International Journal of Research in Medical Sciences
Janagam C et al. Int J Res Med Sci. 2017 Dec;5(12):5227-5231
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20175382

Original Research Article

Study of ascitic fluid cytology in ovarian tumors

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Received: 01 November 2017
Accepted: 17 November 2017

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ABSTRACT

Background: The objectives of this study were to examine the validity of ascitic fluid cytology in the detection of pathological findings, to examine the percentage of false positive and false negative results in the cytology of ascitic fluid and to determine the validity of peritoneal cytology in relation to the histopathological type of the ovarian tumour.
Methods: This retrospective study, over a period of 6 months, included 106 peritoneal cytology findings. The experimental group included 106 cytology findings obtained from patients who presented with an abdominal lump/mass with ascites and diagnosed with ovarian tumors clinically. They included 88 benign ovarian tumours (83%) and 18 malignant ovarian tumors (17%). Patients with other causes of ascites were excluded from the study.
Results: The sensitivity of peritoneal cytology is 90%, specificity is 96.5%, positive predictive value is 85.7%, and negative predictive value is 97.6%. In 1.8% of patients, the peritoneal cytology showed false negative results, while in 2.8%, the results were false positive. False negative results were found in one case of teratoma with squamous cell carcinoma and one case of yolk sac tumor. False positive results were found in 2 cases of tuberculous-salpingo-oophoritis and one case of chronic salpingo-oophoritis due to reactive mesothelial proliferation, mistaken for adenocarcinoma.
Conclusions: Peritoneal cytology of ascitic fluid is highly specific and sensitive for detection of ovarian malignancies, particularly in grade 3 and grade 4 disease, since most of the patients with ovarian malignancies present to us at advanced stage of the disease.

Keywords: Ascites, Ovarian carcinoma, Peritoneal fluid cytology

INTRODUCTION

Ascites is a large amount of fluid accumulated in the abdomen. Under normal conditions, several litres of peritoneal fluid are produced daily, and it is not accumulated but effectively absorbed.

Ascites of malignant aetiology appears in only 10% of all ascites cases.[1] Malignant ascites most frequently presents in gynaecological and gastrointestinal carcinomas. A combination of malignant ascites and carcinomatosis of the peritoneum is present in 15-30% of cases.[2]

Ascites can be exudative and transudative. Transudates make up 90% of ascitic fluids and they are caused by conditions of non-malignant aetiology. This fluid is clear, with a small number of cells and low level of albumin. An exudate is usually malignant, cloudy, with a greater number of cells and a higher level of proteins than transudate.[3]

It is believed that the pathogenesis of malignant ascites is multifactorial and that the most important pathogenetic mechanisms include increased vascular permeability, lymphatic drainage obstruction, increased difference in

hydrostatic pressure and reduced difference in oncotic pressure.[4]

Ascites is the most common complaint of patients with ovarian carcinoma. In 54% of patients with peritoneal carcinomatosis, ascites was the first detectable sign of malignancy.[5]

More than two-thirds of patients that present to us in the hospital have grades III and IV of the disease. Survival rate in advanced stages (III and IV) is 5-20%.[6]

The purpose of this study is to test the validity of ascitic fluid cytology in the detection of malignancy in ovarian tumors, to test the percentage of false positive and false negative results of ascitic fluid cytology and to determine the validity of peritoneal cytology in relation to the histopathological type of ovarian tumour.

METHODS

A retrospective analysis was used for the research which included 106 peritoneal cytology results during a period of 6 months from April 2017 to September 2017. The study group was composed of 106 cytological findings of ascitic fluid obtained from female patients who presented with an abdominal lump or mass with concomitant ascites and clinically diagnosed with ovarian tumors, later proved on histopathology.

Cytological findings of ascitic fluid and peritoneal cavity effusion were sampled and examined microscopically in the Department of Pathology, after centrifugation following which the sediments were collected, used for preparing smears on slides, fixed in isopropyl alcohol for one hour and stained with Haematoxylin and Eosin.

