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ORIGINAL ARTICLE

Accuracy of intraoperative consultation for ovarian tumours: Experience in an Indonesian teaching hospital

Dyah FAUZIAH, Rovi ANGGORO*

Department of Anatomical Pathology, Faculty of Medicine Universitas Airlangga/ Dr.Soetomo Hospital Surabaya

Abstract

Background: Ovarian tumours are a very heterogeneous group of tumours, consisted of non-neoplastic and neoplastic lesions. Preoperative diagnoses in most conditions are inconclusive due to similar clinical, radiological and laboratory findings. Intraoperative consultation is crucial because it can provide rapid diagnosis leading to a suitable surgical management for the patients. *Objective*: To obtain profile, accuracy and concordance rates of ovarian intraoperative consultation in Dr. Soetomo Hospital Surabaya, a teaching hospital in Indonesia. *Materials and Methods*: Observational retrospective study, using data from archives of intraoperative consultation reports in Dr. Soetomo General Hospital Surabaya within 2012-2016 period. There were 734 cases of ovarian intraoperative consultations, all then proceed to permanent sections. Accuracy, sensitivity, and specificity rates were calculated. *Results*: Overall accuracy was 89.5%. Sensitivity for benign, borderline and malignant cases were 98.49%, 71.19% and 84.01%, respectively. Specificity were 90.32%, 95.11% and 98.72%, respectively. *Conclusion*: Intraoperative consultation for ovarian tumours has a reliable diagnostic value in benign and malignant lesion, but lower value in borderline tumours.

Keywords: Ovary, intraoperative consultation, accuracy, sensitivity, specificity

INTRODUCTION

Ovarian tumours are a very heterogeneous group of tumours, consisted of neoplastic and non-neoplastic lesions. Neoplastic tumours include surface epithelial, germ cell, sex-cord stromal and metastatic tumours. Ovarian cancer is the seventh most commonly diagnosed cancer among women in the world, with estimated 239.000 new cases and 152.000 deaths annually.[1] Indonesian cancer profile by WHO showed 7.6% mortality rate for ovarian cancer.[2] Department of Obstetrics & Gynecology, Division of Oncology of Dr. Soetomo Hospital Surabaya recorded 561 cases of surgically managed ovarian tumours for 2014 – 2016 period.

Various non-neoplastic lesions could also cause ovarian enlargement, most common are endometriotic cyst, follicle cyst and infection process. While surgical management varies considerably depending of the nature of the lesion, preoperative diagnosis is seldom available. Serum marker Ca-125 is not specific for malignancy, since it could give normal result particularly in early stage of malignancy and conversely high in non-neoplastic cases such as endometriosis and pelvic inflammatory disease.[3,4] Imaging also has limitations in the accurate diagnosis of ovarian tumours especially in large heterogeneous lesions. In such cases, intraoperative consultation is invaluable for enabling rapid diagnosis to help gynecologists plan appropriate surgical management accordingly.[5,6] Anatomical Pathology Laboratory of Dr. Soetomo Hospital Surabaya recorded 744 intraoperative consultations for ovarian tumors in 2012 – 2016 period.

Intraoperative diagnosis in ovarian tumours comprise macroscopic, imprint cytology and frozen section. Pathologists are advised to formulate a differential diagnosis based on the lesion's gross appearance, age of the patient, additional relevant clinical information and microscopic examination.[6]

**Address for correspondence*: Rovi Anggoro, Department of Anatomical Pathology, Faculty of Medicine Universitas Airlangga / Dr. Soetomo Hospital Surabaya, Jalan Mayjen Prof Dr. Moestopo no 47, Surabaya 60131 – East Java, Indonesia. Phone: +6231-5020251, +6231-5020252, +6231-5020253 Ext. 151, 182, 153. Fax: +6231-5026333. Email: *rovi.anggoro@gmail.com, ang_df01@yahoo.com.*

This retrospective study aims to evaluate the accuracy of intraoperative consultation for ovarian tumours compared to the permanent sections in our center and to analyse the causes of diagnostic discrepancies, to help improve the intraoperative consultation diagnosis in the future.

MATERIALS AND METHODS

Records of all intraoperative consultations for ovarian tumours in Anatomical Pathology Department of Dr. Soetomo Hospital Surabaya between January 2012 – December 2016 were analysed. There were 744 cases, all were compared with the final diagnosis on permanent sections. Ten cases were deferred and dropped from the data. Data then analysed statistically to determine overall accuracy, sensitivity and specificity of each benign, borderline and malignant group of tumours. This study had been approved by Dr. Soetomo Hospital Surabaya ethical committee (Reference number: 0060/KEPK/II/2018).

