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Primary and metastatic mucinous adenocarcinomas of the ovary: Evaluation of the diagnostic approach using tumor size and laterality

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Abstract

Objective. To evaluate the usefulness of the recently proposed algorithm (Seidman JD, Kurman RJ, Ronnett BM. Primary and metastatic mucinous adenocarcinomas in the ovaries: incidence in routine practice with a new approach to improve intraoperative diagnosis. Am J Surg Pathol 2003;27:985–93 [5]) that classifies mucinous adenocarcinomas of the ovary as primary when they were unilateral ≥10 cm and as metastatic when they were unilateral <10 cm or bilateral.

Methods. Malignant ovarian neoplasms, which were resected in Chiang Mai University Hospital between 1992 and 2003, were histologically reviewed. Mucinous adenocarcinomas involving the ovary were identified. The medical records and radiologic materials were reviewed in correlation with the pathologic features to identify the primary site.

Results. There were 74 cases of mucinous adenocarcinomas; 16 were primary ovarian; 52, metastatic; and 6 of indeterminate primary site (primary versus metastatic). Primary mucinous adenocarcinomas had a mean size of 16.4 cm and bilateral involvement in 13%. Metastatic mucinous adenocarcinomas had a mean size of 11.7 cm and bilateral involvement in 77%. Excluding the 6 tumors of indeterminate primary site, the proposed algorithm correctly classified primary and metastatic tumors in 84% of 68 cases. Of 21 unilateral mucinous adenocarcinomas ≥10 cm, 62% were primary ovarian. Of 5 unilateral tumors <10 cm, 80% were metastatic. Of 42 bilateral mucinous adenocarcinomas, 95% were metastatic.

Conclusion. The algorithm provided high accuracy in the overall prediction of primary and metastatic mucinous adenocarcinomas of the ovary, with major strength in the identification of metastatic tumors by bilaterality or size <10 cm. However, the prediction of primary mucinous adenocarcinomas by unilaterality and size ≥10 cm was less reliable than previously reported. Due to the overlapping features between primary and metastatic tumors and the higher frequency of the latter, the possibility of metastases should always be borne in mind in the evaluation of mucinous adenocarcinomas of the ovary.

Keywords: Ovary; Mucinous tumor; Mucinous adenocarcinoma; Primary tumor; Metastatic tumor; Tumor size; Tumor laterality

Introduction

The ovary is a frequent site for metastatic involvement [1]. Metastatic mucin-producing adenocarcinomas to the ovary frequently cause diagnostic confusion with primary ovarian mucinous adenocarcinoma [2–5]. As ovarian metastatic lesions can be the initial presentation of the patients without previously recognized primary cancers, the metastatic nature of the tumor is not suspected preoperatively in many cases [6–8]. Careful intraoperative exploration of the intra-abdominal organs and intraoperative pathology consultation is important in the evaluation and diagnosis of metastatic tumors. However, intraoperative distinction between primary and metastatic mucinous adenocarcinomas on frozen sections can be difficult. In a recent study of primary and metastatic mucinous adenocarcinomas in the ovaries, Seidman et al. proposed an algorithm based on tumor size and laterality that correctly classified mucinous adenocarcinomas in 90% of all 50 cases and 83% of tumors after the exclusion of signet ring cell carcinomas and primary microinvasive tumors [5]. Based on the proposed algorithm, mucinous adenocarcinomas were classified as

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primary when the tumors were unilateral and ≥10 cm (correct prediction 82%) and as metastatic when they were bilateral or unilateral and <10 cm (correct prediction 95%). This algorithm is simple and may serve as a useful guide in the intraoperative evaluation of ovarian mucinous adenocarcinomas [5].

In another series comparing metastatic mucinous adenocarcinomas and selected stage I primary mucinous adenocarcinomas of the ovary, Lee and Young [4] reported a greater proportion of metastatic mucinous adenocarcinomas >10 cm compared to that of Seidman et al. (48% versus ~34%) [5]. The bilaterality rate of metastatic tumors in both studies was comparable (75%). Combination of tumor size and laterality was not evaluated in Lee and Young's study [4]. It is uncertain whether the proposed algorithm would provide a similar result in different settings. We believe that the algorithm should be tested for its reproducibility in another hospital series before applying to routine practice. The purpose of this study was to review primary and metastatic mucinous adenocarcinomas in our practice setting and evaluate the usefulness of the algorithm using tumor size and laterality in the diagnosis.

Materials and methods

Consecutive cases of malignant ovarian neoplasms, either primary or metastatic, were searched from the surgical pathology files of the Department of Pathology, Faculty of Medicine, Chiang Mai University (CMU) between January 1992 and December 2003 (12-year period). The histologic slides were reviewed, and the diagnoses were classified according to the 2003 WHO classification [9]. Distinction between primary and metastatic tumors was based on recent diagnostic criteria [2–4,10]. Clinicopathologic data of all metastatic tumors (hospital and referral cases) were reported in another study [11]. For inclusion in this study, the ovaries had been resected at CMU Hospital. The diagnosis of primary mucinous adenocarcinoma required exclusion of the possibility of metastatic tumors by reviewing the medical records, radiologic materials, and available follow-up outcome. Advanced-stage mucinous adenocarcinomas showing suggestive features, but not fulfilling the diagnostic criteria for metastases [2,10] and not having definite extraovarian primary tumors, were considered as tumors of indeterminate primary site (primary versus metastatic). Metastatic tumors with microscopic ovarian involvement were excluded because they rarely cause diagnostic problems.