All results were statistically processed, tabulated and calculated so as to obtain the sensitivity, specificity, positive predictive value and negative predictive value.

RESULTS

Age wise distribution of ovarian tumors showed that most of the ovarian tumors occurred between 21-40 years, of which majority were benign, whereas, most of the malignant tumors occurred above the age of 40 years, except one case of yolk sac tumor that occurred in a 31-year-old female patient.

The histopathological distribution and ascitic fluid cytology findings in various benign and malignant ovarian tumors in the study is presented in Tables 1 and 2.

Of the 88 benign tumors, the highest percentage of patients had serous cystadenomas (61.4%), followed by mucinous cystadenomas (19.3%) and dermoid cysts/mature cystic teratomas (11.4%). There were also 2 cases of fibroma and fibrothecoma, 1 case of mucinous cystadenoma with Brenner tumor and 1 case of mucinous cystadenoma with borderline Brenner component that were reported.

All these cases were negative for malignant cells on ascitic fluid cytological examination. However, there were 2 cases of tubercular salpingo-oophoritis and 1 case of non-specific chronic salpingo-oophoritis that were clinically diagnosed and sent as ovarian tumors.

Table 1: Benign ovarian tumors (total 88= 85 true negative + 3 false positive).

HPE	Ascitic fluid (-/+ for malignant cells)	No. of cases	%
Serous cystadenomas	Negative	54	61.4
Mucinous cystadenomas	Negative	17	19.3
Dermoid cysts	Negative	10	11.4
Fibroma /Fibrothecoma	Negative	2	2.
Mucinous cystadenoma with Brenner tumor	Negative	1	1.2%
Mucinous cystadenoma with borderline Brenner	Negative	1	1.2
Tuberculoussalpingo-oophoritis	False positive	2	2.3
Non –specific chronic salpingo-oophoritis	False positive	1	1.2

Table 2: Malignant ovarian tumors (total 18= 16 true positive + 2 false negative).

HPE	Ascitic fluid cytology (+/- for malignant cells)	No. of cases	%
Papillary serous cystadenocarcinoma	Positive	10	55.6
Krukenberg tumors	Positive	3	16.7
Mucinous cystadenocarcinoma	Positive	2	11.1
Endometrioid carcinoma	Positive	1	5.6
Yolk sac tumor	False negative	1	5.6
Teratoma with SCC	False negative	1	5.6

Ascitic fluid examination showed inflammatory cells and numerous reactive mesothelial cells that were mistaken for adenocarcinoma cells and reported as positive for malignant cytology, leading to 3 false positive cases. Hence, though these 3 cases of tubo-ovarian masses were of inflammatory pathology, they were still included in the study, to emphasise the importance of differentiating

reactive mesothelial cells that are often confused with adenocarcinoma cells in cytopathology. (Figure 1 and Figure 2).

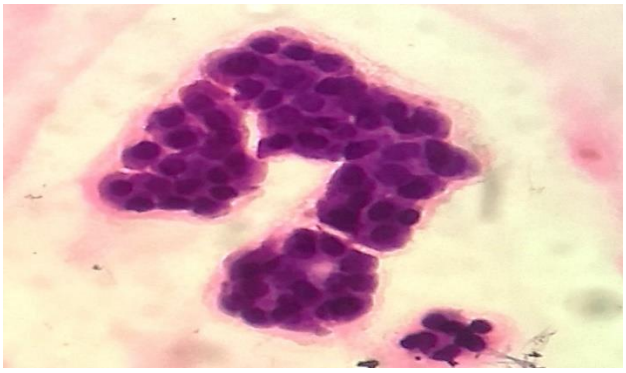

Figure 1: Photomicrograph of reactive mesothelial cells showing rounded cell borders and dense eosinophilic cytoplasm. (H and E, 400x).

