

Use of percutaneous needle biopsy in the investigation of solitary pulmonary nodules

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ABSTRACT Percutaneous needle biopsies were performed on 683 patients with solitary pulmonary nodules during 1976–84. A cytological diagnosis of malignancy was made from the first biopsy in 473 patients (69%). A second biopsy was performed in 43 patients, a diagnosis of malignancy being made in a further 16 cases (37%). Histological material was available for comparison with cytological findings in 203 patients. Cytological examination was reliable in the diagnosis of malignancy with a high yield (75%) and low false positive rate (1.5%). Specific benign lesions were correctly diagnosed in 10 patients (1.5%). There was a false negative rate for the diagnosis of malignancy of 18% for the patients with a subsequent histological diagnosis. This compares with a false negative rate of 9% overall; the true rate probably lies between these figures. These results imply that a cytology report indicating no evidence of malignancy, but not diagnostic of a specific benign condition, does not reliably exclude a malignant lesion. In this series cytological typing was not accurate at predicting the cell type determined by histological examination (61% agreement) and was not able to discriminate between small cell and non-small cell lung cancer.

Introduction

Percutaneous needle biopsy is commonly used in the investigation of pulmonary nodules that are unlikely to be visualised bronchoscopically.¹ Most clinicians use some form of fine gauge needle to provide a sample, which is adequate for microbiological and cytological examination but rarely for histological examination. To assess the role of this technique in the management of patients with solitary pulmonary nodules, we have reviewed our experience retrospectively and determined the diagnostic yield and accuracy of cytology in our unit.

Methods

The records of all patients undergoing percutaneous needle biopsy at Papworth Hospital in the period 1 January 1976–31 December 1984 were examined and the results of cytological examination of needle biopsy specimens and, where available, subsequent his-

tological examination of surgical or necropsy specimens were noted. Biopsies were performed by a consultant radiologist or radiologists in training; they used a fine gauge (20 G or 22 G) aspirating needle or a 21 G Rotex screw biopsy needle (Ursus Konsult) and the material obtained was used to make a cytology smear preparation. One to three passes were made, the number depending on the appearance of the smear and the ease with which the lesion was sampled. All biopsies were of intrapulmonary masses that measured 1 cm or more in diameter on the chest radiograph. Fluoroscopic guidance was used as described previously.² The material obtained was examined by the same cytopathologist (VB) and classified as being malignant, as showing a specific benign condition such as a hamartoma, or as showing "no evidence of malignancy." Tumours were subdivided into five groups: (1) squamous carcinoma; (2) adenocarcinoma; (3) undifferentiated tumour; (4) small cell tumours; (5) other tumours.

Any tumour that could not be specifically typed was classified as an undifferentiated tumour.

Results

CLINICAL OUTCOME

Percutaneous needle biopsies were performed on 683

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patients over a nine year period. Figure 1 summarises the fate of all patients in this study. A positive diagnosis of malignancy was made from the first biopsy in 473 patients (69%). Of these 473 patients, 140 had a thoracotomy. The remainder were considered inoperable for reasons of age, lung function, or evidence of metastases. A necropsy was subsequently

performed on 10 patients with inoperable lesions, so that 150 cases diagnosed as malignant by needle biopsy had histological material for comparison with cytological specimens. There were three false positive patients with a pseudolymphoma and an eosinophilic granuloma were misdiagnosed as having undifferentiated carcinoma from the cytological specimens and a pulmonary infarct was misdiagnosed as squamous carcinoma.

An inadequate specimen was obtained from two patients (0.3%), in whom the procedure was not repeated as the original radiographic abnormalities resolved. A definite diagnosis of a benign condition was made by needle biopsy in 10 patients (1.5%). Five had tuberculosis diagnosed by culture of the organisms, one a mycetoma, one a rheumatoid nodule, and three hamartomas. Subsequent radiographic follow up of these patients for at least two years showed either no change in appearance or resolution of the lesion.

