Folia Medica Indonesiana Vol. 49 No. 2 April - June 2013 : 119-123

DIAGNOSTIC ROLE OF INTRA OPERATIVE OVARIAN CYST FLUID CYTOLOGY IN DETERMINING MALIGNANCY

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ABSTRAK

Keganasan kista ovarium umumnya merupakan nukleoplasma pada organ genitalia wanita. Metode potong beku intra operatif sangat penting dan membantu dalam diagnosis kecurigaan keganasan kista ovarium. Namun, metode potong beku tidak tersedia pada beberapa rumah sakit, khususnya di negara berkembang. Tujuan dari penelitian ini adalah untuk menjelaskan peran diagnostic sitologi cairan kista intra operatif. Penelitian ini dilakukan di Departemen Patologi RS Dr. Soetomo, Surabaya, Indonesia selama tiga bulan pada tanggal 1 November 2012 sampai 31 Januari 2013. Ada tiga puluh kasus cairan kista ovarium. Sitologi melalui pemusingan cairan kista yang diperoleh aspirasi intra operasi. Hasil sitologi dibandingkan dengan diagnosis histopatologi sebagai standar emas. Secara keseluruhan akurasi, sensitivitas dan spesifisitas diagnosis sitologi cairan kista ovarium intra operatif adalah 86,7%, 76,5% dan 100%. Nilai prediktif positif dan negatif adalah 100% dan 76,5%. Pemeriksaan sitologi cairan kista ovarium yang diperoleh dengan aspirasi intra operatif menunjukkan spesifisitas yang tinggi dan nilai prediktif positif. ***(FMI 2013;49:119-123)***

Kata kunci: *cairan kista ovarium*

ABSTRACT

Malignancy of the ovarian cyst is a common neoplasms of female genital organs. Frozen section is an important and helpful method in intra operative diagnosis of suspiciously malignant ovarian cyst. But frozen section facilities are not available at many hospitals, especially in developing countries. The aim of this study is to determine the role of intra operative cytological diagnosis of ovarian cyst fluid. The present study was conducted in Pathology Department Dr. Soetomo hospital, Surabaya, Indonesia on Novembre 1st 2012 until January 31st 2013. Thirty cases of ovarian cyst fluid by intra operative aspiration were collected. Cytological smear were prepared by centrifuging cyst fluid obtained by intra operative aspiration. Cytological result were compared with histopathological diagnosis as the gold standard. Overall the accuracy, sensitivity and specificity of intra operative cytological diagnosis of ovarian cyst fluid were 86,7%, 76,5% and 100%, respectively. The positive and negative predictive value were 100% and 76,5%. Cytological examination of ovarian cyst fluid obtained by aspiration intra operative demonstrated high specificity and positive predictive value. ***(FMI 2013;49:119-123)***

Keywords: *ovarian cyst fluid, cytology.*

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INTRODUCTION

Malignancy of the ovarian cyst is one of the most common cased in Pathology Departemen Dr. Soetomo hospital. Prompt diagnose for the malignancy is used to frozen section (histopathology) as gold standard is important to do definitive therapy Unfortunately, complication of examination method and facilities must be complete caused examination malignancy of the ovarian cyst is difficult to do by hospital with facilities disability. It have reported that examination malignancy of the ovarian cyst with aspiration pre operative method had risk for spreading tumor in peritoneum cavity (Bibbo et al 2008, Lee at al 2003, Cibas 2009). Frozen section in intra operative is used for diagnosis malignancy of the ovarian cyst. However in development country included Indonesia, Frozen section facilities are not available in a lot of hospital (Bibbo et al 2008, Cibas 2009, Shahid et al 2011, 2012, Ghaemmaghani et al 2007). Intra operative cytological cyst fluid examination is an alternative solution used for understanding a malignancy of the ovarian cyst in the hospital with frozen section facilities disability.

If cytological cyst fluid method is compared by histopathology there is a similarity in sensitivity and specificity with histopathology method. Moreover, advantages of cytological method are simple, cheap and

easy to do. Although studies about malignancy of ovarian cyst are excessive there is no information which is talk about cytology cyst fluid in intra operative for diagnosis the malignant ovarian cyst. The purpose of this study was to understand a malignancy of ovarian cyst by intra operative cytological cyst fluid method. the Evaluation for cytological cyst fluid method based on characteristic malignant cells that loss its ability binding with others, so it will be free in the cyst fluid.

