The etiopathogenesis of MOC is not completely understood. Unlike EOC and clear cell ovarian carcinoma, MOC is thought to derive from germ cells, with no relationship to ectopic endometrial tissue.

In contrast with such assumption, our case showed morphological and immunophenotypical features of MOC but arose in a seromucinous lesion; multiple foci of endometriosis were also observed. We decided to make a diagnosis of EOC with GI-type differentiation rather than MOC since the tumor appeared to be of endometrioid lineage. However, it is clear that such diagnosis does not completely fit our case. In fact, the mucinous differentiation found in EOC maintains Müllerian features, as discussed above. On the other hand, a GI-type mucinous differentiation is typical of MOC. The correct definition of the presented case might be found through comparison with endometrial carcinoma. “Müllerian-type” mucinous differentiation is quite common in endometrial endometrioid carcinomas. GI-type mucinous differentiation is less common and appears associated with worse prognosis.

Regarding pure GI-type endometrial carcinomas, they have been recognized as a separate histotype in the current (2020) WHO classification. The presented case shows evident overlap with such entity. Indeed, diagnostic criteria for GI-type endometrial carcinoma include the absence of an overt endometrioid component, positivity for GI markers and negativity for estrogen and progesterone receptors. The pathogenesis may also be similar. Indeed, GI-type endometrial carcinoma seemingly arises in a background of GI-type mucinous metaplasia of the endometrium. In our case, diffuse intestinal-type metaplasia was found in the precursor seromucinous lesion. The possibility of GI-type tumors arising from Müllerian precursors is also supported by previous studies. In fact, there are reports of mucinous cystadenomas with mixed Müllerian and GI phenotype and a benign seromucinous tumor with intestinal type metaplasia.

Our case supports the existence of a GI-type ovarian carcinoma different from MOC, which is associated with endometriosis and may be the ovarian analogous of GI-type endometrial carcinoma. Despite appearing morphologically and immunophenotypically identical to MOC, such GI-type ovarian carcinoma might have a more aggressive behavior. In fact, MOC with expansive pattern are typically indolent neoplasms, generally diagnosed at early stage and often managed by observation alone. On the other hand, GI-type endometrial carcinomas are consistently described as aggressive tumors, often showing bilateral adnexal involvement even in the absence of deep myometrial invasion. Consistently with the latter one, our case showed involvement of lymph-nodes, omentum, pelvic peritoneum and colorectal-wall, despite the expansive growth pattern. Therefore, this GI-type ovarian carcinoma might require a more aggressive clinical management.

Conclusions

Our case may represent the ovarian counterpart of endometrial GI-type carcinoma. The real prevalence of such entity is difficult to define, given its morphological and immunophenotypical overlap with MOC. Hopefully, further studies may help to improve the biological definition of such entity and its recognition in the common clinic-pathological practice.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Statement of Ethics

All procedures performed in this study were in accordance with the ethical standards of the Hospital Ethics Committee and with the 1964 Helsinki Declaration. Written informed consent was obtained from the patient for publication of this case report.

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Authors’ Contribution

Conceptualization, A.T., A.S., N.D.; methodology, G.A., F.I.; software, M.V.; validation, GF.Z., D.A.; formal analysis, G.S.; investigation, A.R; data curation, GF.Z.; writing—original draft preparation, A.T.; writing—review and editing, A.S., N.D.; project administration, GF.Z. All authors read and approved the final manuscript.
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