A needle biopsy cytology report with "no evidence of malignancy" but no specific diagnosis was obtained in 198 patients (29%). Figure 2 shows the further management of this group of patients. A diagnosis was obtained from other investigations in 19 patients (sputum cytology, bronchoscopy, culture of aspirated material, or radiographic follow up). Twelve of the patients had inoperable malignant lesions while seven had treatable infections or lesions that resolved on subsequent radiographs. Clinical suspicion of malignancy was sufficient to proceed directly to thoracotomy in 42 patients, 28 of whom did have malignant lesions while 14 had benign conditions. In 47% of the patients the negative needle biopsy cytology report was compatible with the clinical features and radiographic appearances, and the result was accepted. Follow up of these patients is incomplete as some were discharged to the care of their general practitioner while others were followed up in hospital clinics, but none is known to have developed or died from lung cancer. A second needle biopsy was performed in 43 patients, yielding a positive diagnosis of malignancy in 16 (37%), three of whom had operable lesions. Of the remaining 27 patients with two negative needle biopsy results, 18 were not investigated further and one had a positive third needle biopsy. Histological material was available from thoracotomy or necropsy for eight patients of this group of 27, five whom had a malignant lesion.

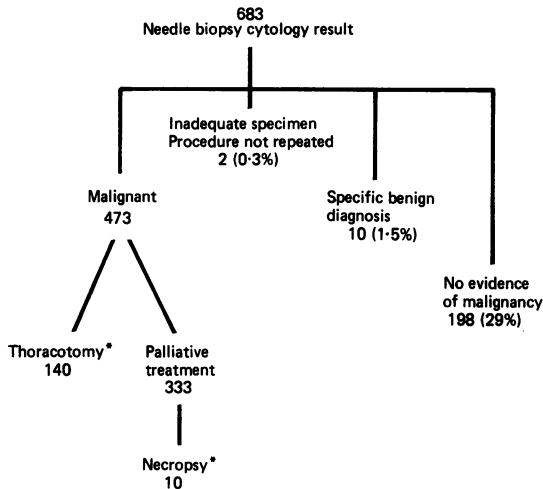


Fig 1 Outcome in 683 patients who had a needle biopsy.

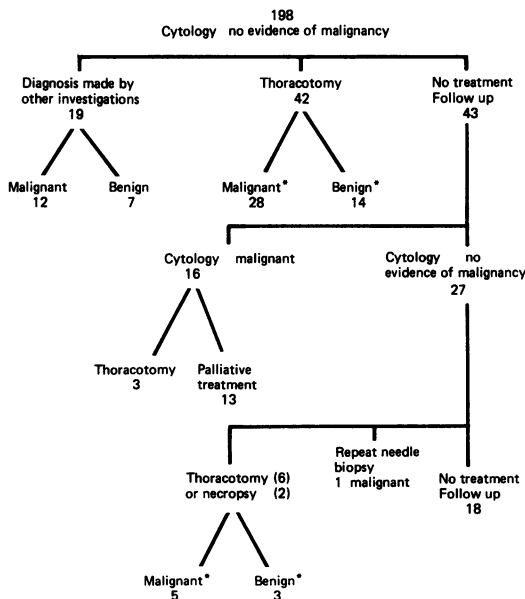


Fig 2 Management and outcome in the 198 patients whose first needle biopsy specimens were reported to show no evidence of malignancy.

VALUE OF NEEDLE BIOPSY

In this series of 683 patients there were 112 patients whom one or two needle biopsies provided no evidence of malignancy and who were assumed to have a benign lesion on the basis of radiographic and clinical

*Use of percutaneous needle biopsy in the investigation of solitary pulmonary nodules***Table 1** Accuracy of cytological diagnosis of malignant and benign lesions from percutaneous needle biopsy specimens compared with histological diagnosis in 203 patients who underwent the two procedures

Cytology report	No of patients	No (%) of patients with histological confirmation
Malignant	150	147 (98)
No evidence of malignancy	53	17 (32)
Total	203	164 (81)

condition at follow up. Three hundred and thirty three patients who had a cytological diagnosis of malignancy were considered inoperable and had no necropsy. It is against this background that the overall estimates of false positive rate (three patients, 0.4%) and false negative rate (62 patients, 9%) must be viewed.

Cytology results from the needle biopsies were compared with the histological diagnosis made in the 203 cases where surgical or necropsy material was available (tables 1 and 2). A cytological report of malignancy was made in 150 cases and was correct in all but three, giving a false positive rate in these 150 cases of 1.5%. Of the 53 patients who had no cytological evidence of malignancy, 36 had histological evidence of malignancy, giving a false negative rate of 36 in 203 (18%). The overall agreement of cytology with histology in the diagnosis of malignancy was 81%.