MATERIALS AND METHODS

This study was a prospective study held in Dr. Soetomo Hospital for three months starting from November 1st 2012 until January 2013. Sample are obtained from suspiciously malignant ovarian cyst fluid by an operational laparotomy which met indication operational frozen section. After ovarian cyst tissue received, aspiration cyst fluid did by needle 23G. Then, cyst fluid are centrifuged with speed 3.000 rpm during 5 minutes. Supernatant are removed, it will be made a smear on object glass from sediment materials sample. Afterwards, fixation is did by water dry method and Diff Qiuk spread. Next, microscopic evaluation is did. All these method need ten until fifteen minutes time. Overall, the result will be classified on Benign and Malignant. It's called benign if the appearance benign cells or non-neo-plastic or are not appear atypical malignant in cytology. The, all sample are compared by histophatological diagnosis by hematoxylin-eosin spread as golden standard diagnosis. Malignant histopathological result is involved borderline criteria, primary malignant or metastases. Then, cytological result is compared by histopathological diagnosis as a golden standard and made table 2x2. Correlation test based on statistical analysis about accuracy.

RESULTS

In this study collected there were 30 sample intra operative ovarian cyst fluids. Sample study was between 11 and 59 years old. On 30 cases based on cytology result there were 17 cases showed benign cytology, 7 cases of atypical cells and 6 cases showed malignant cytology. The final results of this study showed histopathology in 13 cases of benign, 4 borderline tumor cases and 13 cases showed malignant histopathology.

Comparison result between ovarian cyst fluid cytology and histopathology obtained 13 cases of positive, 12 cases negative, 4 cases negative false and not obtained positive false case. Calculation has resulted in specificity, sensitivity and accuracy of 76.5%, 100% and 86.7%. While the positive predictive value was 100% and a negative predictive value was 76.5%.

Table 1. The result of cytologic and histophatologic diagnosis

No	Age (years old)	Cytology Result	Histopathology Result
1	29	Benign	Endometrial cysts
2	39	Benign	Endometrial cysts
3	37	Benign	Endometrial cysts
4	34	Malignant	Serous Cystadenocarcinoma
5	39	Benign	Endometrial cysts
6	34	Atypical	Serous Cystadenocarcinoma
7	44	Benign	Mucinous Cystadenoma
8	33	Atypical	Clear Cell Carcinoma
9	48	Benign	Endometrial cysts
10	44	Benign	Serous Cystadenoma
11	51	Benign	Ovarian struma
12	22	Benign	Mucinous Cystadenoma
13	55	Atypical	Mucinous Cystadenocarcinoma
14	49	Malignant	Endometrioid Adenocarcinoma
15	25	Benign	Mature Cystic Teratoma
16	52	Benign	Serous Cystadenocarcinoma
17	18	Benign	Serous Tumor Borderline
18	59	Benign	Mucinous Tumor Borderline
19	47	Atypical	Endometrioid Adenocarcinoma
20	11	Atypical	Immature Teratoma
21	25	Atypical	Immature teratoma
22	36	Benign	Mucinous Tumor Borderline
23	49	Benign	Endometrial cysts
24	33	Benign	Mucinous Cystadenoma
25	49	Benign	Mucinous Cystadenoma
26	37	Malignant	Serous Cystadenocarcinoma
27	33	Atypical	Mucinous Tumor Borderline
28	38	Malignant	Mucinous Cystadenocarcinoma
29	55	Malignant	Serous Cystadenocarcinoma
30	34	Malignant	Serous Cystadenocarcinoma

Table 2. Correlation between ovarian cyst fluid cytology and histopathology result

Histopathology Result	Number of case	Cytology	
		Benign	Malignant
Endometrial cysts	6	6	
Serous Cystadenoma	1	1	
Serous Tumor Borderline	1	1 (NF)	
Serous Cystadenocarcinoma	6	1 (NF)	5
Mucinous Cystadenoma	4	4	
Mucinous Tumor Borderline	3	2 (NF)	1
Mucinous Cystadenocarcinoma	2		2
Endometrioid Adenocarcinoma	2		2
Clear Cell Carcinoma	1		1
Mature Cystic Teratoma	1	1	
Ovarian struma	1	1	
Immature Teratoma	2		2
Total	30	17	13

NF = Negative False

DISCUSSION

Thirty cases of ovarian cysts in this study consisted of 6 cases non-neoplasm and 24 cases non-neoplasm. The

non-neoplasm was non neo-plastic cysts of endo-metriosis. Ultrasound picture of ovarian endo-metriosis cyst were various as benign or malignant.

