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A COMPARISON BETWEEN PLEURAL FLUID ASPIRATE CYTOLOGY AND BLIND PLEURAL BIOPSY HISTOPATHOLOGY IN PATIENTS SUSPECTED TO HAVE MALIGNANT PLEURAL EFFUSION

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ABSTRACT

Background: Pleural effusion remains the most common manifestation of pleural pathology. Cytopathological examination of the pleural fluids is a fast, efficient and non-invasive diagnostic method. Identification of malignant pleural effusions bears critical importance in treatment and prognosis. Blind pleural biopsy histopathology is helpful to reach an etiological diagnosis of exudative pleural effusion, particularly when malignancy is suspected or when results of detailed pleural fluid study are inconclusive, especially in a set up where thoracoscope is not available. **The aim of the study:** The aim of this study was to investigate the cytopathologic diagnoses in malignant pleural effusions and compare it with blind pleural biopsy histopathology, and assess the value of both tests. **Patients and Method:** A total of 201 pleural effusion cases diagnosed to have malignancy in 2011, the data collected from (early detection of cancer laboratories, teaching laboratories and thoracic surgery laboratories) in (Baghdad Medical city Complex) were retrospectively identified as the study group. cytopathological evaluation of pleural fluid alone was done in 113 cases, histopathological pleural biopsy alone was done in 51 cases, and both investigations were done in 37cases. Cytological, histopathological and both are presented as a percentage and compared. **Results:** Of the total 201 pleural effusion cases, 89(44.2%) were females and 112 (55.8%) were males. The age range was between (21-80) with a mean value of (54.6±12.4). The study show that pleural fluid cytology alone was 50.4% malignancy +ve, and closed pleural biopsy histopathology alone was 25.5% malignancy +ve, both tests are +ve in 75.7%.Over all test pleural fluid cytopathology was 54% malignancy +ve, and closed pleural biopsy was 30.7% malignancy +ve. **Conclusion:** Cytopathological examination of pleural fluid is the most valuable diagnostic method for suspected malignant pleural effusions which may have various etiological causes. The sensitivity of pleural tissue biopsy histopathology in the diagnosis of malignant pleural effusion is lower than that of cytopathological evaluation of pleural fluid. Very few cases negative on cytopathology can be diagnosed by biopsy histopathology.

INTRODUCTION

Pleural effusion is a common condition encountered by both chest physicians and chest surgeons in Iraq, and diagnosis of the cause is often difficult. The relative frequency of causes of pleural effusion are known to vary in different parts of the world.[1] Cancer is, however, becoming more common as a cause than it was a decade ago.[2]

Malignant Pleural Effusions

Pathogenesis

The lymphatic system of the parietal pleura plays a major role in the resorption of pleural liquid and protein. Interference with the integrity of the lymphatic system between the parietal pleura and mediastinal lymph nodes can result in a pleural effusion. Tumor involvement of the pleura causes mesothelial thickening, and, on occasion, marked pleural fibrosis.[3]

Postmortem studies suggest that most pleural metastases arise from tumor emboli to the visceral pleural surface, with secondary seeding to the parietal pleura.[4,5] Other possible mechanisms include direct tumor invasion (in lung cancers, chest wall neoplasms, and breast carcinoma), hematogenous spread to parietal pleura, and lymphatic involvement. A malignant tumor can cause a pleural effusion both directly and indirectly. Interference with the integrity of the lymphatic system anywhere between the parietal pleura and mediastinal lymph nodes can result in pleural fluid formation.[5,6] Direct tumor involvement with the pleura may also contribute to the formation of pleural effusions. Local inflammatory changes in response to tumor invasion may cause increased capillary permeability, with resultant effusions.[7]

Causes of Malignant Pleural Effusion

The most important causes are listed in (table 5).

