Research Journal of Medical Science

Serous Effusions: A Clinicopathological Study

Mahendra Patil, S.R. Upadhey and Avinash Mane
Department of Pathology, Krishna Institute of Medical Sciences, 415110 Karad, Maharashtra, India

Key words: Effusions, fluid, clot, transudate or exudate, pleural

Corresponding Author:
Avinash Mane
Department of Pathology, Krishna Institute of Medical Sciences, 415110 Karad, Maharashtra, India

Page No.: 319-322
Volume: 9, Issue 6, 2015
ISSN: 1815-9346
Research Journal of Medical Sciences

Abstract: The term serous effusion refers to the fluid collected in the three serous cavities namely-pleural, peritoneal and pericardial. Various disease processes may disturb this equilibrium and can lead to accumulation of larger amount of fluids, leading to effusion. Depending upon the disease process the nature and composition of fluid may vary. Fluid tapping, a minimally invasive diagnostic as well as therapeutic procedure with serous fluid examination is a well-established method for determining the etiology of effusions. In case of clinical suspicion of malignant effusion, typing of fluid into exudate or transudate and wet mount preparation for abnormal cells may be done before examination of fixed smears for malignant cells as we did not find any transudative fluid positive for malignancy.

INTRODUCTION

The term serous effusion refers to the fluid collected in the three serous cavities namely-pleural, peritoneal and pericardial. Normally these cavities contain only a small amount of fluid which is maintained in dynamic equilibrium. Various disease processes may disturb this equilibrium and can lead to accumulation of larger amount of fluids, leading to effusion. Depending upon the disease process the nature and composition of fluid may vary. Effusion fluid is a very common specimen received in clinical pathology laboratory and analysis of the same can diagnose or can provide clue towards the disease. A variety of tests can be performed on serous fluids. These include chemical profile to decide whether it is transudate or exudate, cytological tests with cell counts and differential counts, smears for malignant cells, microbiological examination like Gram and Ziehl-Neelsen staining, culture for bacteria, fungi and mycobacteria, etc. Thus, primary, metastatic tumors and non-neoplastic conditions like infections can be diagnosed by fluid examination. Clinicians rely on the reports of effusion fluids for the diagnosis and etiology of the diseases and also for assessing the therapeutic response.

Aim of the study: Study of serous effusions with their clinicopathological correlation.

Objectives of the study: To classify serous effusions into transudates and exudates and arrive at an etiological diagnosis with the help of cytological, biochemical and microbiological findings. To correlate these findings with clinical diagnosis.

Literature review: Serous effusions are accumulation of fluid other than blood in excess of the normal small amount in serous cavities. The main 3 cavities are: pleural, peritoneal and pericardial (Shidham and Atkinson, 2006). The para-testicular space is the forth space but is not of significance in clinical cytology. The

first microscopic study of cytology of serous effusions was reported by Lambert in 1845 (Hajdu, 1977). Luke and Klebs described and illustrated malignant cells in an effusion ((Hajdu, 1977; Sears and Hajdu, 1987). Reider recorded mitotic activity for the first time, in the cells freely floating in a fluid medium, in peritoneal fluid of carcinoma ovary (Shidham and Atkinson, 2006). Bahrenberg found epithelial cells in two cases of peritoneal fluids which later revealed carcinoma involving peritoneum on autopsy (Zemansky, 1928). Widal and Ravaut carried out the first systematic study of effusions and they tried to separate tuberculous pleural effusions from others (Spriggs, 1997). Paddock (1940), classified fluids into transudates and exudates by using specific gravity, cell count and protein content of pleural fluid (Paddock, 1941). Later studies revealed limited role of specific gravity, importance of protein (Carr and Power, 1958) and non- usefulness of white cell count (Light *et al*., 1972) in differentiating exudates from transudates (Carr and Power, 1958). Sujathan *et al*. (2000) in their study using ethanol-acetic acid and formalin as fixative in preparation of cellblock for body cavity effusion, described that this method was very simple, rapid and cost effective since no additional materials was required. Washiya *et al*. (2012) described effective method of three dimensional nuclear estimation; for discrimination of cytomorphologically in discriminable malignant mesothelioma from reactive mesothelial hyperplasia.

