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Mucinous tumors of the ovary: Diagnostic challenges at frozen section and clinical implications

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ABSTRACT

Objective. Frozen section (FS) diagnosis of mucinous tumors of the ovary can be quite difficult due to the size of these tumors, heterogeneity and potential risk of metastasis from gastrointestinal (GI) neoplasms. Given the paucity of data on this subject, our objective was to determine the reliability of FS diagnosis in ovarian mucinous tumors.

Methods. A retrospective review of 73 consecutive ovarian mucinous tumors submitted for frozen section (FS) evaluation between January 2004 and November 2009 was conducted. FS and final pathology results, in addition to patient characteristics, were collected. Univariate analysis was performed evaluating predictors of FS reliability.

Results. The average tumor size was 19.7 cm (0.8–50 cm). The FS and final pathology diagnosis were concordant in 66% (48/73) of the cases. Of the 25 (34%) discordant cases, 8 (11%) were downgraded and 17 cases (23%) were upgraded. Of the 44 tumors interpreted as LMP on FS, 14 (32%) were malignant at final diagnosis (26% ovarian, 7% GI) and 8 (18%) were benign. Of the 23 benign tumors on FS, 13% were upgraded to either LMP or malignant at final diagnosis. Tumors with a malignant diagnosis on FS were 100% concordant with final diagnosis. Univariate analysis did not reveal any correlation with the FS diagnosis and patient age, tumor size or presence of bilateral disease.

Conclusions. Our study showed a 34% rate of discordance between FS and final diagnosis. Given that 5 cases (7%) were of GI origin, intraoperative assessment of the appendix should be performed in all mucinous ovarian tumors.

Introduction

Mucinous carcinoma of the ovary historically accounted for approximately 11.6% of all primary epithelial ovarian carcinomas, although recent reports suggest it may be <3% with improved methods of distinguishing gastrointestinal primaries from primary ovarian epithelial carcinomas [1]. Correct intraoperative histopathologic interpretation is imperative in order to perform the appropriate operation. In general, in cases where an early stage malignant ovarian tumor is suspected, surgical staging involves total hysterectomy, bilateral salpingo-oophorectomy, omentectomy and lymph node sampling; in cases of borderline tumors, the extent of the surgery may be modified in order to preserve the patient's fertility. Therefore, the accuracy of frozen section (FS) diagnosis in ovarian tumors is critical, especially in patients who desire fertility preservation. Pre-operative CA-125 levels are also less commonly elevated in patient with mucinous tumors making intraoperative decisions even more important. In a review by Kolwijck et al., only 34% patients with mucinous carcinoma had a CA-125 level >35 U/mL [2]. Mucinous tumors have been noted in the literature to be associated with increased inaccuracy on FS diagnosis as compared to serous tumors, but no significant series on the FS diagnoses of mucinous tumors have been reported [3,4]. This is especially important as overdiagnosis of borderline neoplasms may result in unnecessary surgical intervention and underdiagnosis may result in a second surgery, increase tumor spread and lead to inadequate adjuvant therapy [5]. In this study, we aimed to review the accuracy of FS diagnosis of all mucinous ovarian tumors and determine the reliability for surgical staging.

Materials and methods

All consecutive ovarian masses with either a FS or final pathologic diagnosis of mucinous tumor of the ovary at Magee-Womens Hospital of the University of Pittsburgh Medical Center, from January 2004 to November 2009 were identified and included in this study. Consultative specimens and cases that did not have FS were excluded.

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Institutional review board approval for medical record and pathology report review was obtained. At intraoperative consultation, gross examination and a FS of one or more sections were performed depending on tumor size and the degree of suspicion. The 5 μm sections were frozen in a cryostat, stained with hematoxylin and eosin and were interpreted by the gynecologic pathologists. At the time of frozen section, typically only the most suspicious gross lesions would undergo microscopic examination. The current protocol for tumor sampling at our institution is to submit 2 sections per 1 cm of maximum tumor diameter (e.g. a 20 cm tumor would result in 40 sections for final review). Any area that seems suspicious grossly would also be sectioned under the current protocol.

The pathology reports from the FS and permanent sections were reviewed and the following data was collected: maximal diameter of tumor (in centimeters), patient's age, FS and final diagnosis, the presence of bilateral tumors, the presence of endometriosis and surgical staging. Two masses were found to have a final pathologic diagnosis of low malignant potential with foci of microinvasion on final pathology. In this study, they were classified as final diagnosis of low malignant potential, not as malignancies.

Statistical analysis was performed using PASW Statistics 18.0 software. Univariate analysis was performed looking at predictors of accuracy on frozen section. Variables that were analyzed included patient's age, tumor size, presence of bilateral disease, and presence of endometriosis. Chi-square test and Student's *t*-test were used for univariate analysis for categorical variables and continuous variables, respectively. A p value of less than 0.05 was considered statistically significant.

