 DOI: 10.18231/2394-6792.2017.0041

Diagnostic approach to pleural effusions

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Abstract

Introduction: Aspiration of serous cavities is a simple and relatively noninvasive technique to achieve the diagnosis of cause of pleural effusion. Cytological examination of pleural fluid obtained by tapping is a simple, inexpensive, diagnostic modality of the cause of pleural effusion and further helps in treatment and follow up of the patients. Not only the infective causes, it also helps in cancer patients either primary or metastatic effusions both in diagnosis and management.

Materials and Method: This study on pleural fluid cytology was done on 100 cases in Adichunchanagiri Institute of Medical Sciences B G Nagar for a period of 2 years. Relevant and available clinical information regarding age, sex, symptoms and accompanying signs were obtained from the patients. Pleural fluid was analysed for gross appearances and cytological analysis for cell count, cell type and malignant cells.

Results: 100 samples of pleural fluid were received. Incidence of pleural effusion was more in males compared to females with a male to female ratio of 1.6:1. In the benign effusions, various clinical conditions noted were Pulmonary tuberculosis, Pneumonia, and anemia with hypoproteinemia, CCF, and Pulmonary infarction. Exudative effusions were more (84%) compared to transudative effusions (16%). Out of 100 samples received clinical diagnosis of malignant effusions was made in 10 cases and 3 cases which were diagnosed as tuberculous effusion turned out to be malignant effusion by cytology.

Conclusion: Pleural fluid cytology is one of the easy, inexpensive mode of diagnosis for the cause of pleural effusion, which also helps in the treatment and management of patients. It can be done in any rural set up with basic facilities where sophisticated techniques are not available.

Keywords: Pleural Fluid, Cytological Analysis, Tuberculosis, Malignant Effusion.

Introduction

Pleural cavity is a potential space between the parietal pleura and visceral pleura. It consists of some amount of fluid called pleural fluid which is normally less than 25ml. Pleural fluid is produced by parietal lining and absorbed by visceral lining.(1)

Grossly the normal pleural surface is smooth, glistening, and semitransparent. Microscopically it is lined by layers like mesothelial cell layer, elastic, and deep fibroelastic layer. The size of human mesothelial cell ranges from 16.4+/-6.8 to 41.9+/-9.5 µm. Its surface is covered with microvilli, measuring approximately 0.1 microns in diameter and up to 3 µ in length. The nuclus is ovoid with a prominent nucleolus. The cytoplasm has moderate to abundant organelles like mitochondria, rough endoplasmic reticulum, golgi apparatus and glycogen granules. The mesothelial cells have typical tight junctions.(2)

Aspiration of serous cavities is a simple and relatively noninvasive technique to achieve the diagnosis of cause of pleural effusion. Cytological examination of pleural fluid obtained by tapping is a simple, inexpensive, diagnostic modality of the cause of pleural effusion and further helps in treatment and follow up of the patients. Not only the infective causes, has it also helped in cancer patients either primary or metastatic effusions both in diagnosis and follow up. Cellularity yielded is good in pleural fluid tapping as the cells lining the cavity will be shed in the effusions which gives cells from wider area as compared to pleural biopsies where we get cell material from a single focus. However doing cell block in pleural fluid is more advantageous since it gives better architectural patterns and material can be taken for immunohistochemistry and other ancillary techniques.

Materials and Method

The study was done for two years from 2014 to 2016 in Adichunchanagiri Institute of Medical Sciences, B G Nagar. Ethical clearance was obtained from the institutional ethical clearance committee. Clinical details were taken like age, and sex, of the patient with the relevant clinical symptoms like cough, expectoration, chest pain, fever, and weight loss. The pleural fluid was tapped under aseptic precautions by the clinicians and sent to our pathology laboratory. The received pleural fluid was immediately processed. Gross Examination of Pleural fluid was done for –volume, colour and clarity. A drop of pleural fluid was taken on a slide with a drop of toludine blue stain added on it, to see the cells in wet mount preparation. Microscopic examination of pleural fluid is done. Total cell count is done using neubauers counting chamber with WBC diluting fluid as the diluent. Differential cell typing is done after centrifuging the remaining pleural fluid at 2000 rpm for 5 minutes. Centrifuged smears are prepared from the sediment and stained with haematoxylin and eosin stain, leishman and giemsa stain. Centrifuged sedimented smears were

studied for cell type whether predominant cells are neutrophils or lymphocytes. Smears were also scanned for reactive mesothelial cells and malignant cells. If malignant cells were found morphological criteria like cellularity, pattern of arrangement of malignant cells with nuclear and cytological features are considered. After studying all the available clinical data, based on morphology the smears were divided as inflammatory, benign, suspicious and malignant lesions.

Discussion and Results

The pleural cavity is a potential space that is present between the visceral and parietal pleura, which covers the entire surface of the lung, including the interlobar fissure and the parietal pleura including the inner surface of thoracic cage, mediastinum, and diaphragm.

