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Cytological Evaluation of Pleural Fluid with Special Reference to Malignancy in a Tertiary Care Centre

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ABSTRACT

Cytological examination of body fluids not only helps for the diagnosis of cancer but also for staging and prognosis of diseases as well as regarding etiology of effusion. Cell block and immunocytochemistry are essential adjunct to cytomorphology in suspicious cases and substantially improves diagnostic accuracy.

A total of 255 pleural fluid samples received over an one & a half years period were analysed.and stained by MGG and PAP. Cell block and immunocytochemistry (EMA, Calretinin and CD20) were performed to aid the diagnosis in clinico-radiologically diagnosed malignant cases.

Total 32 cases (12.6%) were found to be malignant and out of which metastatic adenocarcinoma was found to be the most common cause of malignant effusion followed by metastatic squamous cell carcinoma and mesothelioma. The most common primary lesion in malignant pleural effusion was found to be carcinoma lung (65.62%) followed by carcinoma breast (12.5%).

Cytology is a useful tool to detect malignant effusions. Cell block must be performed in paucicellular cases and immunocytochemical staining in difficult cases to differentiate metastatic epithelial cells from reactive mesothelial cells.

KEYWORDS Immunocytochemistry, metastatic adenocarcinoma, reactive mesothelial cells, cell block

INTRODUCTION

The pleural cavity is lined by two serous membranes. The fluid between the membranes is called serous fluid**,** and it provides lubrication between the parietal and visceral membrane.[1] Effusions are classified clinically as transudative or exudative.[2]

Cytological examination of serous fluids is of paramount importance not only in detecting cancer cells, but it also reveals information regarding various inflammatory conditions of serous membranes and various infections.[8] Cytology is more sensitive than blind biopsy for detecting serosal malignancy [3], presumably because fluid provides a more representative sample. Estimates of sensitivity of cytology for diagnosing serosal malignancy range from 58% to 71%.[3,4] The specificity of a cytologic diagnosis is quite high: false-positive diagnoses occur in less than 1% of cases.[5,6]

The cell block method is one of the traditional method used for processing cytological material and was described in the literature as early as 1900.[7] Apart from increased cellularity, better morphological details are obtained by cell block method as there is a better conservation of architectural features like arrangement of cells, cytoplasmic and nuclear details.[8]

Immunocytochemistry is an essential adjunct to cytomorphology in selected cases and substantially improves diagnostic accuracy.[9]

MATERIALS AND METHOD

This study was carried out in the Department of Pathology, Guahati Medical College and Hosipital, Guwahati, North-East India from July 2014 to January 2016. A total of 255 cases of pleural effusion were reported in the cytology section. The study was approved by Institutional ethical committee of Gauhati Medical College and Hospital, Guwahati.

20-30 ml of pleural fluids were collected by thoracentesis and subjected to physical, chemical and cytological examination.

The fluids received were stained with May-Grunwald-Giemsa stain and Papanicolaou stain for cytological evaluation.

In doubtful cases sections were made from the cell block and were stained with Haematoxylin and Eosin stain and if necessary immunocytochemical stains to differentiate between reactive mesothelial cells and adenocarcinoma cells using Epithelial membrane antigen and calretinin. Adenocarcinoma shows positive for EMA but negative for calretinin, reactive mesothelial cells show positive for calretinin and negative for EMA, mesothelioma shows positive for both EMA and calretinin. CD20 was performed in suspected lymphoma cases.

RESULTS

In our study of 225 cases, the maximum number of pleural effusions were found to be 41-50 year old age group (24.71%) followed by 51-60 years (16.48%). There was male predominance (62.35%) over female.. The most common clinico-radiological diagnosis was tuberculosis followed by malignancies (68 cases). 85.09% effusions were exudative and 14.91% were transdative.

Out of 68 cases of clinico-radiologically diagnosed malignancy with pleural effusion, 20 cases were diagnosed as metastatic adenocarcinoma, 03 cases were metastatic squamous cell carcinoma, 32 cases show reactive mesothelial cells and remaining 11 cases were suspicious cytologically which is detailed in Table 1.