RESULTS

There were 744 cases of ovarian tumours in which intraoperative consultations were done. The diagnosis of intraoperative consultation were deferred in 10 cases; one case due to extensive necrotic tissue, one case due to non-representative sample (a small fibrotic tissue), three cases due to discordant macroscopic and microscopic findings (all three were large teratomas weighed more than 1 kg, grossly malignant with solid fleshy areas and necrotic parts but the frozen sections taken failed to show evidence of immature or neuroepithelial elements), and five cases of mesenchymal tumours in which determination of malignancy required thorough evaluation of permanent section (including mitotic count) and immunohistochemistry studies. Cases with deferred intraoperative diagnosis were excluded in this study. Permanent sections were made in all 734 cases.

The age group ranged from 10 to 80 years and the mean age was 44.8±12.8 years. Permanent diagnosis after intraoperative diagnosis showed that the most common non-neoplastic lesion was endometriotic cyst (117 cases). The most common benign, borderline and malignant neoplasm was mature teratoma (71 cases), mucinous borderline tumour (44 cases) and mucinous carcinoma (86 cases), respectively (Table 1).

Table 2 shows the comparison of frozen and paraffin sections diagnosis. There were 77 discordant diagnosis, with 69 false negative cases and 8 false positive cases. The discordance occurred mostly in mucinous borderline tumour cases. Twenty-four cases diagnosed mucinous borderline tumour intra-operatively turned out to be mucinous carcinoma in final diagnosis (Table 3).

Statistical analysis found overall accuracy of intraoperative consultation in ovarian tumours was 89.5%. Sensitivity was 98.49%, 71.19% and 84.01% for benign (non-neoplastic lesions included), borderline and malignant lesions, respectively. Specificity was 90.32%, 95.11% and 98.72% for benign (non-neoplastic lesions included), borderline and malignant lesions, respectively (Table 4).

DISCUSSION

Overall, statistical analysis found that accuracy of intraoperative consultation for ovarian tumours in this study was 89.5%. Previous studies also stated that the accuracy of intraoperative consultations for gynecology pathology ranged from 86 to 97%.[3,5,7] High specificity was found for all three groups of tumours, 90.32% for benign lesions (non-neoplastic lesions included), 95.11% for borderline tumours and 98.72% for malignant tumours. These findings are also in accordance with previous studies.[5,8]

In this study, sensitivity was 98.49%, 71.19% and 84.01% for benign (non-neoplastic lesions included), borderline and malignant lesions, respectively. Many other studies also had the same findings, that the sensitivity of intraoperative consultation is high for benign and malignant tumours but tend to be lower in borderline tumours, particularly mucinous tumours.[3,5,9]

From total 734 cases, there were discordant diagnoses in 77 cases. The main cause was sampling errors, especially in false negative cases. These mostly happened in highly heterogeneous tumours like mucinous tumours and teratomas. Frozen section may fail to sample the most severe lesion or frankly malignant area in a limited number of sections intraoperatively.[10] Forty-seven (61%) misdiagnoses in our study were in mucinous tumour group. Because mucinous tumours are notorious for their histologic heterogeneity with malignant foci sometimes representing only a small component, it is important to open and carefully examine each cyst, sampling the most suspicious areas as many

TABLE 1. Histological types according to permanent section results

Diagnosis	Cases (n)	(%)
Non neoplastic lesions		
Endometriotic cyst	117	15.94
Abscess	12	1.63
Lutein cyst, simple cyst, etc	10	1.36
Benign Neoplasms		
Mature teratoma	71	9.67
Mucinous cystadenoma	68	9.26
Serous cystadenoma	25	3.41
Fibroma	13	1.78
Seromucinous cystadenoma	7	0.95
Serous adenofibroma	3	0.41
Thecoma	2	0.27
Brenner tumour	2	0.27
Mucinous adenofibroma	2	0.27
Benign mesenchymal tumour	1	0.14
Borderline Neoplasms		
Mucinous borderline tumour	44	5.99
Serous borderline tumour	13	1.78
Seromucinous borderline tumour	1	0.14
Sertoli-Leydig moderately differentiated	1	0.14
Malignant Neoplasms		
Mucinous carcinoma	86	11.72
Serous carcinoma	77	10.49
Endometrioid carcinoma	59	8.04
Clear cell carcinoma	40	5.45
Adult granulosa cell tumour	18	2.45
Immature teratoma	8	1.09
Adenocarcinoma (NOS)	8	1.09
Dysgerminoma	7	0.94
Yolk sac tumour	7	0.94
SCC arising in teratoma	7	0.94
Mixed Malignant Mullerian Tumour	5	0.68
Signet ring cell carcinoma	5	0.68
Metastatic carcinoma	4	0.54
Seromucinous carcinoma	3	0.41
Non Hodgkin Lymphoma	2	0.27
Malignant stromal tumour (Sertoli-Leydig tumour, poorly differentiated)	2	0.27
Undifferentiated carcinoma	1	0.14
Mixed germ cell tumour	1	0.14
Embryonal carcinoma	1	0.14
Melanoma	1	0.14
Total	**734**	**100**