Reactive mesothelial cells have mild nuclear variability, some prominence of the nucleoli, and maintenance of N:C ratio. Nuclear pleomorphism and macronucleoli are absent which helps them to differentiate from malignant cells. Reactive changes in mesothelial cells can be seen in Pulmonary infarction, Cirrhosis, radiation, chemotherapy, systemic diseases, traumatic irritation, underlying neoplasm's, chronic inflammation, foreign substance and infection.[3] Cytoplasm of most mesothelial cells has PAS positive granules concentrated at the periphery and representing neutral mucopolysaccharides.

Cell counts

Red blood cell count: Analysis of fluid for the presence of red blood cells is routinely performed. Light and co-workers reported that RBC counts of >100,000cells/mm^3 are seen only with malignancy, trauma or pulmonary infarction. RBC count of >10,000cells/mm^3 have been commonly seen in malignancy and infection (including tuberculosis) but are also frequently noted in cirrhosis and congenital heart failure.[4]

White Blood Cell count: A value of 1000cells/mm^3 separates transudates from exudates. Transudates are most often lymphocytic, but they may show a predominance of polymorphonuclear leucocytes up to 13% of time. Monocytosis is most consistent with malignancy, where as a low number of mesothelial cells is suggestive of tuberculosis.[4]

Cell population in benign effusions

- Mesothelial cells
- Macrophages (Histiocytes)
- Blood cells
- Miscellaneous other cells
- Mesothelial cells Appears as sheets of polygonal cells, about 20µm in diameter, that are usually separated from each other by clear gaps or windows. Single cells are usually spherical or oval.

Typically, macrophage measures 15-20µm have a round cell shape with the variable cell borders that can be well or ill defined. They may appear singly or in loose clusters. When in clusters, the cytoplasmic borders may not be well maintained and the peripheral contours of the group may appear smooth or knobby. Nuclei are kidney shaped, peripheral in location. Nucleoli are indistinct,[5]

Pleural fluid analysis:[6] The normal volume of liquid in pleural spaces averages 0.1-0.2 ml/kg body weight. The rate of turnover of pleural fluid is rapid and may exceed 1 lt/day. The rate of fluid entry and efflux is almost equal so the volume of pleural fluid remains virtually constant.

The first diagnostic step in the evaluation of a pleural effusion is to determine if it is a transudate or exudates.

Gross characteristics of the Fluid:[7]

Characteristics	Significance
1. Clear and straw-colored	Most transudates Some exudates
2. Reddish tinge to bloody	If not traumatic tap, suggests tumor, pulmonary infarction or trauma
3. Turbid, Yellow	Suggests infection, including tuberculosis
4. Turbid, green	Suggests rheumatoid pleuritis
5. Cloudy, Milky white	Chylothorax (Chylous effusion
6. Thick, Yellow, Metallic sheen	Pseudochylothoraxchyliform effusion,
7. Pus(with or without) putrid odour	Empyema
8. Viscous, haemmorhagic	Suggests malignant mesotheliomas
9. Anchovy colour	Suggests amoebic liver abscess ruptured in to pleural space.

Microscopic examination: Diagnostic problem may arise in diagnosis of malignancy by the morphological study of serous effusions whenever there is little or no morphological distinctions as for example between reactive mesothelial cells and poorly differentiated malignant cells. In such situation to avoid grave clinical implications guarded or ambiguous reports little clinical values are common.[8] Most of the fluid received in the cytology laboratory contains blood clots or small bits of tissue from the lesion while preparing the slide. These bits remain in bottle and not available for microscopy.[9]

Cell block prepared from residual fluid and tissue can be particularly useful for identification of tumors that cause diagnostic difficulties in smears. This technique is simple, reproducible, and safe. Further the effectiveness of cellblock lies in the availability of diagnostic material for further histological examination, histochemistry and IHC studies for better classification of the tumor and identification of infectious causes with microbiological stains.[10]

The disadvantage of the cell block technique is delay in the diagnosis when compared to conventional smears and sometime risk of loosing material during processing. Some mesothelial cells because of centrifugation artifacts may form rosettes or pseudoacini that can be the source of misdiagnosis.[11]

Drug induced pleural effusion: Pleural effusion as a reaction to drug have been described with only small number of agents like nitrofurantoin, dantrolene, methysergide, bromocriptine, procarbazine, practolol and methotextrate. Nitrofurontoin and dantrolene cause eosinophilic pleural effusion.[12]

Malignant pleural effusion: Neoplasms are responsible for higher percentage of pleural effusion. There is an exponential increase in incidence of malignant effusion in routine clinical practice.