Figure of endometriosis cysts a multilocular with various wall thickness, not infrequently gives a figure nodule on the wall of cell so resembles a neoplasm, and suspected a malignant (Woodward et al 2001). The endometriosis cyst case based on cytology picture there is no sign of malignancy. Three of six cases showed a background containing hemosiderophage, 2 cases showed hemosiderophage with inflammatory neutrophils cells, whereas 1 case of erythrocytes. Three of six cases obtained endometrial glandular cells, whereas 3 cases endometriosis cyst was not found endometrial cells. Endometrial glandular cells are arranged in groups or sheet. The cells are small with less obvious boundaries. The nucleus of cell was round to oval with inconspicuous nuclei. The cytoplasm were thin, sometimes bubbly. Component of endometrial stroma is relatively rare in cytological preparation (Cibas 2009, Koss & Melamed 2006)

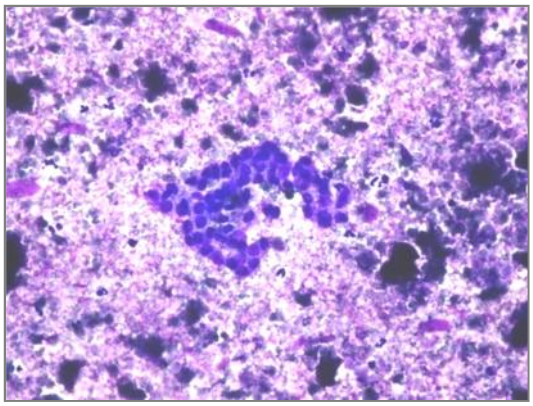

Figure 1. Endometriosis cyst. Background containing erythrocytes degeneration with macrophage containing hemosiderin.. And also appear endometrial glandular cells in the sheet.

Tumors are derived from epithelial cell surface is the most common ovarian neoplasms. Similarly, in this study, 20 cases (67%) were derived from ovarian cyst epithelial cell surface as serous tumors, mucinous tumors, endometrioid and clear cell. Most of the literature mentions that serous tumor type is the most type and followed by mucinous tumors, but the most type in this study were mucinous and followed by serous tumor (Lee et al 2003, Ellenson & Pirog 2010, Rosai 2011)

In this study we found 8 cases of ovarian cysts on epithelial cell types were serous. 5 of 8 cases serous tumors were serous cystadenocarcinoma. Microscopic picture shows glandular pattern, papillary or syncytial groups. Multinucleated tumor cells with round prominent nuclei. Comparison between nucleus and cytoplasm were high so it was looked thin and pale cytoplasm. 1 of 8 cases of Serous tumors in this study was serous ovarian cystadenoma. This microscopic picture only showed an amorph materials, did not obtain epithelial cells lining the cysts. It was found that 1 case of Borderline Serous tumors and 1 case Serous cystadenocarcinoma which consists of both liquid Cysta and distribution of macrophages. Cytology couple of Serous tumors often appears hypocellular (Bibbo et al 2008, Bandyopadhyay et al 2012, Perez-Guillermo& Orell 2012). These conditions result to a false negative cases.

In this study there were 9 cases, four cases, was Mucinous Cystadenoma based on the results of histopathology, 2 cases shows a figure mucinous epithelial cells resembling high endocervix epithelial cells in columnar -shaped, with basal nuclei with pale cytoplasm containing mucin matrix. It can be found epithelial cells resembling goblet cells. These cells may in group resembling ribbons, in sheets or individually. Two cases of Mucinous Cystadenoma in this study, it was only showed mucin matrix and distribution of macrophages. It was also found three cases Mucinous Borderline tumors in histopathological results. Two of them only showed mucin matrix and distribution of macrophages, whereas there was a case showed groups of epithelial cells in sheets with a slightly enlarged heart, seemed atypical. Whereas the other 2 cases were Mucinous cystadenocarcinoma with a picture of group and distribution of epithelial cells in columnar shaped, containing mucin with enlarged and pleomorphic nucleus.

In this study obtained 2 cases with histopathological results Endometrioid Adenocarcinoma. Endometrioid Adenocarcinoma cytology is not specific, such as adeno-carcinoma in general, consists of epithelial cells anaplasi, these cells are round, elongated columnar, granular eosinophilic cytoplasm irregular destroyed, solid or cribiform shape. Sometimes found differentiated carcinoma (Cibas 2009, Shahid et al 2012, Perez-Guillermo& Orell 2012). In this study, there was 1 contain lots of blood with 3 groups obtained columnar cells with atypical nuclei. Cysts were obtained from macroscopic evaluation cysts tissue containing blood. In ovarian cyst with extensive hemorrhage, tumor cells would be difficult to obtain cyst fluid for cytological evaluation.