Metastatic invasive adenocarcinomas with at least some degree of mucin production were classified as mucin-producing adenocarcinomas. Determination of primary sites for metastatic tumors was based on the clinicopathologic review. For the diagnosis of metastatic tumors of unknown primary site, the pathologic features of the ovarian lesions must be diagnostic of metastases [2,10]. Metastatic mucin-producing adenocarcinomas were further classified, based on the predominant component (involving >50% of the histologic materials), into the following groups: mucinous adenocarcinoma, adenocarcinoma with predominant endometrioid-like (pseudoendometrioid) appearance, and signet ring cell carcinoma. Only the metastatic mucinous adenocarcinoma group was further analyzed and compared with primary and indeterminate mucinous adenocarcinomas.

The data regarding age, tumor size (maximal dimension), and laterality of all cases of mucinous adenocarcinomas (primary, metastatic and indeterminate) were collected. The histologic features of all mucinous adenocarcinomas were recorded including architectural grade and the presence of the following features: confluent epithelial pattern, nodular growth pattern, surface implants, ovarian hilar involvement, lympho-vascular space invasion, minor signet ring cell component, and co-existing ovarian lesion [2,4]. Architectural grading was based on the proportion of solid tumor area as follows: grade 1, <5%; grade 2, 5–50; and grade 3, >50%. Confluent epithelial pattern was defined by complex arrangement of malignant epithelial cells, with little or no intervening stroma, exceeding 10 mm^2 in area [2,9,10]. Co-existing primary ovarian lesions must be clearly different from mucinous adenocarcinoma components. A benign or borderline (low malignant potential) mucinous tumor component was not considered as a co-existing ovarian lesion for primary mucinous adenocarcinoma. For evaluation of the proposed algorithm [5], cases of primary and metastatic mucinous adenocarcinomas were tabulated by laterality (unilateral versus bilateral) and tumor size (<10 versus ≥10 cm).

Results

During the study period, there were 238 cases of primary ovarian epithelial carcinomas resected at CMU Hospital, 16 of which (6.7%) were primary mucinous adenocarcinomas. Primary mucinous adenocarcinomas were stage I in 11 cases (69%), stage II in 2 (13%), stage III in 2 (13%), and stage IV in 1 case (6%). There were 6 mucinous adenocarcinomas of indeterminate primary site (primary versus metastatic). Ninety cases of metastatic mucin-producing adenocarcinomas to the ovary were identified. The large intestine was the most common primary site for ovarian metastases (29 cases or 32%). For further analysis of metastatic mucinous adenocarcinomas, 15 adenocarcinomas with predominant endometrioid-like appearance and 23 signet ring cell carcinomas were excluded. The excluded tumors originated from the large intestine (17 cases), stomach (10 cases), appendix (2 cases), cervix (1 cases), and unknown primary site (8 cases).

Table 1 shows information on 74 mucinous adenocarcinomas including 16 primary ovarian; 52 metastatic; and 6 of

Table 1
Comparison of selected clinicopathologic features of mucinous adenocarcinomas involving the ovary in each category (primary, metastatic, and indeterminate primary site)

Category	No.	Mean age (range) (year)	Mean size (range) (cm)	Bilaterality (%)	Size <10 cm (%)	Unilateral and size ≥10 cm (%)
Primary	16	48 (32–75)	16.4 (8.0–25.0)	2 (13)	1 (6)	13 (81)
Metastatic	52	49 (21–85)	11.7 (3.0–29.0)	40 (77)	22 (42)	8 (15)
Large intestine	12	46 (27–66)	13.8 (5.0–29.0)	9 (75)	4 (33)	2 (17)
Intrahepatic bile duct	10	54 (41–74)	11.4 (3.0–20.0)	6 (60)	4 (40)	3 (30)
Extrahepatic bile duct and gallbladder	7	52 (21–66)	11.1 (6.0–17.0)	7 (100)	4 (57)	0
Stomach	2	59 (32–85)	11.8 (11.0–12.5)	2 (100)	0	0
Appendix	2	58 (54–61)	19.5 (19.0–20.0)	2 (100)	0	0
Breast	2	31 (26–35)	4.5 (4.0–5.0)	2 (100)	2 (100)	0
Cervix	10	47 (31–63)	10.6 (5.0–18.0)	6 (60)	5 (50)	2 (20)
Unknown	7	48 (32–62)	10.8 (5.0–21.0)	6 (86)	3 (43)	1 (14)
Indeterminate primary site	6	60 (49–75)	12.8 (6.5–20.0)	4 (67)	2 (33)	1 (17)