Table 1: Distribution of clinico-radiological diagnosis with that of cytological diagnosis

Clinico-radiologically diagnosed as malignancy	No. of cases	Cytology			
		Metastatic adenocarcinoma	Metastatic squamous cell carcinoma	Suspicious of malignant cells	Reactive mesothelial cells
Ca. lung	45	13	03	08	21
Ca. breast	11	04	-	01	06
Ca. ovary	05	02	-	-	03
Mesothelioma	02	-	-	02	-
Unknown primary	01	01	-	-	-
Hematolymphoid malignancy	04	02 cases positive for malignant cells			02
Total no. cases	68	20 (adeno)	03 (squamous)	11 (suspicious)	32 (reactive)

EMA positivite but calretinin & CD20 negaive (metastatic

adenocarcinoma and SCC) was seen in 28 cases out of 68 cases of clinico-radiologically malignant cases. Both EMA & calretinin positivite but CD20 negaive (mesothelioma) was seen in 02 cases. Only CD20 positive (hematolymphoid malignancies) was seen in 02 cases and only calretinin positive (reactive mesothelial cells) was seen in 36 cases. Out of 11 suspicius cases 05 cases were metastatic adenocarcinoma and 02 case were mesothelioma which is detailed in Table 2.

Table 2: Staining status of EMA, Calretinin and CD20 in clinico-radiologically diagnosed malignant cases

Cytology findings of clinico-radiologically diagnosed malignant cases	Cytology smeras	EMA +ve, Calretinin -ve, CD20 -ve	EMA -ve, Calretinin +ve, CD20 -ve	EMA +ve, Calretinin +ve, CD20 -ve	EMA -ve, Calretinin -ve, CD20 +ve
Metastatic adenocarcinoma	20	20	0	0	0
Metastatic squamous cell carcinoma	03	03	0	0	0
Suspicious cells	11	05 (adenocarcinoma)	04 (reactive mesothelial cells)	02 (mesothelioma)	0
Hematolymphoid malignancies	02	0	0	0	02
Reactive mesothelial cells	32	0	32	0	0
Total	68	28	36	02	02

Distribution of final cytological findings of all pleural effusion cases after confirmation by immunocytochemistry shows that out of 255 cases, 32 cases (12.6%) were found to be positive for malignant cells. The remaining cases were benign inflammatory and transudative effusion which is detailed in Table 3.

Table 3: Distribution of final cytological findings of all pleural effusion cases after confirmation by immunocytochemistry in clinico-radiologically diagnosed malignant cases

Cytological category	No. of cases	Percentage
Non-inflammatory transudative	38	14.9%
Inflammatory	185	72.5%
Malignant	32	12.6%
Suspicious	0	0%
Total	255	100%

In our study, out of 32 malignant pleural effusion, metastatic adenocarcinoma is found in 25 cases (78.12%), metastatic SCC in 03 cases (9.38%), mesothelioma in 1 case (6.25%) and hematolymphoid malignancies in 1 cases (6.25%) which is detailed in Table 4. Furthermore, the most common primary neoplasm in malignant pleural effusion was found to be lung origin (65.62%) followed by breast origin (12.5%).

Table 4: Distribution of different types of malignant pleural effusions

Types of malignant cells	No. of cases	Percentage
Metastatic adenocarcinoma	20 + 05 = 25	78.12%
Metastatic squamous cell carcinoma	03	9.38 %
Mesothelioma	02	6.25%
Hematolymphoid malignancies	02	6.25 %
Total	32	100%

