

An audit of the clinical investigation of pleural effusion

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Abstract

Background Pleural aspiration with pleural biopsy is advised for the investigation of pleural effusion. The clinical investigation of pleural effusion in a group of teaching hospitals was audited with reference to adequacy and diagnostic value of sampling procedures.

Methods A retrospective review of case records of all patients investigated for pleural effusion during an eight month period was performed. The records of 112 patients, age range 16-91 years, who underwent 150 procedures were reviewed.

Results Microbiology samples were obtained from 137 procedures, of which five provided a positive culture, including one for mycobacteria. Cytology samples were obtained from 145 procedures though approximately two thirds of samples were less than the recommended 30 ml. The pleural biopsy rate was 30%, varying from 0% in general or thoracic surgery to 68% in thoracic medicine (thoracic surgeons carried out thoracoscopy). Twenty nine per cent of pleural biopsy samples were of poor quality. The complication rate was 2% for aspiration alone, and 4% for aspiration plus biopsy. The sensitivity of the first diagnostic procedure for a diagnosis of malignancy or tuberculosis was 53% for cytology alone, 50% for biopsy alone and 72% for cytology plus biopsy.

Conclusion The samples obtained from pleural aspiration and biopsy in the initial investigation of pleural effusion are often inadequate. Further education is necessary to improve the quantity and quality of specimens submitted for histological and cytological examination.

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Pleural effusion is a common clinical problem, the investigation of which may take place in a variety of hospital departments. Standard teaching recommends that initial investigation of a pleural effusion should include cytological and microbiological examination and estimation of protein content in the fluid with closed needle pleural biopsy except when contraindicated.^{1,2} The purpose of this study was to audit routine practice in a group of teaching hospitals. The assessment included an analysis of the frequency of cytological and biopsy requests, the adequacy of cytology and biopsy samples, the results of microbiological tests, complications associated with the procedures

and the relationship of the results of investigation to clinical outcome.

Methods

Patients with an undiagnosed pleural effusion admitted to the Aberdeen Teaching Hospitals during an eight month period from June 1989 to January 1990 were identified retrospectively by examining the records of the chemical pathology, cytology, pathology and microbiology departments. Case records of these patients were reviewed and details of pleural aspiration and biopsy procedures recorded. The number and volume of pleural cytology specimens recorded on the pathology report were noted, with the cytological diagnosis. Pleural fluid protein concentration was recorded. The pathology reports on all pleural biopsy samples were reviewed with respect to adequacy of the specimen and biopsy diagnosis. Microbiological findings from direct smear and culture of fluid were recorded. The final clinical diagnosis was noted, account being taken of all the information available. In some cases this included findings from subsequent thoracoscopy, bronchoscopy or other diagnostic procedure, results of post mortem examination, or a further review of case records 8-16 months after the procedure. Thoracoscopy and procedures in which frank pus was aspirated were excluded from the analysis.

ANALYSIS

The sensitivity of cytology, biopsy and the two combined in detecting bronchial carcinoma, all cancers and cancer plus tuberculosis was calculated when satisfactory specimens were obtained according to the formula:

$$[\text{true positives}/\text{true positives} + \text{false negatives}] \times 100\%$$

Results

A total of 112 patients who underwent 150 diagnostic pleural procedures were identified. The sources of samples and numbers of patients according to department are shown in table 1. The final clinical diagnoses were as follows: cardiac or renal failure, 18 patients; pneumonia or pulmonary embolism, 28; bronchial carcinoma, 26; other carcinomas, 22; lymphoma or leukaemia, 8; mesothelioma, 3; tuberculosis, 4. In three cases, no definite final clinical diagnosis could be established from the case records.

FLUID CYTOLOGY

Cytology specimens were obtained on 145 (97%) occasions. The volume of cytology fluid

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Table 1 Sources of samples

Source	Samples	Patients
General medicine	57	46
Thoracic medicine	40	22
Oncology	14	13
Thoracic surgery	6	5
Geriatrics	15	10
Surgery	10	10
Other	8	6

received by the laboratory ranged from 1 ml to 2000 ml with 62% being less than 30 ml, the minimum volume recommended by our laboratory. The cytological diagnosis was: negative, 66%; carcinoma, 21%; lymphoma, 4%; mesothelioma, 1%. In all, 6% of samples were inadequate, usually owing to delay in samples reaching the laboratory, resulting in cell degeneration. The diagnosis of tuberculosis was suggested in three patients by a predominance of small lymphocytes in the fluid, and was confirmed by examination of pleural biopsy samples taken at the time of the first aspiration in one patient and at subsequent aspirations in the other patients. In another patient, with hairy cell leukaemia, where pleural biopsy was contraindicated, the diagnosis of tuberculosis was presumptive until culture of the fluid yielded *Mycobacterium tuberculosis*.