Classification of effusions: The primary pathogenic process doesn't involve the serous surfaces. Purely transudative effusions occurring most commonly in the peritoneal cavity are associated with cardiac, renal and hepatic failure. Exudates are characterized by high protein content, i.e., above 3g dL^{-1} and specific gravity >1.015 (Paddock, 1940, 1941). The cellular content is higher, composed of inflammatory cells or neoplastic cells in cases of neoplastic serous involvement. Exudates are formed when the capillary permeability is increased, lymphatic flow is decreased or both mechanisms operate together. This commonly occurs with damage to the capillary wall which allows escape of protein and cellular constituents into the serous cavity (Naylor, 2008). Signs and symptoms depend upon the site of involvement and the nature of the underlying disease. Commonly noted symptoms are breathlessness, chest pain and discomfort in case of pleural effusion and abdominal distension in case of ascites (Mc Pherson and Pincus, 2006). Signs of heart failure with muffled heart sounds, hypotension and cardiomegaly on X-ray chest examination may be suggestive of pericardial effusion. Large amount of effusion fluids can be detected easily on clinical examination, however small amount of fluids require additional diagnostic aids like ultrasonography and other radio-imaging studies such as, Computerized Tomography (CT-Scan) for detection of effusion. Recognition of even smaller amounts of fluid is important because of its influence on staging and prognosis in cases of malignancy (Cheson, 1985).

MATERIALS AND METHODS

The present study is a two year hospital based descriptive observational study of Examination of serous effusions and their clinical correlation, done at our hospital and research centre from May, 2011 to April, 2013 which includes 267 cases.

Inclusion criteria: All pleural, ascitic, pericardial and peritoneal fluids were included in the study. In case of pleural effusion, ascites and pericardial effusion, clinicians collected fluids under aseptic precautions, into three parts. First and the second part were sent for cytological and biochemical analysis, where as the third part collected in a sterile, clean, dry container was sent for microbiological analysis. The samples collected intra-operatively after instilling normal saline into the abdominal cavity during exploratory laparotomy were included in the study and were labeled as peritoneal fluid.

Exclusion criteria: Other fluids like synovial and CSF were excluded as these are not serous fluids.

RESULTS AND DISCUSSION

As indicated in Table 1, we received majority of the samples from our hospital accounting for 98% (262 samples) of total cases whereas 2% (5 cases) were referred from outside. Out of 5 cases received from outside; 3 cases (60%) were found to be positive for malignancy where as in-house samples showed positivity of 7.6% (20 cases).

Total 59 fluids showed presence of clot, i.e., 22%. Out of 59 clots maximum were seen in pleural fluid (35/59) (Table 2). Out of 237 pleural, ascitic and pericardial fluids, 99 (41.8%) were transudates and 138 (58.2%) were exudates. Peritoneal fluids were excluded from the classification Table 3.

Out of 267 cases, 71 (26.6%) were known cases of malignancy. Liver cirrhosis was next common (64 cases-24%) followed by tuberculosis (40 cases-15%) (Table 4).

Table 1: Distribution of samples as per source

Sample source	No. of cases	Positive for malignancy
In-house	262	20 (7.6%)
Lab case	5	3 (60%)
Total	267	23

($p = 0.0189$, statistically significant)

Table 2: Distribution of fluids having clot formation

Clot/Types	Pleural	Ascitic	Peritoneal	Pericardial	Total
Present	35 (30.7%)	15 (12.5%)	8 (26.7%)	1 (33.3%)	59 (22.1%)
Absent	79 (69.3%)	105 (87.5%)	22 (73.3%)	2 (66.7%)	208 (77.9%)
Total	114	120	30	3	267

Table 3: Distribution of fluids as transudates and exudates

Types	Pleural	Ascitic	Pericardial	Total
Transudate	31 (27.1%)	67 (55.8%)	1 (33.3%)	99 (41.8%)
Exudate	83 (72.9%)	53 (44.2%)	2 (67.7%)	138(58.2%)
Total	114	120	3	237

Table 4: Distribution according to clinical diagnosis

Diagnosis	Pleural	Ascitic	Peritoneal	Pericardial	Total
GI, Hepatic					
Liver cirrhosis	4	60	-	-	64
Enteritis	-	4	-	-	4
Pancreatitis	1	2	1	-	4
Respiratory					
Pneumonia	3	-	-	-	3
Empyema	4	-	-	-	4
COPD, Bronchitis	6	-	-	-	6
Tuberculosis	36	3	-	1	40
Other systems					
Cardiac cause	4	3	-	-	7
Renal disease	3	1	-	-	4
Hypoproteinimia	-	1	-	-	1
Miscellaneous					
PIH, IUD	1	1	-	-	2
Hypothyroid	-	1	-	-	1
HIV	4	1	-	-	5
Leptospirosis	2	-	-	-	2
DKA	-	1	-	-	1
Multiple	13	5	-	-	18
Unknown	14	1	-	2	17
Neoplastic					
Benign	-	1	12	-	13
Malignant	19	35	17	-	71
Total	114	120	30	3	267

Table 5: Distribution according to clinical diagnosis and positive for malignancy

Diagnosis/Fluid	Total	Fluid positive
Malignancy present	71	19
No-malignancy	196	4
Total	267	23

As indicated in Table 5, out of 71 samples received from known cases of malignancy only 19 (26.7%) effusions were positive for malignancy on cytological examination whereas 4 fluid samples having no clinical history of malignancy were found to be positive, i.e., 2% (4/196). All malignant effusions were found to be exudates (23/23) ($p<0.0001$, statistically significant).