In this study, we found that one case with histopathology result Carcinoma Clear cell. Figure of cytology carcinoma clear cell is a big cell, eccentric prominent nuclei. The cytoplasm appears broad, vacuole, thin and eosinophilic in Papanicolaou staining. Sometimes seems hyaline extracellular material that smeared pink, especially with Romanowsky staining (Cibas 2009, Perez-Guillermo & Orell 2012, Gherardi 2009). In this study, sample containing similar cell, but was not find hyaline extracellular matrix. In this study, was found that 4 cases of ovarian cysts were derived from germ cell tumors component, 1 case was Mature Teratoma, 1 case of Ovarian struma, and 2 cases Immature teratoma. Both the mature teratoma and immature teratoma found keratin debris, epithelial cells carcinoma a-nucleated, squamous epithelial cells mature, sometimes obtained a granular (Bibbo et al 2008, Cibas 2009, Perez-Guillermo & Orell 2012, Kocjan 2006). While in immature teratoma found small nucleated cells groups, thin hyper-chromatic cytoplasm, seemed atypical. There was 1 ovarian struma case only contain cyst fluid cytology, tumor cells was not obtained

There were 24 cases of ovarian cyst neoplasm showed various number of tumor cells. 8 out of 24 cases showed a-cellular cytology sample, it was only containing the cyst fluid without tumor cells. 4 of 8 cases showed malignant histopathology results. Limitations on ovarian cyst fluid cytology samples in this study were found a-cellular sample. Cole et al 2011 in his research has reported that as much as 33% of all samples classified as ovarian cysts pauci-cellular and 6% classified as non diagnostic. Should have to know that ovarian cysts cytology samples by aspiration methods have not high adequately percentage. Some studies found no adequately sample reaches 18 to 80% (Wojcik & Selvaggi 1994, Dietrich et al 1999, Papathanasiou et al 2004). In this study, there were 4 negative false cases. The whole negative false cases showed a-cellular sample. Clinicians should be vigilant when cytology samples are not adequately classified, on that condition possibility of malignancy cannot be ruled out (Cole et al 2011). In this study did not find a positive false case.

In this study was found an accuracy of ovarian cyst fluid intra-operative cytology diagnostic was 86.7%. This figure is similar to Khan's study were 89.9% (Khan et al 2009). Cytological study conducted by Shahid et al (2011) about ovarian cysts showed higher accuracy were 95.8%. In that study cytology samples obtained by different techniques, by scraping and gluing sample on a glass object method (Shahid et al 2011). Some researchers tried to combine cytological evaluation with a various method to improve diagnostic. Athanassiadou and Grapsa 2005, suggested that additional methods of examination e.g cytometry or immunocytochemistry may improve diagnostic possibilities, especially in borderline cases.

Sensitivity of ovarian cyst fluid cytology intra operative diagnostic in this study was 76.5%. This value is similar to study conducted by Khan who has reported sensitivity was 79.2%. Several studies reported that diagnostic of cyst fluid cytology has low sensitivity only 25 to 50% (Moran et al 1993, Papathanasiou et al 2004, Cole et al 2011). It reflects of desquamasi malignant cells in the ovary is not always easy to happen (Cole et al 2011, Papathanasiou et al 2004, Khan et al 2009, Moran et al 1993). Specificity value in this study was 100%. Similarly by various studies reported high specificity between 95.8% and 100% (Cole et al 2011, Shahid et al 2011, Papathanasiou et al 2004, Moran et al 1993). However histopathological methods can detect malignant cells so there are not atypical cells detected.

In this study was showed a positive predictive value of 100%. It means that 0% chance of someone not suffer from malignant ovarian cysts if result of cytology indicate to malignancy. Negative predictive value in this study was 76.5%, means 23.5% possibility of someone having malignant ovarian cysts although cytology results showed benign.

CONCLUSION

Cytological examination of ovarian cyst fluid obtained by aspiration intra operative demonstrated high specificity and positive predictive value.

ACKNOWLEDGMENT

The author thanks to Tatit Syahadani Alfirdausi for her contribution in preparing the layout of the manuscript.

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