PROTEIN CONTENT

Pleural fluid protein concentration ranged from 8 g/l to 65 g/l, with a wide spectrum of values in all diagnostic groups (figure 1).

PLEURAL BIOPSY

Pleural biopsy samples were obtained on 46 (30%) occasions; 28 patients had pleural biopsy on one occasion, seven on two occasions, and one on four occasions. A pleural punch (Abrams) was used in 25 cases and a cutting needle (Tru-Cut) in 11. Pleural biopsy rates varied between specialties (figure 2) from 68% in thoracic medicine to 18% in general medicine and none in thoracic or general surgery. The absence of closed needle biopsy samples in thoracic surgery reflects the

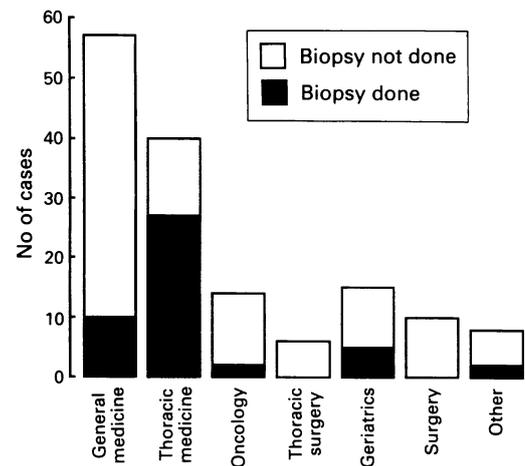


Figure 2 Numbers of pleural aspiration procedures performed by each specialty. Shaded areas indicate procedures where a pleural biopsy sample was also obtained.

availability of thoracoscopy. The mean (SD) number of tissue fragments received by the laboratory was 3 (2). The diagnoses according to the biopsy were: pleurisy or negative, 45% of biopsies; carcinoma, 13%; lymphoma, mesothelioma and tuberculosis, each 4%. A large number of biopsy samples (29%) were inadequate for diagnosis. These either did not contain recognisable pleural tissue or, rarely, had extensive crush artefact. The proportion of inadequate biopsy samples was similar for the pleural punch (6/25) and cutting needle biopsies (3/11).

MICROBIOLOGICAL INVESTIGATIONS

Fluid was sent for microbiological investigation on 137 (91%) occasions. Positive cultures were obtained from four samples, the organisms being *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Klebsiella pneumoniae*, and *Str milleri*. Mycobacterial culture was positive in only one of the four cases of tuberculosis.

COMPLICATIONS

Complications which required active treatment occurred in four cases. Aspiration alone resulted in a pneumothorax in two patients, whereas aspiration combined with biopsy resulted in one pneumothorax and one late empyema, the latter occurring in a patient with a post-pneumonic effusion. The rate of complications requiring treatment was thus 2% for aspiration alone and 4% for aspiration combined with biopsy.

VALUE OF ASPIRATION AND BIOPSY

The sensitivity of cytology and biopsy and the combination at the first aspiration in establishing the final diagnosis of malignancy and tuberculosis was assessed (table 2). Where adequate specimens were obtained, there was a substantially higher sensitivity when both cytology and biopsy specimens were obtained than with either procedure alone.

