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RESEARCH ARTICLE

Role of Intraoperative Frozen Section in Surgical Management of Ovarian Masses

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ABSTRACT

Introduction: Accuracy of intraoperative frozen section diagnosis is very important in ovarian masses as the diagnosis and course of surgery is usually determined by frozen section examination. There is scant data on this topic from this part of the world.

Aims and objectives: To determine accuracy of intraoperative frozen section for appropriate surgical management of ovarian masses and discuss the reasons for discordancy.

Materials and methods: Retrospective analysis of all patients subjected to the exploratory laparotomy for suspected ovarian mass who underwent intraoperative frozen section at Aga Khan University Hospital from January 2006 till December 2014.

Results: Data from 295 patients were analyzed. The mean age was 40.7 years. The final histologic diagnosis revealed benign lesion in 232 (78.6%), borderline in 17 (5.8%), and malignant in 46 (15.6%) cases. The final histologic diagnosis agreed with the frozen section in 288 cases with an accuracy of 97.6%. In seven discordant cases, there were no false positives, and the false negative rate was 2.4%. Sensitivity was highest in the benign and borderline group (100%) and lowest in the malignant group (93.4%), while specificity was highest in malignant (100%) and lowest in the benign group (92%). Tumor size more than 10 cm, borderline, or mucinous histology were significant predictors for discordancy in our study.

Conclusion: Intraoperative frozen section with its high accuracy is a sensitive tool to guide us regarding the surgical management of patients with ovarian masses. This technique is less reliable when we are dealing with large >10 cm masses, mucinous, or borderline tumors.

Keywords: Frozen section, Ovarian neoplasm, Surgery.

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INTRODUCTION

There are three major categories of ovarian neoplasm: Benign, borderline, and malignant; different from each other based on their biological characteristic, treatment, and prognosis.[1] Ovarian cancer is the leading cause of death among all cancers of female genital tract and leading indication of all gynecological surgeries.[2,3] The overall lifetime risk of ovarian cancer in general population is 1.5%, while the overall risk of malignancy in an ovarian neoplasm is 13% in premenopausal women and 45% in postmenopausal women.[4]

Prior to opting for any surgical management, it is imperative to differentiate the ovarian mass into benign, borderline, or malignant.[5] This is usually evaluated through certain serological and radiological tests like ultrasound, computed tomography (CT) scan, and CA125 assay.[6] Despite improvements in these techniques, the diagnosis remains difficult due to significant false positive and false negative results. No single method is completely sensitive or specific for ovarian malignancy.[7] Therefore, intraoperative histopathological consultation is required to differentiate ovarian mass into benign, borderline, and malignant form.

The intraoperative frozen section has a great impact on diagnosis of ovarian masses. Histopathological findings from frozen section help us in staging and thereby enable us to select appropriate surgical management. If histopathology shows borderline ovarian mass, conservative or fertility preserving surgical approach can be opted instead of radical approach.[8] Many studies have previously assessed the efficacy of intraoperative frozen section for ovarian masses with overall accuracy ranging from 86 to 97%.[9] However, there is paucity of data on this topic in Pakistan. Hence, the present study was conceived to determine the accuracy of intraoperative frozen section for diagnosing the nature of ovarian masses.

MATERIALS AND METHODS

Institutional Review Board approval was obtained to review the medical records of all patients subjected to the

exploratory laparotomy for suspected ovarian mass who underwent intraoperative frozen section at Aga Khan University Hospital from January 2006 till December 2014.

All cases referred for intraoperative frozen section from outside Aga Khan University Hospital and intraoperative frozen section done for other malignancies of female genital tract were excluded from the study.

In the present study, we reviewed 295 ovarian masses submitted for frozen section. In all specimens, tissue samples were processed following standard protocol for intraoperative histology. After being examined macroscopically for size, consistency, surface irregularities, and vegetation, two to three samples were taken by the attending pathologist from suspicious areas. Frozen sections were cut on Shandoneryotome FSE machine. Specimens were frozen in a cryostat and 5 µm sections were stained with hematoxylin and eosin (H&E). The slides were examined by the attending pathologist. Subsequently, for permanent sections, the specimen was fixed overnight in 10% buffered formalin. Grossed and adequate representative sections were taken according to the standard guidelines. The permanent sections were initially evaluated on H&E stains. Special immunohistochemical stains were performed in some cases for confirmation of diagnosis and tumor typing.

The data was obtained from histopathology and gynecology department. Medical records of all patients were reviewed and relevant demographic, clinical, and pathologic information was acquired. Patient's characteristics, like age, marital status, parity, menopausal status, ultrasonographic features, CA-125 level, were checked. The final diagnosis of the paraffin-embedded tissues was compared with the intraoperative frozen section result.