Malignant disease involving the pleura is common. It is the second leading cause of exudative pleural effusions after parapneumonic effusions and approximately 50% of all patients with metastatic cancer develop malignant pleural effusions.[8]

Nearly all neoplasms have been reported to involve the pleura. In most studies, however, lung carcinoma has been the most common neoplasm, accounting for approximately one third of all malignant effusions. Breast carcinoma is the second most common. Lymphomas, including both Hodgkin's disease and non-Hodgkin's lymphoma, are also an important cause of malignant pleural effusions. Tumors less commonly associated with malignant pleural effusions include ovarian and gastrointestinal carcinomas. In 5 to 10% of malignant effusions, no primary tumor is identified.[6,9]

Pleural effusions occurring in patients with known primary cancers may be malignant, paramalignant, or nonmalignant in origin. Malignant effusions are due to pleural metastases and most commonly occur with primary malignancies of the lung and breast (table 5). Paramalignant effusions are not associated with pleural metastases or direct pleural involvement by the malignancy (table 11). Obstruction of the lymphatics by enlarged mediastinal lymph nodes, atelectasis and pneumonia from a tumour obstructing a bronchus, and a chylothorax due to invasion of the thoracic duct are some instances where paramalignant effusions may occur. Nonmalignant effusions are unrelated to the primary malignancy. Differentiation of these three forms of pleural effusions is important as the treatment and prognosis of the patient may vary.[10]

Malignant pleural effusions generally portend a poor prognosis with the average survival time following diagnosis of a malignant pleural effusion being 3 to 6 months. Effusions due to nonmalignant causes, on the other hand, may be potentially treatable.[10]

The term "paramalignant effusions" is reserved for those effusions that are not the direct result of neoplastic involvement of the pleura but are still related to the primary tumor.[28] Important examples include postobstructive pneumonia, with a subsequent parapneumonic effusion; obstruction of the thoracic duct, with the development of a chylothorax; pulmonary embolism; and transudative effusions secondary to postobstruction atelectasis and /or low plasma oncotic pressures secondary to cachexia. Treatment of the primary tumor can also result in pleural effusions. Important causes in this category include radiation therapy and such drugs as methotrexate, procarbazine, cyclophosphamide, and bleomycin. Finally, concurrent nonmalignant disease, such as congestive heart failure, may account for an effusion seen in a patient with cancer.[11]

Although parapneumonic effusions take first place in the etiology of exudative pleural effusions, malignant effusions are seen to be the most common when fluids that require thoracentesis are taken into account. Lung and breast cancers are the most common cause of malignant pleural effusions. The most common cause of malignant effusion in women is breast and ovary cancer metastasis while lung cancer and malignant mesothelioma affect both sexes equally.[3]

The presence of malignant effusion is of great importance the regarding treatment and prognosis. For example, the presence of malignant effusion in lung cancer eliminates the possibility of surgical treatment while it is a sign of advanced disease and short survival in tumors of other organs.[6]

The discovery of malignant cells in pleural fluid and/or parietal pleura signifies disseminated or advanced disease and a reduced life expectancy in cancer patients.[4] Median survival following diagnosis ranges from 3 to 12 months and is dependent on the stage and type of the underlying malignancy. The shortest survival time is observed in malignant effusions secondary to lung cancer and the longest in ovarian cancer, while malignant effusions due to an unknown primary have an intermediate survival time.[12]

Pleural fluid cytology

Cytopathological examination of pleural fluids is a fast, efficient and non-invasive diagnostic method. Identification of malignant pleural effusions bears critical importance in treatment and prognosis.[13]

Cytopathologic investigation is known to have a high diagnostic value in malignant pleural effusions.[14]

Malignant pleural effusion can be diagnosed only by demonstrating malignant cells in pleural fluid or pleural tissue.[15] Pleural fluid cytology in the diagnoses of malignant pleural effusion had a sensitivity of 40 to 90% and average to about 62 %.[16-21] Most experts agree that

when the initial evaluation of pleural fluid is nondiagnostic, especially when neoplastic disease is suspected, parietal pleural biopsy should considered.[22]

Lastly, the greater the number of separate specimens submitted for cytologic examination, the higher will be the percentages of positive reports. Not only do multiple specimens allow examination of more material, pleural fluid which has recently accumulated following a thoracentesis is likely to contain freshly shed and better preserved cells. In the study by Light, if 3 separate specimens are submitted, the diagnostic yield increased from an initial 60% to nearly 80%.[10]

Pleural biopsy histopathology

Biopsy has traditionally been performed blindly using a needle described by Abrams in 1958.[23] The role of blind biopsy in diagnosing malignant effusion has been questioned because its diagnostic sensitivity is less than that of image-guided and thoracoscopic pleural biopsies.[24]