Discussion

The results of this study highlight a number of

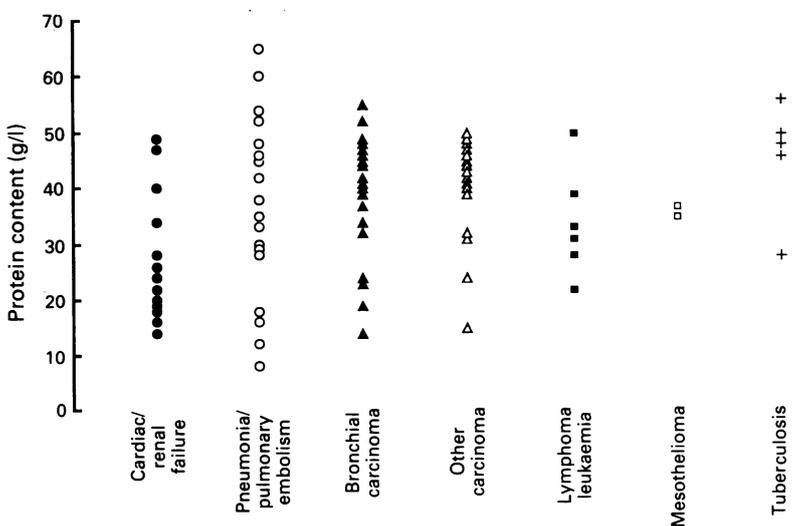


Figure 1 Protein content of pleural fluid samples in each diagnostic category.

Table 2 Sensitivity of cytology and biopsy examinations for final diagnosis

Final diagnosis	Cytology	Biopsy	Cytology plus biopsy
Bronchial carcinoma (n = 26)	60 (25)	43 (7)	67 (9)
Malignancy, all types (n = 59)	53 (55)	45 (11)	69 (13)
Malignancy plus tuberculosis (n = 63)	53 (59)	50 (12)	72 (14)

Values in parentheses are numbers of samples.

problems in the routine clinical investigation of pleural effusion.

The optimum volume of pleural fluid required for cytological diagnosis is not known and, to establish this, a prospective study would be required. Sahin³ has suggested that 35–50 ml of fluid should be obtained for full assessment of a pleural effusion and our laboratory empirically advises that a minimum of 30 ml should be submitted. This was done on only 38% of occasions.

Although protein content of pleural fluid is frequently measured, it appears to be of little value as a diagnostic indicator. Some authors^{3–5} have suggested that it is a useful guide to diagnosis, a concentration of 30 g/l or above being associated with malignancy or tuberculosis, and a concentration of less than 30 g/l with cardiac failure.^{4,5} Our findings, however, are similar to those of Melsom⁶ and demonstrate a substantial overlap in protein concentration between diagnostic groups. These data suggest that protein concentration is a poor guide to diagnosis and emphasise the need for more specific investigation.

Routine submission of samples for microbiological investigation is important since, although the yield of positive cultures is low, a positive result is of great clinical significance.

Pleural biopsy was performed in only 30% of all procedures, although much more frequently by the thoracic medicine unit. This may be due to lack of experience among junior staff, lack of availability of pleural biopsy needles on wards without a special interest in thoracic medicine and reluctance of senior medical staff to subject patients to biopsy examination. The number of biopsy samples taken was often inadequate, as indicated by the low number of tissue fragments received by the laboratory. It is well established that, owing to the patchy nature of pleural disease, the likelihood of obtaining a positive diagnosis of malignancy is increased when multiple samples up to ten are taken.⁷ Many of the biopsy samples were taken by junior staff (senior house officers and junior registrars), and the poor quality of some samples due to crush artefact and absence of pleural tissue may reflect their inexperience. An inadequate biopsy rate of 20% has been reported in a previous series of biopsies performed by interns and residents in Philadelphia.⁸ Increasing the number of biopsy samples taken may reduce this problem.

Complications were infrequent, relatively minor, and comparable with other published series. Scerbo *et al*⁹ observed complications in four of 222 procedures and Mungall *et al*⁷ described four pneumothoraces, none requiring treatment, among 55 procedures. In both

these series, the number of operators was limited and they were presumably more experienced than those in our study. In a comparable study, where pleural aspirations were performed by a range of junior staff, pneumothorax requiring intubation occurred in 4% of 129 procedures.¹⁰ Other potential complications, including re-expansion pulmonary oedema and spread of tumour along the needle track,^{1,2} were not observed in our study.

The sensitivity of the diagnostic procedures in this study compares favourably with other published data. For a diagnosis of malignancy, reported sensitivities for cytology alone vary from 22% to 87%,^{7,11} while for biopsy alone sensitivities vary from 40% to 72%.^{7–9} Prakash and Reiman¹² found in their series that pleural biopsy samples were positive when cytology was negative in only 7.1% of 281 malignant pleural effusions. They suggested that biopsy thus provided a relatively small increase in sensitivity and that cytology alone should be the initial investigation of choice in patients in whom malignant disease is suspected. However, as in the present study, most authors observe improved sensitivity when the two procedures are combined.^{7,9} It is also important that, as in our study, cytology specimens are examined by an experienced cytopathologist.