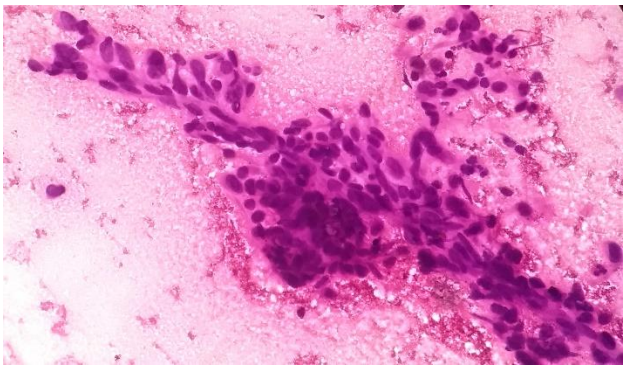

Figure 2: Photomicrograph of papillary serous carcinoma metastatic deposits in ascitic fluid showing papillae lined by round to oval tumor cells with pleomorphic nuclei (H and E, 400x).

Among the 18 malignant tumors, most of the cases were serous cystadenocarcinomas, constituting 55.6% of cases and the most common ovarian malignancy. We also reported 3 cases of bilateral Krukenberg tumors, 2 cases of mucinous cystadenocarcinomas and 1 case of endometrioid carcinoma of ovary. All these cases were positive for malignant cells on peritoneal fluid cytological examination. However, one case of yolk sac tumor and another case of teratoma with squamous cell carcinoma were reported as negative for malignant cells on cytological examination of ascitic fluid, leading to 2 false negative results.

The above-mentioned case of dermoid cyst was an interesting case. On gross examination, the ovarian cyst measured 11x9x6 cm. Cut section showed pultaceous material with hair and a greyish white solid area measuring about 3x3cms, (Figure 3) from which multiple sections were given that revealed squamous cell carcinoma component on histopathological examination (Figure 4).

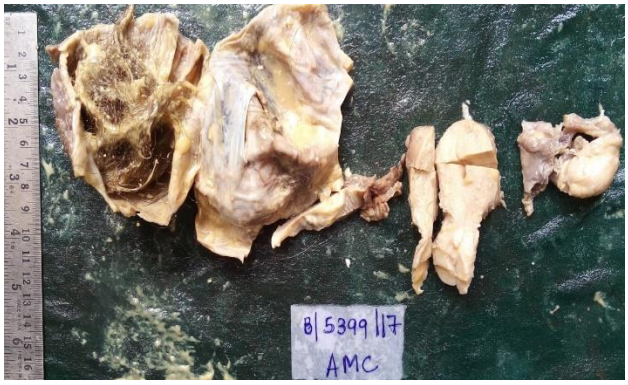

Figure 3: Gross photo of dermoid cyst-ovary showing pultaceous material and hair along with separate grey-white solid area measuring 3 x 3cms.

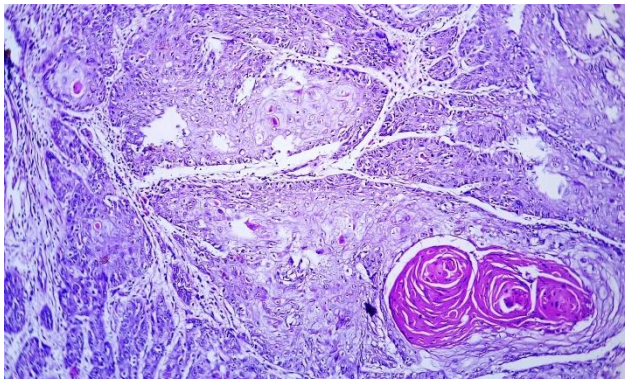

Figure 4: Photomicrograph of dermoid cyst-ovary showing nests and sheets of atypical squamous cells with keratin pearl formation (H and E 100x).

The following parameters were calculated as follows: (Table 3).

Table 3: Ascitic fluid cytology findings in correlation with histopathology.