Abrams' biopsy is used for the diagnosis of malignant pleural disease in many centres, although a recent randomized controlled trial has shown that CT-guided cutting-needle biopsy has a greater sensitivity (sensitivity 87 % in CT-guided biopsy group vs. 47% in Abrams' group).[25]

Several types of pleural biopsy needle are available: Cope, Abrams, Radja, Trucut, Ramel. There is no difference between the needles in relation to diagnosis.[26-29]

The diagnostic yield in pleural biopsy increases as the disease becomes more advanced.[18,30] The blind percutaneous biopsies of the costal (parietal) pleura reported a diagnostic yield of 39 to 75% and probably average to about 45%.[16,20,23]

The relatively low yield of blind pleural biopsy is due to several factors, including early stage of disease with minimal pleura involvement, distribution of tumor in areas not sampled during blind biopsy, and operator inexperience.[15,17,21]

However, studies have shown that 7 to 12% of patients with malignant effusions may be diagnosed by pleural biopsy when fluid cytology is negative.[31,32]

Combined pleural biopsy with cytologic analysis of the pleural effusion was more beneficial than any single method in identifying malignant pleural effusion.[31,32]

In one prospective study of 414 cases, U.B.Prakash and H.M.Reiman found that the presence of pleural malignant disease was established cytologic study in 162 patients (57.6%), by needle biopsy in 123 (43%), and by either cytologic analysis or biopsy in 182 (64.7%).[14]

Prognosis of Malignant Pleural Effusion

Median survival 3-12 months from diagnosis; shortest in lung cancer, longest in mesothelioma and ovarian cancer. Pleural fluid pH <7.3 tends to be associated with shorter survival (median survival 2.1 months) and decreased success of pleurodesis.[33]

Table 1: Causes of Malignant Pleural Effusions in Two Different Series.

	Spriggs and Boddington[34]		Anderson et al[35]	
Tumor	***n***	**%**	***n***	**%**
Lung carcinoma	275	43	32	24
Breast carcinoma	157	25	35	26
Lymphoma and leukemia	52	8	34	26
Ovarian carcinoma	27	4	9	7
Sarcoma (including melanoma)	13	2	5	4
Uterine and cervical carcinoma	6	1	3	2
Stomach carcinoma	18	3	1	1
Colon carcinoma	9	1	0	0
Pancreatic carcinoma	7	1	0	0
Bladder carcinoma	7	1	0	0
Other carcinoma	23	4	6	4
Primary unknown	40	6	8	6
Total	634		133	

Table 2: Causes of paramalignant pleural effusions.[36]

Local effects of tumor
Lymphatic obstruction
Bronchial obstruction with pneumonia
Bronchial obstruction with atelectasis
Trapped lung
Chylothorax;
Superior vena cava syndrome
Systemic effects of tumor
Pulmonary embolism
Hypoalbuminemia
Complications of therapy
Radiation therapy
Early
Late
Chemotherapy
Methotrexate
Procarbazine
Cyclophosphamide
Mitomycin/bleomycin

PATIENTS AND METHODS

This was a comparative study carried out at Baghdad medical complex during the year 2011. This study was performed on 201 cases with pleural effusion that had been diagnosed to have malignancy, collected from (early detection of cancer laboratories, teaching laboratories, thoracic surgery laboratories) were retrospectively evaluated and included in this research.

Statistical analysis

SPSS (statistical package for social science), version 18\ IBM.US.\2007 was used for entering and analysis of patients data.

Descriptive statistics were performed; frequencies and percentages of variables were calculated for gender, Age groups distribution, pleural biopsy Histopathology and pleural fluid Cytology.

A comparative statistics then had been performed and (two by two contingency) tables had been performed, then sensitivity and specificity of the tests had been calculated.

KAPPA statistics had been used to find the Percent agreement of validity of diagnosis by both tests.

Chi square and Pearson's correlation tests were used for comparison among variables and to calculate P.value.

In all statistical procedures level of significance (P.value) was two sided and set at P≤ 0.05 to be considered as significant.

Finally all data and results had been presented in tables and or graphs.

RESULTS

The total number of patients was (201), Men to Women ratio was 1.26**:** 1.