For a diagnosis of tuberculosis, histological examination of pleural biopsy samples has a sensitivity of 61–71%,^{8,9} and culture of pleural fluid and biopsy material combined with histological examination of the biopsy samples may raise the sensitivity to 90%.³

Our results suggest that in the initial investigation of an undiagnosed pleural effusion there remains a good case for combining pleural biopsy with aspiration cytology. However, there is a need to educate medical staff, particularly in units without a thoracic specialty input, regarding the value of closed needle pleural biopsy samples, and to improve the quantity and quality of fluid and biopsy samples obtained in all units. One approach may be for the thoracic medicine unit to provide an aspiration and biopsy service. This would be a substantial commitment, since our figures suggest that about 225 procedures would be done each year in our hospitals. An alternative is to educate all staff who may be required to perform these procedures, and we are now preparing an educational video for this purpose.

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Adventitia

Charlie's Club

The first club of thoracic surgeons was founded by George Mason of Newcastle upon Tyne. It was called Brown's Club because they met in the hotel of that name in Mayfair. Almost all the thoracic surgeons in the country were members. There were not many of them in 1948—I remember that the meeting of the association took place in a ward in the London Chest Hospital just after I got there in November 1948, and there were about 15 members there. Now, of course, there are 10 times as many.

Charlie's Club was set up about six months after Brown's Club at the London Chest Hospital. Fifteen newly appointed consultants met and agreed that they should meet once a year behind closed doors and report to each other the two most ghastly errors that they had made during the previous year. There is no doubt that the spiritual father of this club was Sir Clement Price Thomas ("Pricie" to us all). He was the most formidably honest surgeon I have ever met—and I have known a lot of them, notably among the members of our club.

I must now digress. Perhaps the accolade for honesty should go to my revered colleague Vernon C Thompson. In the early 1950s he was to go to Oxford to report to the British Thoracic Association a series of 300 thoracoplasties that had been done at the country branch of the London Chest Hospital at Arlesey without any deaths. At that time a 5% mortality rate was respectable. He met me in the corridor and said, "They will not believe this—I will make it 250 cases." I believe he did. I was much afraid, having been recently appointed to the staff, that I might be responsible for the ending of this quite remarkable series. In fact I was not. The number eventually reached 347 before an unfortunate senior registrar spoiled the record.

It was I who perpetrated the original "Charlie" and published it. I was doing my first solo lobectomy. It was my second lobectomy! Training was not the same in the late 1940s as it is now. I was intending to take out the left lower lobe and "inadvertently" divided the left main

bronchus. I reanastomosed it and all went well. Having just been promoted from being Pricie's RSO, I was in the Brompton shortly afterwards. I told him what had happened. His reaction was, "Well done, my boy." The next day I confessed to my dear chief, Sir Thomas Holmes Sellors, who was known to the whole society as "Uncle Tom." He said, "Oh dear." He was perhaps the greatest delegator of all time and almost certainly the best technical surgeon of his era. I worked for and with him for nearly 30 years and we never had a cross word. I shall never forget the dinner which was held at the Apothecaries Hall, to which all his ex-senior registrars had been invited (and most of them came or sent messages) when he got his knighthood. Every one of them, totally unprompted, got up and spoke with the affection which he richly deserved.

During the 30 years the club remained largely in operation the level of reporting of errors was maintained, as its diary shows. Six of the 18 members became presidents of the Thoracic and Cardiac Surgeons' Association and one became the president of the Royal College of Surgeons of Ireland. Two of them also were presidents of the Thoracic Society.

We pooled statistics and it was the custom that the president for the year wrote the paper. The last one was in 1983, when we collected the follow up for operations on 8781 patients with bronchial carcinoma. But for one or two backsliders it would have been 10 000.

Lastly, in the anecdotal vein, I have a wonderful story about my third dear colleague at the London Chest Hospital — Donald Barlow. He showed a film at our annual meeting one year; he was passing an oesophagoscope down his own oesophagus like a sword swallower. I congratulated him about this film and said, "Donald, you must have had a great deal of practice at this." He replied, "You must think I'm crazy. I did it only once, just for the film." Few people would believe this story, but those who knew him would have no difficulty in doing so.—JACK R BELCHER