TABLE 2: Comparison of intraoperative diagnosis and final formalin fixed paraffin embedded (FFPE) histopathological diagnosis (gold standard)

		Paraffin Sections (gold standard)			
		Benign	**Borderline**	**Malignant**	**Total**
Frozen Section	Benign	326	14	25	365
	Borderline	3	42	30	75
	Malignant	2	3	289	294
	Total	331	59	344	734

False negative False positive

TABLE 3: Discordant diagnosis, intraoperative diagnosis compared with final permanent histopathological diagnosis

Intraoperative Diagnosis		**Permanent Sections**	
Diagnosis	**n**	**Diagnosis**	**n**
Benign lesions	**39**		
Mucinous adenoma	17	Mucinous borderline tumour	9
		Metastatic mucinous carcinoma (secondary tumour)	4
		Mucinous carcinoma	3
		Clear cell carcinoma	1
Serous adenoma	4	Serous borderline tumour	3
		Serous carcinoma	1
Endometriosis cyst	3	Endometrioid carcinoma	2
		Serous papillary carcinoma	1
Mature teratoma	6	SCC arising in mature teratoma	4
		Immature teratoma	2
Adenofibroma	1	Malignant Mixed Mullerian Tumour (MMMT)	1
Benign lesions, not specified	8	Malignant ovarian tumour, DD: 1. Adult granulosa cell tumour 2. Dysgerminoma	1
		Immature teratoma	1
		Serous carcinoma	1
		Serous borderline tumour	1
		Signet ring cell carcinoma	1
		Endometrioid carcinoma	1
		Smooth muscle of uncertain malignancy potential	1
		Dysgerminoma with extensive necrosis	1
Borderline tumour	33		
Mucinous borderline tumour	28	Mucinous carcinoma	24
		Mucinous adenoma	3
		Endometrioid carcinoma	1
Serous borderline tumour	5	Serous carcinoma	5
Malignant tumour	5		
Malignant, not specified	3	Suspicious for Sertoli-Leydig intermediate differentiation with heterologous component	1
		Struma ovary	1
		Benign mesenchymal tumour with extensive necrosis	1
Mucinous carcinoma	2	Mucinous borderline tumour	2

TABLE 4: Sensitivity, specificity, Positive Predictive Value and Negative Predictive Value of Intraoperative Consultation Diagnosis in Ovarian Tumours

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Benign	98.49	90.32	89.32	98.64
Borderline	71.19	95.11	56	97.42
Malignant	84.01	98.72	98.3	87.5

as time allows. Cytology imprint also can be used to complement sampling multiple areas for less-consuming time. As we all know, technical factor which could also causes difficulty in diagnosis is the quality of sections prepared with frozen section technique limits the evaluation of cellular detail. So, the combination of frozen section with cytology imprint is recommended to help overcome this problem in most settings. The pathologist experience and skill are also an important factor.[8,11]

There were 8 false positive cases in our study. Three cases diagnosed as borderline tumours intraoperatively turned out to be benign, three cases diagnosed as malignant tumours intraoperatively turned out to be borderline tumours, and two cases diagnosed as malignant tumours intraoperatively turned out benign in permanent sections.

We present here two false positive cases. The first was a 55 years old female with suspected malignant solid cystic ovarian tumour. Gross examination found 220 grams multiloculated cyst with solid area. Frozen section showed closely packed glands layered by atypical-looking cells, lead to adenocarcinoma diagnosis intraoperatively. In permanent corresponding sections, the closely packed glands turned out to be benign thyroid follicles, and the final diagnosis was struma ovary (FIG. 1).

The second false positive case was a 65 years old woman with 5000 grams ovarian tumour. Gross examination found a thick walled unilocular cyst filled with thick yellowish substance. Frozen section showed a thick fibrous tissue with focal hypercellular area, consisted of cells with round and monotonous nuclei, vaguely resembled acinar structure. This finding, considered along with gross appearance (huge tumour size and necrotic areas inside the cyst) rendered the intraoperative diagnosis as malignancy. In permanent sections, after extensive samplings, the tumour was mostly consisted of edematous fibrous tissue, and the hypercellular area turned out to be severe infiltration of inflammatory cells (FIG. 2).