Ascitic fluid cytology	Positive for malignant cells 21 cases	Negative for malignant cells 85 cases
Histopathology	Malignant -18 Benign -3 (false positive)	Benign -83 Malignant-2 (false negative)

- Sensitivity = (True positive/True positive + False negative) x 100 = (18/18+2) x 100 = 90%
- Specificity = (True negative/True negative + False positive) x 100 = (83/83+3) x 100 = 96.5%
- Positive predictive value = (True positive/True positive + False positive) x 100 = (18/18+3) x 100 =85.7%
- Negative predictive value = (True negative/True negative + False negative) x 100 = (83/83+2) x 100 = 97.6%
- False positivity = (3/106) x 100 = 2.8%
- False negativity = (2/106) x 100 = 1.8%.

DISCUSSION

The main cytological characteristics of malignant ascites are increased number of leukocytes and positive cytology for the presence of malignant cells. A positive cytological finding represents an important predictive factor in prognosis and recurrence.

The reason for false positive cytological results is inadequate interpretation of reactively altered mesothelial cells.[7] These cells are enlarged, arranged grape like clusters with rounded cell contours and they have a dense cytoplasm, a big nucleus with a nucleolus and may contain vacuoles. On the other hand, adenocarcinoma cells show high nucleo-cytoplasmic ratio with irregular pleomorphic nuclei and prominent nucleoli and show focal acinar or papillary arrangement.

This led to 3 false positive results in our study (2.8%). False positives were found in 3 cases of tubo-ovarian masses that were later diagnosed as tubercular salpingo-oophoritis (2 cases) and non-specific chronic salpingo-oophoritis on histopathology. According to another study by Oscar L, peritoneal cytology can be false positive in 4.5% of cases and also describe a relatively high percentage of false negative findings which exceeds 20%.[7] The reasons for such a high percentage of false negative cytological results of ascitic fluid may be in the bad distribution of cells in the sampled ascitic fluid, bad preparation, or insufficient cell exfoliation, and since cytology is a subjective method, errors may be due to inadequate interpretation of findings.[7] In our study, however, false negative results were found only in 1.8% cases. These included 2 cases of yolk sac tumor and teratoma with squamous cell carcinoma, respectively.

The sensitivity of peritoneal cytology stated in a study by Runyon et al can be upto 97%, depending on the study, disease stage and peritoneal inclusion.[8] In our study, the sensitivity was 90% because majority of the patients presented with advanced stage of ovarian carcinoma.

Specificity in our study was 96.5%. The examination of total validity of cytology in study by Karoo et al[9] showed somewhat lower sensitivity which was 60% and high specificity of almost 100%.

According to a study by Zuna et al, the sensitivity of peritoneal cytology was 82.9% and specificity was 98.1%.[10] As per a study by Cheng et al, sensitivity of peritoneal fluid cytology was 94%.[11] These correlated well with the present study.

The result of primary cytology of ascitic fluid is an important parameter in the diagnosis, staging, therapeutic approach and disease prognosis. The result of secondary cytology after the treatment is also an important independent prognostic marker which is highly correlated with the optimal effect of surgical treatment, recurrence and overall survival rate. In positive secondary cytology, survival is 13 to 32 months, while in negative cytology, it is > 48 months.[12]

CONCLUSION

In our study, we concluded that peritoneal cytology of ascitic fluid is a highly specific (96.5%) and sensitive (90%) test in malignant ovarian tumors, especially in advanced stages of malignancy with which most of our patients present in our hospital. It greatly aids in supporting the diagnosis, in predicting the prognosis and chance of recurrence of the tumor, that in turn helps in proper management and treatment of the patients. In 1.8% cases, peritoneal cytology had false negative results and in 2.8% cases, it showed false positive results, which can be prevented by more careful microscopic examination and experience.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Janagam C, Atla B. Study of ascitic fluid cytology in ovarian tumors. Int J Res Med Sci 2017;5:5227-31.