A significant difference had been found within gender; male were more likely to have malignant pleural effusion rather than female, table 1 and figure 1.

Table 3: Distribution of cases by gender.

Gender	Frequency	Percent
Female	89	44.2
Male	112	55.8
Total	201	100

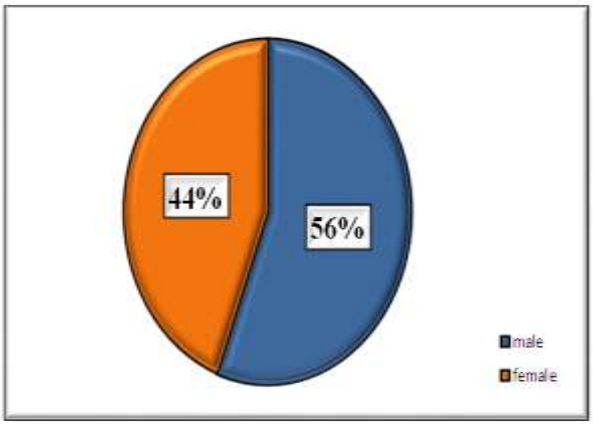

Figure 1: Distribution of patients by gender (Male to Female ratio is 1.26: 1).

The total mean age was (54.6 ± 12.4) year and the range was (21 – 80) year, it had been found, with a high significance, that malignancy tend to be more prevalent with advancing ages, rather than younger age; about 64% of cases were older than 50 year, table 2.

Table 4: Age group distribution of all cases.

Age group	Frequency	Percent
21 - 30	8	3.98%
31 - 40	26	12.94%
41 - 50	38	18.91%
51 - 60	61	30.35%
> 60	68	33.83%
Total	201	100.0%

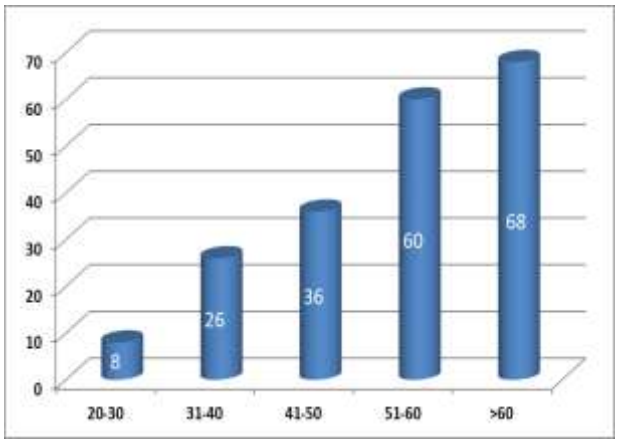

Figure 2: Age group distribution of all cases.

Table 3 shows the frequencies and percentage of patient who were send for histopathology, cytology or both, Pleural fluid cytopathology was performed for about 113 patients and it revealed malignancy in 57 patients (50.4%), pleural biopsy histopathology was performed for 51 patients and it had revealed malignancy in 13 of them(25.5%), while both investigation were performed simultaneously for 37 patients, out of them according to the results of both test 28 (75.7%) were having malignancy, table 3.

Table 5: Distribution of patients by type of test performed.

Test		Finding		Total
		Malignancy	No malignancy	
Pleural fluid CP	Count	57	56	113
	% within Test	50.4%	49.6%	100%
Pleural biopsy HP	Count	13	38	51
	% within Test	25.5%	74.5%	100%
Both	Count	28	9	37
	% within Test	75.7%	24.3%	100%
Total	Count	98	103	201
	% within Test	48.8%	51.2%	100%

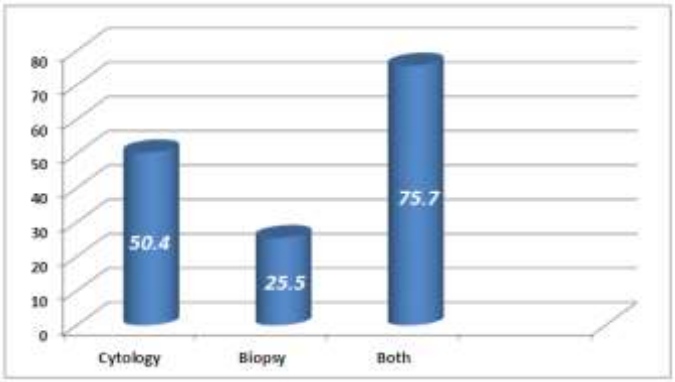

Figure 3: Distribution of patients by type of test performed.