Statistical Analysis

IBM Statistical Package for the Social Science (SPSS), version 19 was used for data analysis. Sensitivity and specificity values were calculated by using 2 × 2 contingency tables. Categorical variables were compared by using chi-square test. Continuous variables were tested for the normality of distribution, and compared using Student's t-test.

RESULTS

From January 2006 to December 2014, 295 patients underwent frozen section test for evaluation of ovarian masses in our University Hospital. The mean age was 40.7 years (6–80 years). Sixty-two women (21.0%) were unmarried, 54 (18.3%) were nulliparous, and majority, i.e., 182 (61.7%) were multiparous. Majority of the women were premenopausal, i.e., 205 (69.5%) and the remaining were postmenopausal 90 (30.5%). Epithelial neoplasms (51.2%), endometriomas (13.6%), and germ cell neoplasms (12.9%) were the most frequent histological diagnosis in our patients.

Table 1: Frequencies of different histological types

	Frequency	*Percentage*
Epithelial	151	51.2
Germ cell	38	12.9
Sex cord stromal	19	6.4
Endometrioma	40	13.6
Simple cyst	18	6.1
Hemorrhagic cyst	14	4.7
Metastatic tumor	1	0.3
Others	14	4.7
Total	295	100.0

Table 2: Comparison of frozen section diagnosis *vs* final paraffin diagnosis

		Final histology			
		Benign	*Borderline*	*Malignant*	*Total*
Frozen section	Benign	232	4	1	237
	Boderline	0	13	2	15
	Malignant	0	0	43	43
Total		232	17	46	295

Table 3: Diagnostic value of frozen section

	Benign (%)	*Borderline (%)*	*Malignant (%)*
Sensitivity	100	100	93.4
Specificity	92	99	100
Positive predictive value	97.8	86	100
Negative predictive value	100	99	98

Frequencies of various histological features are shown in Table 1.

The final histologic diagnosis revealed benign lesion in 232 (78.6%), borderline in 17 (5.8%), and malignant in 46 (15.6%) cases. The final histologic diagnosis agreed with the frozen section in 288 cases with an accuracy of 97.6% (Table 2). Five cases of benign tumor were upgraded as borderline (n = 4) and malignant (n = 1) on final histology. In two cases, intraoperative frozen section diagnosis of borderline was later classified as malignant. All frozen section diagnosis of malignant masses were concordant with the final paraffin diagnosis.

Sensitivity, specificity, positive, and negative predictive values are shown in Table 3. In seven discordant cases, there were no false positives. All of these cases were false negatives (2.4%) on intraoperative frozen section.

DISCUSSION

Intraoperative frozen section is an important diagnostic tool, which is very helpful in determining the malignant

potential of ovarian masses.[10] Frozen section diagnosis of ovarian tumor is of paramount importance to determine the appropriate surgical procedure, as the results of which is essential to prevent over- or undertreatment of ovarian tumor. Especially in younger subjects, preservation of fertility by conservative management or loss of fertility by radical management is determined by the accurate diagnosis of ovarian mass by frozen section biopsy results; fertility can be preserved in cases with benign or borderline ovarian tumor.

At least one section is required for each 1 cm diameter of the tumor mass to rule out malignancy in borderline tumors. The accuracy of frozen section biopsy in diagnosing the malignant potential of ovarian masses range from 89.8 to 97%.[10-13] The accuracy of frozen section biopsy in our study is 97.6%. Our study also shows that the sensitivity and specificity of frozen section biopsy in diagnosing the benign ovarian tumor is 100 and 92% respectively and the sensitivity and specificity of the frozen section in diagnosing borderline ovarian tumor is 100 and 99% respectively. The sensitivity and specificity of the frozen section biopsy in diagnosing malignant ovarian tumor is 93.4 and 100% respectively. The positive predictive value of frozen section biopsy in benign, borderline, and malignant tumor is 97.8, 86 and 100% respectively. The negative predictive value of frozen section biopsy in benign, borderline and malignant tumor is 100, 99 and 98% respectively. Our study shows that sensitivity, specificity, positive predictive values, and negative predictive values of frozen section biopsy are high in diagnosing benign, borderline, and malignant tumor.