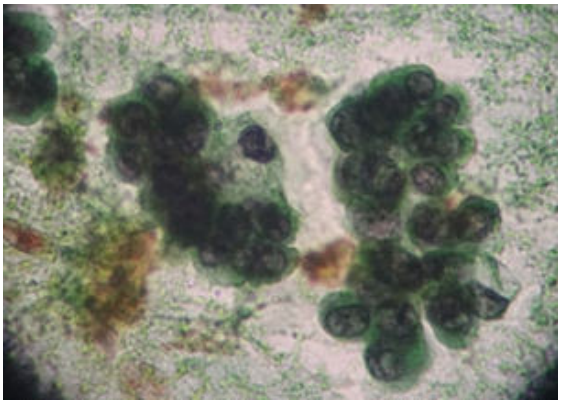

Fig1: Metastatic adenocarcinoma in PAP (10x40X

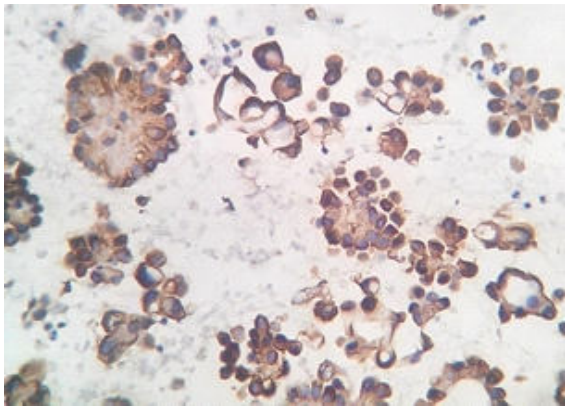

Fig2: EMA positive in Metastatic adenocarcinoma (10x40X)

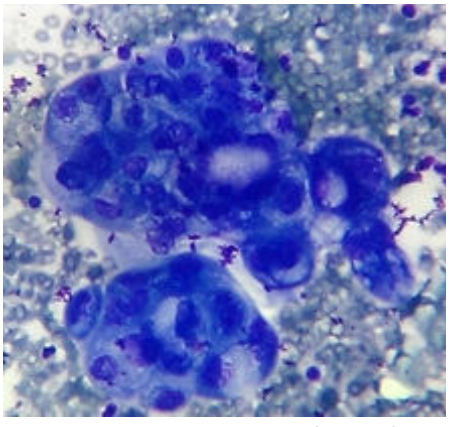

Fig3: Malignant mesothelioma in MGG (10x40X)

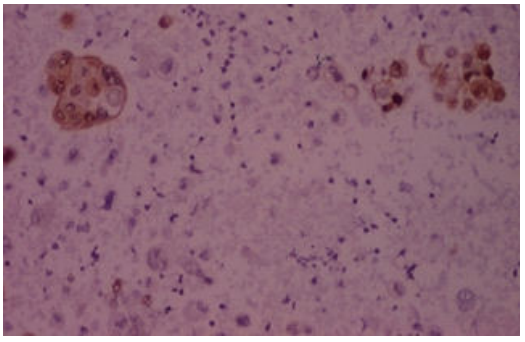

Fig4: Calretinin positive in mesothelioma (10x40X)

DISCUSSION

In our study of 255 cases, the commonest age group of pleural effusion was found to be 41-50 years with male preponderance (62.35%) which is in aggrement with Khan Y et al[11], Khan FY et al[12]

and Grandhi B et al[19].

In this study, 85.09% cases were found to be exudative type and remaining 14.91% were transudative which is in aggrement with Kushwaha R et al[10] and Khan FY et al[12].

Out of 255 cases, 32 cases (12.6%) were found to be malignant which is in aggrement with Khan FY et al[12], Dagli AF et al[13] and Rehan M et al[18].

In our study, the most common primary lesion in malignant pleural effusion was found to be carcinoma lung (65.62%) followed by carcinoma breast (12.5%) and carcinoma ovary (6.25%), mesothelioma etc which is in aggrement with Kacprzak G et al[15] and Yahya ZM et al[17]. Amongst the malignant pleural effusion , the most common type of malignancy was found to be metastatic adenocarcinoma (78.12%) in aggrement with Cakir E et al[14] and Gupta S et al[16].

In terms of sensitivity and specificity of cytological examination, suspicious cases were regarded as negative for malignancy for statistical purposes. When the cytological diagnosis were compared with the final immunocytochemical diagnosis, the encountered sensitivity of effusion cytology for detecting malignant cells was 78.13% with 100% specificity which closely resembled to the study done by Yahya ZM et al[17] and Grefte JMM et al[20].

CONCLUSION

From the present study it can be concluded that effusion cytology is a useful tool to distinguish between benign inflammatory and malignant pleural effusions. From cytology it is possible to type the tumor in a substantial number of cases. Metastatic adenocarcinoma is the commonest type of malignant pleural effusion and the most common primary site is of lung. In the identification of malignant cells in effusion and its differentiation from cells showing reactive and degenerative changes are diagnostic difficulties in some of the cases. In these problematic cases, additional immunocytochemistry acts as an important ancillary diagnostic tool to aid the diagnosis.

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