Table 6: Comparison between Pleural biopsy HP and pleural fluid aspirate CP according to the total number of tests.

Test		Finding		Total
		Malignancy	No Malignancy	
Pleural fluid CP	Count	81	69	150
	% within Test	54%	46%	100%
Pleural biopsy HP	Count	27	61	88
	% within Test	30.7%	69.3%	100%
Total*	Count	108	130	238
	% within Test	45.4%	54.6%	100%

*****The total represents the total number of tests that performed and not the patients number.(37 patients had performed both tests (37 CP and 37 HP, simultaneously).

DISCUSSION

In this study the males was 112 (58.2%), the females was 89 (44.8%), and the male to female ratio is 1.26:1. A significant difference had been found within gender; male were more likely to have lung malignancies rather than female. (Table 3 and figure 1). We have no explanation for the greater number of women included in our study. Previous authors have suggested that more females will have a malignant pleural effusion because breast cancer is the second most common cause of a malignant pleural effusion.[35]

The age of the patients ranging between (21-80) years with total mean age was (54.6 ± 12.4) years. on the other hand it had been found, with a high significance, that malignant pleural effusion tend to be more prevalent with advancing ages, rather than younger age; about 64% of cases were older than 50 year.(table 4, figure 2).

The pleural fluid cytopathology done alone in 113 patients and it revealed malignancy in 57 patients (50.4%), pleural biopsy histopathology alone was performed for 51 patients and it had revealed malignancy in 13 of them (25.5%), while both investigation were performed simultaneously for 37 patients, out of them according to the results of both test 28 (75.7%) were having malignancy (Table 5).

Considering the focal nature of pleural involvement by metastatic tumor, it is not surprising that the success in diagnosis for biopsy is less than that of cytology.

According to the total number of tests (The total represents the total number of tests that performed and not the patients number.37 patients had performed both tests 37 cytopathology and 37 histopathology, simultaneously), the patients whom did pleural fluid

cytology was 150 patients and found malignancy in 81 patients (54%), the patients whom did pleural biopsy histopathology was 88 patients and found malignancy in 27 patients (30.7%) (Table 6).

In this study it had been significantly found that pleural fluid cytopathology has higher sensitivity results rather than pleural biopsy histopathology.

The diagnosis of malignancy by blind pleural biopsy histopathology alone in this study is lower than to the experience of other authors (possibly due to lack of experience to do perfect technique of pleural biopsy). The blind percutaneous biopsies of the costal (parietal) pleura reported a diagnostic yield of 39 to 75% and probably average to about 45% [16-20, 23]. Several authors have reported a higher percentage of "positive" diagnoses, and others have recorded a lower yield.[37]

The diagnosis of malignancy by pleural fluid cytopathology alone in this study is similar to the experience of other authors. Also several authors have reported a higher percentage of "positive" diagnoses, and others have recorded a lower yield.

In general, cytopathologic study of the pleural fluid establishes the diagnosis more frequently than pleural biopsy. This is because the costal parietal pleuron is not involved in about 50% of patients with malignant pleural disease. Nonetheless, tumour cells will be present in the pleural fluid only if the tumour involves the pleural surface. Subserosal tumours often have negative cytology but may be detected by pleural biopsy. Hence the combination of cytology and pleural biopsy can increase the rate of definitive diagnosis from 73% to 90%. This is similar to the diagnostic rate of 80% by obtaining 3 separate pleural fluid cytopathological examination as mentioned above. The choice between repeated thoracentesis or pleural biopsy in addition to thoracentesis should therefore be made clinically, based on the fitness of the patient to undergo each procedure and the operator's expertise.[10]

Percutaneous pleural biopsy should be reserved for the second thoracentesis if the initial pleural fluid cytological examination is negative. If the second cytological examination and initial pleural biopsy are negative, a third cytological examination and second pleural biopsy soon after usually is not diagnostic.[38]

Suspicion of patients to have malignant pleural effusion in this study was built on history (the patients had malignancy in lung, breast, ovary. etc), examination, chest x-ray findings, CTS findings (all taken from patients case sheets, from laboratories requests for cytopathological and histopathological examination and from laboratories files of the patients), positive results of pleural fluid cytological examination, positive results of pleural biopsy histopathological examination.