Results

A total of 73 cases were reviewed. The average ovarian tumor size was 19.7 cm (range 0.8 to 50 cm). The median age for all patients was 52 years old (range 26–83). Five patients had bilateral ovarian disease.

Diagnoses by FS of mucinous tumors were concordant with final pathology in 48 of the 73 cases (65.7%). Of the discordant cases, overdiagnosis occurred in 8 benign cases (11%) that were interpreted as LMP on FS. Underdiagnosis occurred in 17 cases (23%) at the time of FS. Eleven malignant lesions were interpreted as LMP on FS; 2 borderline lesions were interpreted as benign on FS; 1 malignant tumor was interpreted as benign on FS (Fig. 1); and 3 metastatic appendiceal malignancies were interpreted as LMP on FS.

The diagnosis of LMP on frozen section was the most discordant with the final diagnosis. Of the 44 tumors diagnosed as LMP on FS, only 22 (50%) remained LMP at the final diagnosis. Fourteen (32%) were upgraded to malignant on final diagnosis (11 ovarian, 3 appendiceal) and 8 (18%) were downgraded to benign on the final diagnosis. Of the 23 tumors that were benign on FS, 13% were upgraded to either LMP or malignant. Tumors with a malignant diagnosis on FS were 100% concordant with final diagnosis.

Despite 34% cases being disconcordant on FS and final pathology, only in 7 cases (10%) did discordance have clinical impact. Six patients were unnecessarily thoroughly surgically staged due to FS diagnosis of LMP and later the final pathology was benign, and 1 patient with a malignancy diagnosed on final pathology did not undergo surgical staging due to the benign FS diagnosis.

Univariate analysis did not reveal any correlation with the accuracy of frozen section diagnosis and patient age, tumor size or presence of bilateral tumors (Table 1).

Discussion

The aim of intraoperative FS diagnosis for ovarian tumors is to give a preliminary diagnosis of malignancy enabling the surgeon to choose the most appropriate operation, including conservative therapy for young women with low malignant potential tumors. While experienced surgeons and pathologists often note that mucinous tumors are difficult to interpret on FS, there is a paucity of literature giving evidence to this notion. In this retrospective study, we found an overall concordance rate of 66% (48/73) for FS diagnoses of mucinous adnexal tumors. These results are similar with previous studies that had limited cases of mucinous tumors [4,6–9].

While there have been other retrospective studies that have evaluated the utility of FS diagnosis of ovarian masses, these studies have included only small numbers of patients with mucinous histology [4,6–9]. The results of these studies also suggest that mucinous tumors are difficult to diagnose on FS, as confirmed in the present study. In the largest series published with mucinous tumors, Puls et al. included 105 mucinous tumors and found a concordance rate for frozen and final diagnosis of 87%. However, only 26 tumors with a frozen or final diagnosis of LMP were included in this series likely contributing to the improved concordance as compared to our study. In a series by Twaalfhoven et al., of the 176 ovarian masses evaluated, only 45 were mucinous tumors and they found a concordance rate of 80% (36/45) [9]. Interestingly, amongst borderline mucinous tumors included in this analysis, 8 of the 10 were false negatives on frozen section. Ilvan further demonstrated diagnostic problems in cases of mucinous tumors, in that 15 of the 21 cases of disagreement in this study were mucinous tumors — all reportedly due to sampling errors [6]. Houck et al. published the largest series of borderline mucinous tumors. This series included 47 mucinous borderline tumors, of which, 49% had concordant frozen/final diagnosis compared to 71% of serous tumors [4]. This study differed from the present one in that only cases of borderline tumors either on FS or final pathology were included for analysis. The higher overall concordance rate seen

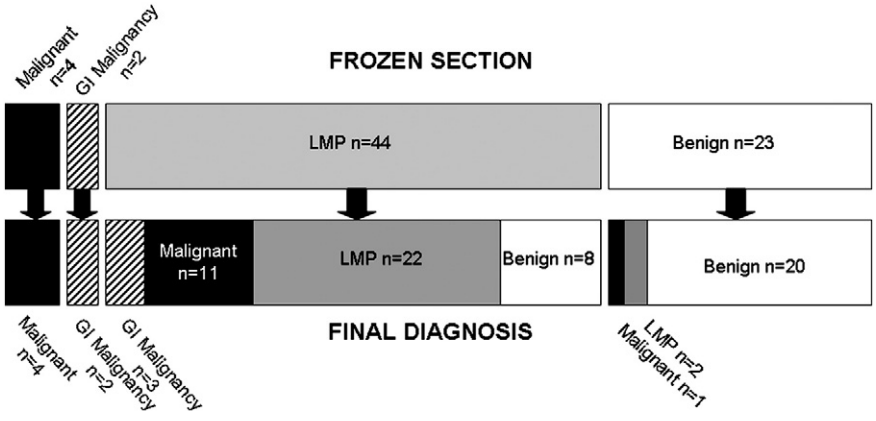

Fig. 1. Comparison of frozen section diagnosis to final pathology diagnosis in ovarian mucinous tumors.