Fluid tapping, a minimally invasive diagnostic as well as therapeutic procedure with serous fluid examination is a well-established method for determining the etiology of effusions. Differentiation between transudate and exudate helps in deciding the management of patient. Conditions like empyema and bacterial peritonitis, etc. can be easily diagnosed on cytology. In case of malignancy presence of effusion indicates advanced disease and careful cytological examination is must to rule out presence of malignant cells; as it changes the stage as well as the treatment modality. Total 267 cases were obtained within a period of 2 years from May, 2011 to August, 2013, in a hospital based prospective and observational study.

CONCLUSION

In case of clinical suspicion of malignant effusion, typing of fluid into exudate or transudate and wet mount preparation for abnormal cells may be done before examination of fixed smears for malignant cells, as we did not find any transudative fluid positive for malignancy. Diagnostic effusion tapping followed by immediate processing of fluid in laboratory may improve cytological outcome. Malignant effusions may not be hemorrhagic in appearance. Rarely effusion may be the first manifestation of malignancy. Immunocytochemistry (ICC) may be required to differentiate reactive mesothelial cells from malignant cells. However; cytomorphological features along with good clinical correlation may provide useful information, wherein there is lack of ICC. Clot processing

can be used as an additional diagnostic tool of value for reporting of effusions. Fluid ADA levels may not only be diagnostic but can also help in ruling out tuberculosis.

REFERENCES

Carr, D.T. and M.H. Power, 1958. Clinical value of measurements of concentration of protein in pleural fluid. New Engl. J. Med., 259: 926-927.

Cheson, B.D., 1985. Clinical utility of body fluid analyses. Clin. Lab. Med., 5: 195-208.

Hajdu, S.I., 1977. Cytology from antiquity to Papanicolaou. Acta Cytologica, 21: 668-676.

Light, R.W., M.I. Macgregor, P.C. Luchsinger and W.C. Ball Jr., 1972. Pleural effusions: The diagnostic separation of transudates and exudates. Ann. Int. Med., 77: 507-513.

Mc Pherson, R.A. and M.R. Pincus, 2006. Henry's Clinical Diagnosis and Management by Laboratory Methods. 21st Edn., W.B. Saunders, St. Louis, Missouri..

Naylor, B., 2008. Pleural, Peritoneal and Pericardial Effusions. In: Comprehensive Cytopathology, Bibbo, M. (Eds.). WB Saunders, Philadelphia, Pennsylvania, pp: 515-577.

Paddock, F., 1941. The relationship between the specific gravity and the protein content in human serous effusions. Am. J. Med. Sci., 201: 569-574.

Paddock, F.K., 1940. The diagnostic significance of serous fluids in disease. New Engl. J. Med., 223: 1010-1015.

Sears, D. and S.I. Hajdu, 1987. The cytologic diagnosis of malignant neoplasms in pleural and peritoneal effusions. Acta Cytologica, 31: 85-97.

Shidham, V.B. and B.F. Atkinson, 2006. Cytopathologic Diagnosis of Serous Fluids. Elsevier WB Saunders, Philadelphia,.

Spriggs, A.I., 1977. History of cytodiagnosis. J. Clin. Pathol., 30: 1091-1102.

Sujathan, K., S. Kannan, A. Mathew, K.R. Pillai, B. Chandralekha and M.K. Nair, 2000. Cyto-diagnosis of serous effusions: A combined approach to morphological features in papanicolaou and may-grunwald giemsa stained smears and a modified cell block technique. J. Cytol., 17: 89-95.

Washiya, K., K. Narumi, T. Noro, S. Hamakawa, N. Furuta, H. Yoshioka and J. Watanabe, 2012. Discriminant analysis of malignant mesothelioma and reactive mesothelium using three-dimensional nuclear estimation. Acta Cytologica, 56: 189-195.

Zemansky, A., 1928. Examination of fluids for tumor cells: Analysis of 113 cases checked against subsequent examination of tissue. Am. J. Med. Sci., 175: 489-503.