In our study, maximal tumor size was significantly larger (>10 cm) in discordant cases, which is in agreement with earlier reports. The diagnosis of borderline tumors that are mucinous is difficult than the borderline serous tumor because the mucinous tumors are larger in size and are heterogeneous in nature.[14] Borderline mucinous tumors tend to have benign, borderline, and malignant areas in the same tumor mass.[15] Our study also shows that there is a statistically significant difference between mucinous tumors diagnosed histologically and frozen section misdiagnosis. The reason for misdiagnosis by frozen section of mucinous tumor is due to the larger tumor size and multilocular tumor (Table 4). There is a statistically significant difference in case of borderline tumors, which were underdiagnosed in frozen section. Of total seven discordant cases, four benign mucinous tumor diagnosed by frozen section were found to be borderline mucinous in final histopathological examination. Two benign epithelial tumors, on final histopathological diagnosis, were serous cyst adenocarcinoma and clear cell adenocarcinoma. One benign teratoma was diagnosed as immature teratoma (Table 5). Metastatic ovarian tumor account for 0.3% of ovarian tumor in our study population. Differentiating metastatic tumor from primary ovarian tumor is essential in intraoperative management of ovarian tumor. Features that suggest metastatic ovarian tumor intraoperatively are bilateral involvement, invasion of lymphatics and vascular tissue, extensive involvement of the surface, and multinodular growth pattern.[16] It is always a challenge for the pathologist to diagnose a metastatic ovarian tumor from the primary ovarian tumor. Cervical metastatic tumor may mimic primary ovarian tumor or mucinous tumor. Cervical tumors that are microinvasive can also metastasize to ovary.

It is always a challenge for the pathologist to diagnose tumor which are mucinous, endometrioid, or mixed pattern with mucinous and endometrioid tumor from primary epithelial tumor of the ovary. It is much more difficult when the tumor is bilateral.[17,18]

Though frozen section biopsy offers a fairly accurate results, there are always some discordance with results of paraffin samples and the reason could be due to limited sampling or misinterpretation. The size of the adnexal tumor mass is very important, which is underscored by the procedure of frozen section biopsy. The frozen section biopsy is a rapid procedure which has to be done

Table 4: Comparison of demographic and tumor related factors among concordant and discordant tumors

Sl. no.	*Variables*	*Concordant cases (n = 288)*	*Discordant cases (n = 7)*	*p-value*
1	Age, mean (SD)	40.8(15.15)	37 (18.66)	0.5
2	Menopausal status			
	Premenopausal	201	4	0.36
	Postmenopausal	87	3	
3	Laterality of tumor			
	Unilateral	248	7	0.35
	Bilateral	40	0	
4	Tumor size			
	<10 cm	164	1	0.02*
	>10 cm	124	6	
5	Histology			
	Mucinous	64	4	0.03*
	Nonmucinous	224	3	
4	Histology			
	Borderline	13	4	0.000*
	Nonborderline	275	3	

Table 5: Histological details of concordant and discordant cases

Sl. no.	*Frozen section diagnosis*	*Final paraffin diagnosis*	*No. of cases*
1	Benign mucinous	Mucinous borderline	1
2	Benign teratoma	Immature teratoma	1
3	Epithelial borderline	Serous cyst adenocarcinoma	1
4	Benign mucinous	Borderline mucinous	3
5	Epithelial borderline	Clear cell adenocarcinoma	1

within the limited timeframe in the operating theater. It offers limited time for the pathologist to take adequate sampling in a given block of the specimen as opposed to the standard paraffin sampling procedure that allows the pathologist to make adequate number of samples to hit at correct and accurate diagnosis of the tumor mass. The operating surgeon and the reporting pathologist must have an effective communication of the clinical picture and the operative picture of the patient, as there are always chances for the pathologist to report a tumor as malignant because of the necrotic area that could have been seen in frozen section but the real clinical picture could have been the tumor mass could have been necrosed because of the torsion of the tumor casing ischemic necrosis which could have been interpreted as tumor necrosis.

In addition to histopathological examination of H&E slides to make the diagnosis, sometimes validation of the diagnosis often requires immunohistochemistry. Complete clinical data always helps the pathologist to correctly diagnose a given sample. The operating surgeon should always examine the abdomen intraoperatively to detect the origin of the tumor.

The quality of frozen section biopsy is determined by the level of the experience of the reporting pathologist. It is also determined by the quality of the frozen section slides, which also plays a major role in arriving at correct diagnosis. The accuracy of the diagnosis of benign, borderline, or malignant tumor in terms of sensitivity, specificity, positive, and negative predictive value is high in hands of experienced gynecological pathologists than in the hands of nongynecological pathologists.[6]

The level of CA125 does not correlate well with the benign and malignant tumor. Also in case of mucinous tumor, the level of expression of CA125 is less. The levels of CA125 may be of help to pathologist if the pathologist could differentiate between mucinous and nonmucinous tumor in frozen section biopsy, as the nonmalignant diagnosis in mucinous tumor is not much reliable.

CONCLUSION

Intraoperative frozen section with its high accuracy is a sensitive tool to guide us regarding the surgical management of patients with ovarian masses. This technique is less reliable when we are dealing with large >10 cm masses, mucinous, or borderline tumors.

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