Malignant Mesotheliomas: It is most commonly due to occupational exposure to asbestos and carries a worst prognosis as age increases.[13]

Metastatic tumors: Lung tumors in males and Breast tumors in females are the malignant diseases most commonly responsible for malignant pleural effusion. Besides the lung and pleura, the primary common sites of malignancy in males were the gastrointestinal tract, Liver and Pancreas. In females, the Breast, Lung, Ovary, Pancreas, Gastrointestinal tract and uterus were in descending order of frequency.[14]

Results

Table 1: Age wise distribution of pleural effusions

Age(Years)	No of Samples	Percentage
1-10	2	2.0
11-20	11	11.0
21-30	7	7.0
31-40	19	19.0
41-50	18	18.0
51-60	23	23.0
61-70	13	13.0
71-80	6	6.0
81-90	1	1.0
Total	100	100.0

Maximum number of samples was in the age group of 51-60 Years. Least number of samples was in age group 1-10 Years. Less number of children are affected compared to olderones

Table 2: Sex wise distributions of pleural effusions

Sex	No of Samples	Percentage
Male	62	62.0
Female	38	38.0
Total	100	100.0

Sherwani et al in the year 2005, in his study on pleural effusions also had concluded that males had more incidence of pleural effusion compared to females.[15]

Table 3: Clinical diagnosis of Pleural effusion samples received

Clinical diagnosis	No of Samples	Percentage
Tuberculosis	52	52
Pneumonia	22	22
CCF	5	5
Anaemia/ Hypoproteinemia	6	6
Pulmonary infarction	2	2
Malignant effusion	13	13
Total	100	100

Among the 100 samples received to our laboratory maximum 52 samples had a clinical diagnosis of Tuberculosis and cytology of these smears showed predominance of lymphocytes. 22 samples were with neutrophils predominance highly cellular which were clinically diagnosed as pneumonia. 13 cases were known malignant effusions for which detailed clinical history was taken and concluded. Rest were transudative causes with few cells in cytology.

Table 4: Nature of Pleural fluid

Nature of fluid	No of Samples	Percentage
Exudative effusions	84	84.0
Transudative effusions	16	16.0
Total	100	100.0

84% 0f the samples are exudative and 16% of samples are transudative effusions.

Light et al in the year 1972 and Sherwani et al in 2005 also showed that exudative effusions were more compared to transudative effusions. Nature of effusion is very important because if the effusion is exudative than further evaluation and investigation is required to find the infective organism like tubercle bacilli or other bacteria causing it. Further management of congestive cardiac failure, Cirrhosis or hypoproteinemia are important.

Table 5: Sex wise distribution of Primary site of malignant effusion

Primary site	Male (n=62)	Female (n=38)	Total (n=100)
Ovary	-	2(5.3%)	2(2.0%)
Breast	-	2(5.3%)	2(2.0%)
Lung	1(1.6%)	-	1(1.0%)

GIT	4(6.5%)	2(5.3%)	6(6.0%)
Unknown	1(1.6%)	1(2.6%)	2(2.0%)
Total	6(9.7%)	7(18.4%)	13(13.0%)

Primary site of malignancy was diagnosed as it was aspirated from a known case of malignancy.

Dekker and Bupp, in their study also had shown that lung was the most common site of primary malignancy.(12)

Table 6: Role of Cytology to establish definite diagnosis

Initial clinical diagnosis	No of Samples	Cytological diagnosis	No of Samples	Concordance co-efficient
Tuberculosis	52	Tuberculosis Malignant effusion	49 3	88.46%
Pneumonia	22	Pneumonia	22	100.0%
Malignant effusion	10	Malignant effusion	10	100.0%

So 3 cases which were diagnosed as Tuberculosis clinically was diagnosed as Malignant effusions by Cytology. We could see the malignant cells in the centrifuged sample of fluid. The cells had pleomorphism with irregular nuclear membrane and prominent nucleoli.

Summary of the results obtained-100 samples of pleural fluid were received- 8 year old boy was affected, and common were the middle aged to elder people affected. Males were affected more than females. Tuberculosis was the common condition seen, Effusion was more of exudative than transudates. Diagnosis of malignant effusions was made in 10 cases and 3 cases which were diagnosed as tuberculous was malignant in our study by cytology. So by cytology these 3 cases which turned out as malignant was useful for the patient and the clinician as the mode of treatment was entirely different for both the conditions.

Conclusion

Pleural fluid cytology is one of the easy, inexpensive, mode of diagnosis for the cause of pleural effusion, like whether it is because of Tuberculosis, Pneumonia, or Malignant effusion which also helps in the treatment and management of patients. Differentiation into transudative or exudative effusion is also important in further management of effusion cases. Pleural fluid analysis can be done in any rural set up with basic facilities where sophisticated techniques are not available. Pleural effusion cytology not only finds the infective cause or the local cause of the effusion, but it also helps in diagnosing the metastatic pleural effusion by cellular details and pattern of arrangement of cells where primary is unknown.

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