In order to gain maximal results in intraoperative consultation's assessment, it is very important to know the epidemiology of each ovarian tumours, relevant clinical information of the patient, macroscopic characteristic of each tumours, and surely the histological findings in frozen section.[9] The major limitations of frozen section are limited number of sections that can be examined, thicker sections compared to permanent sections and freezing artifacts that can obscure the finer details and influence interpretation. Misdiagnoses are mostly caused

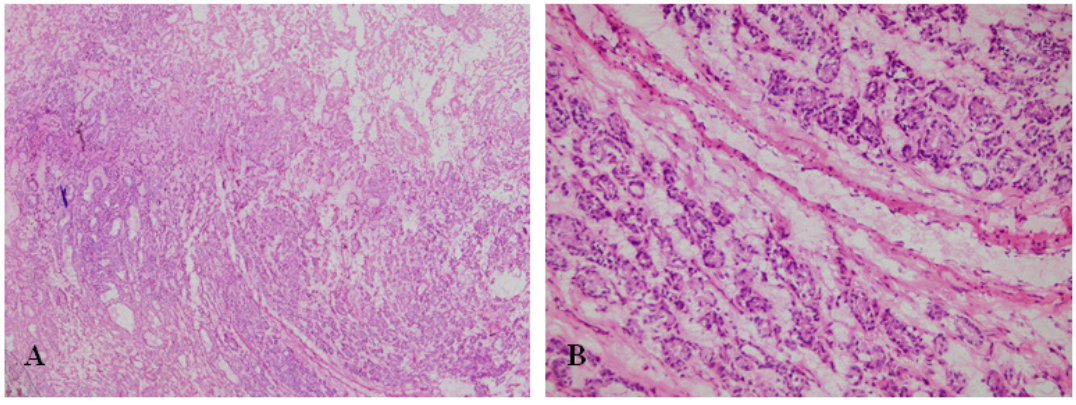

FIG. 1: Struma ovary was interpreted as adenocarcinoma intraoperatively. Frozen section showed closely packed glands structure. (A. H&E; 40x, B. H&E; 200x).

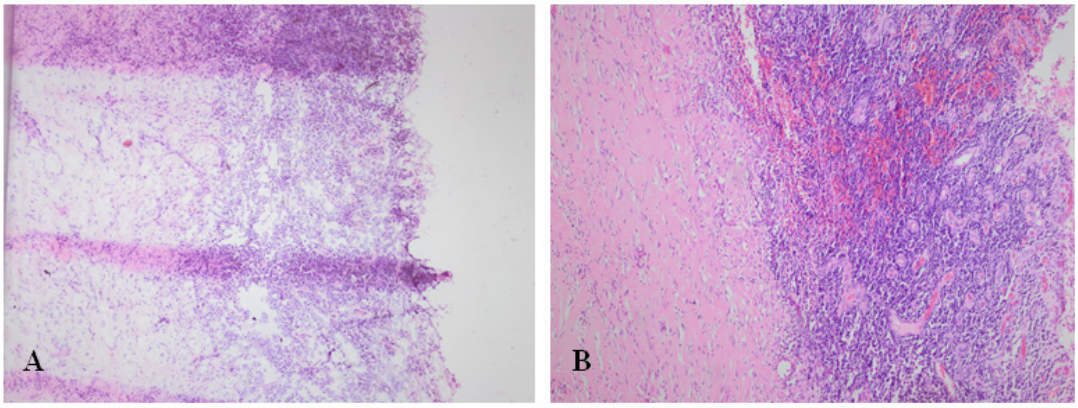

FIG. 2: Fibrous tissue with abundant inflammatory cells was interpreted as malignancy intraoperatively. A. Frozen section showed hypercellular area with vaguely acinar structures (HE, 100x). B. Corresponding section in permanent section showed thick fibrous tissue with abundant inflammatory cells (HE, 100x).

by sampling errors and misinterpretation from the pathologist. Good communication between the gynecology oncologist and pathologist is vital for diagnosis and determination of next appropriate surgical management for the patient, especially in difficult cases.

CONCLUSION

Intraoperative consultation for ovarian tumours is an invaluable tool with decent high accuracy to help clinicians determine the next surgical management. Misdiagnoses mostly caused by sampling errors and misinterpretation from the pathologist. To minimise diagnostic errors, comprehensive knowledge in clinical, radiological, laboratory, cytology and histology findings of each ovarian tumours along with good communication between the clinician and the pathologist is a must.

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