In this study the sensitivity of pleural tissue biopsy histopathology which is done by blind Abram's needle in the diagnosis of malignant pleural effusion was 30.7% which is lower than that of pleural fluid cytology which was 54%.

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CONCLUSION

The findings of this study confirm the usefulness of cytopathological study of pleural fluid and closed needle biopsy of the pleura in the diagnosis of malignant pleural effusion. Cytopathological investigation for pleural fluid is fast, rapid, non-invasive and is very important regarding treatment and prognosis as it constitutes the primary diagnostic step.

This study compared the efficacy of pleural needle biopsy histopathology and pleural fluid cytopathology in the diagnosis of malignant pleural effusion. Cytopathological studies alone yielded a higher percentage of cancer diagnoses than did the biopsies histopathology alone. A diagnosis was established in 75 percent of the patients with malignant pleural effusion when both procedures were performed together. These findings indicate the value of utilizing these techniques concomitantly in the evaluation of patients with malignant pleural effusion.

RECOMMENDATION

1. This study is retrospective study and I found difficulties in collecting of the data because of bad records so we recommended to doing this study prospectively.
2. According to the results of this study combined pleural biopsy HP with CP analysis of the pleural effusion was more beneficial than any single method in identifying malignant pleural effusion so we recommend that they should be doing concomitantly.

REFERENCES

1. Al-Alusi: Pleural Effusion in Iraq. Prospective study in 100 cases. Thorax, 1986; 41: 492-493.
2. Bakir F, Al-Ani F, Talib H, Thwaini J, Al-Shabander N, Rasheed RK. Serous lymphocytic exudate in Iraq: the value of various methods of investigations. Tubercle, 1977; 58: 101-7.

3. Veena BA, Loddenkemper R, Astoul P, Boutin C, Goldstraw P, Hott J Panadero FR, Sahn SA. ATS, Am J Respir Crit Care Med Vol 162. Management of Malignant Pleural Effusions, 1987–2001; 2000.
4. Rodriguez-Panadero F, Borderas Naranjo F, Lopez-Mejias J. Pleural metastatic tumours and effusions: frequency and pathogenic mechanisms in a post-mortem series. Eur Respir J, 1989; 2: 366–369.
5. Meyer PC. Metastatic carcinoma of the pleura. Thorax, 1966; 21: 437–443.
6. Chernow B, Sahn SA. Carcinomatous involvement of the pleura. Is J Med, 1977; 63: 695–702.
7. Andrews BS, Arora NS, Shadforth MF, Goldberg SK, Davis JS. The role of immune complexes in the pathogenesis of pleural effusions. Am Rev Respir Dis., 1981; 124: 115–120.
8. Light RW: Pleural diseases. 4th ed. Philadelphia, Lippincott Williams and Wilkins, 2001; 120-123.
9. Vieta JO, Craver LF. Intrathoracic manifestations of the lymphomatoid diseases. Radiology, 1943; 37: 138–159.
10. K C Ong, V Indumathi, W T Poh, Y Y Ong.The Diagnostic Yield of Pleural Fluid Cytology in Malignant Pleural Effusions. Singapore Med J., 2000; 41(1).
11. John EH, Jeffrey SK. Recent Advances in the Diagnosis and Management of Malignant Pleural Effusions. Mayo Clin Proc., 2008; 83(2): 235-250.
12. Antunes G, Neville E, Duffy J, Ali N. BTS guidelines for the management of malignant pleural effusions. Thorax, 2003; 58: ii29-ii38.
13. Dağlı AF, Küçük Ş, Sezer M, Üçer Ö. Cytopathologic Diagnosis in Pleural Effusion and Cyto-Histopathologic Correlation. Turkish Journal of Pathology. Cilt/Vol. 27, No. 1, 2011; 12-16
14. Prakash UB, Reiman HM: Comparison of needle biopsy with cytologic analysis for the evaluation of pleural effusion: analysis of 414 cases. Mayo Clin Proc 1985, 60: 158-64
15. Sahn SA. Pleural diseases related to metastatic malignancies. Eur Respir J 1997; 10: 1907-13.
16. Strausz J. Pulmonary Endoscopy and Biopsy Techniques. European Respiratory Monograph 1998; 3: 269.
17. Light RW. Diagnostic principles in pleural disease. Eur Respir J 1997; 10: 476-81.
18. Bueno CE, Clemente g, Castro C, Martin M, Ramos SR, Panizo AG et al. Cytologic and bacteriologic analysis of fluid and pleural biopsy specimens with Cope's needle. Study of 414 patients. Arch Intern Med 1990; 150: 1190-4.
19. Motherby H, Nadjari B, Friegel P, Kohaus J, Ramp U, Bocking A. Diagnostic accuracy of effusion cytology. Diagn cytopathol 1999; 20: 350-7.
20. Malcolm DJ, Camp J, Mentzen SJ, Swanso SJ, Sugarbaker DJ. Malignant Effusive disease of pleura and pericardium. Chest 1997; 112: 291-5.
21. Management of Malignant Pleural Effusion. ATS Board of Directors. Am J Respir Crit Care Med 2000; 162: 1987-2001.
22. DeGroot M, Walter G. Thoracoscopy in undiagnosed pleural effusion. S Afr Med j., 1998; 88: 706-11.
23. Abrams LD. A pleural-biopsy punch. Lancet 1958; 1:30–31
24. Maskell NA, Gleeson FV, Davies RJ. Standard pleural biopsy versus CT-guided cutting-needle biopsy for diagnosis of malignant disease in pleural effusions: a randomised controlled trial. Lancet, 2003; 361: 1326–1330
25. Hackbarth JS, Murata K, Reilly WM, Algeciras-SchimnichA: Performance of CEA and CA19-9 in identifying pleuraleffusions caused by specific malignancies. Clin Biochem, 2010, 43:1051-1055
26. Light Rw. Pleural Diseases. Baltimore: Williams and Wilkins, 1995.
27. Cristopher DJ, Peter JV,Cherian AM. Blind pleural biopsy using a tru-cut needle in moderate to large pleural effusion an experience. Singapore Med J, 1998; 39: 169-9.
28. Mc Leod DT, Ternouth Y, Nkanza N. Comparison of the Tru-cut biopsy with Abrams punch for pleural biopsy. Thorax, 1989; 44: 794-6.
29. Morrone N, Algranti E, Borreto E.Pleural biopsy with Cope and Abrams. Chest, 1987; 92: 1050-2.
30. Light RW. Diagnostic principles in pleural disease. Eur Respir J, 1997; 10: 476-81.
31. Hsu C. Cytologic detection of malignancy in pleural effusion: a review of 5255 sample 3811 patients. Diagn Cytopathol, 1987; 3: 8-12.
32. Loddenkemper R, Grosser H, Gabler A, Mai J, Preussler H, Brandt HJ. Prospective evaluation of biopsy methods in the diagnosis of malignant pleural effusions: intrapatient comparison between pleural fluid cytology, blind needle biopsy and thoracoscopy. Am Rev Respir Dis., 1983; 127(Suppl 4): 114.
33. Chapman S, Robinson G, Stradling J, West S. Oxford Handbook of Respiratory Medicine, 2nd Edition, 2009; 47.
34. Al Boddington MM. The cytology of effusions, 2nd ed. New York: Grune & Stratton, 1968.
35. Anderson CB, Philpott GW, Ferguson TB. The treatment of malignant pleural effusions. Cancer, 1974; 33: 916-922
36. Fishman AP, Elias JA, Fishman JA, Grippi MA, Pack AI, Senior RM. Disorders of pleural space. Washington DC. McGraw – Hill, 2008: 1511.
37. Salyer WR, Eggkston C, Erozan YS. Efficacy of Pleural Needle Biopsy and Pleural Fluid Cytopathology in the Diagnosis of Malignant Neoplasm Involving the Pleura. Chest, 1975; 67: 536-539.
38. Anderson CB, Philpott GW, Ferguson TB. The treatment of malignant pleural effusions. Cancer, 1974; 33: 916-922.