ACCURACY OF CELL TYPING OF TUMOURS

Table 2 compares the cell type reports on cytological specimens from the first needle biopsy of malignant lesions compared with the subsequent histological diagnosis based on thoracotomy or necropsy material

Table 2 Cell type reports from needle biopsy specimens in 150 patients with malignant lesions diagnosed cytologically compared with histological diagnosis

Cytology report*	No of patients	No (%) of patients with this cell type diagnosed histologically
Squamous cell carcinoma	97	65 (67)
Adenocarcinoma	20	17 (85)
Undifferentiated carcinoma	19	1 (5)
Small cell	4	1 (25)
Other malignancies	10	9 (90)
Total	150	91 (61)

*First needle biopsy.

There was agreement in 91 of the 150 cases (61%) overall. Cytology was most accurate in the diagnosis of adenocarcinoma, 17 out of 20 patients being diagnosed correctly (85%); the other patients had a squamous cell carcinoma (1) or rare tumours (2). Sixty seven per cent of those reported as having squamous cell carcinomas were diagnosed correctly from cytology specimens, the other 32 patients having adenocarcinoma (24), undifferentiated tumours (2), anaplastic tumours (2), clear cell tumours (2), transitional cell carcinoma (1), and a pulmonary infarct. Nineteen tumours were classified cytologically as undifferentiated but only one (5%) was confirmed as such from histological appearances. The other 18 patients had squamous cell carcinoma (7), adenocarcinoma (6), benign lesions (2), and rare tumours (3). Cytology was poor for diagnosing small cell carcinoma of the bronchus; of four cases with this cytological diagnosis, only one had the diagnosis confirmed histologically and a further histologically proved case had been diagnosed as lymphosarcoma by cytology. Nine out of 10 other specific tumours were correctly diagnosed by cytology.

REPEAT NEEDLE BIOPSIES

A second needle biopsy was performed in 43 of the 198 patients with no evidence of malignancy from the first biopsy. The yield of malignancy at the second biopsy was 37% (16 cases, three confirmed at thoracotomy). There was no evidence of malignancy in 27 patients, six of whom were subsequently found to have cancer at thoracotomy, necropsy, or further lung biopsy (fig 2). The false negative rate for the second biopsy was 14%.

Discussion

Percutaneous aspiration needle biopsy of the lung has become more widely used with the advent of fluoroscopy and image intensification.³ A limited amount of material is obtained, which is usually adequate only for microbiological or cytological examination. The latter may be technically difficult if the sample is distorted in the process of biopsy or during the preparation of the specimen, so that appearances may differ from those seen in exfoliative cytological preparations.⁴

The usefulness of this technique in the investigation of pulmonary nodules depends on the ability to differentiate between benign and malignant lesions, thereby obviating the need for an exploratory thoracotomy. In this series a specific benign diagnosis was made in only 10 patients (1.5%). This figure may be artificially low as most patients with infections, many of whom are immunosuppressed, are inves-

Table 3 Distribution of cell types of lung cancer reported for needle biopsy cytology specimens from 473 patients compared with results in the subgroup of 150 cases for whom histological diagnosis was later available

Cell type	% of needle biopsy specimens with this diagnosis (n = 473)	% with this cell type diagnosed cytologically who later had thoracotomy or necropsy (n = 150)
Squamous cell carcinoma	57	65
Undifferentiated carcinoma	15	13
Adenocarcinoma	22	13
Small cell or other tumours	6	7

tigated by needle biopsy at another site in our district and have not been included in this series. Most negative cytological samples in this series were simply described as showing "no evidence of malignancy." The estimated false negative rate overall was 9%, but in the group for whom histological material was available for comparison (203 of the 683 patients) the false negative rate was 18%. The former figure may therefore be an underestimate as the diagnosis of a benign lesion was presumptive in 112 patients. The figure of 18% may be too high, however, since all patients in whom there was a suspicion of malignancy despite a negative cytology report were sent for thoracotomy, while those with a low index of suspicion were not investigated further. The true false negative rate probably lies between the two figures; this would compare with figures quoted by other authors—that is, from 5% to 16%.⁵⁻⁷ If cytological specimens could have been prepared and examined immediately at the time of biopsy the yield would probably have been improved and the need for repeated biopsies reduced. Unfortunately this facility is not available in our unit. None of the false negative results were due to inadequacy of the specimens for cytological purposes, although this had been a common cause of false negatives in other series. The false positive rate in this series was low, from 0.4% to 1.5%, although other authors have had no false positives.^{5,7,9} Forty two of our patients had a second needle biopsy, with a 37% yield of malignancy. Sargent *et al*⁷ performed second biopsies in 44 cases with a yield of 45% and third biopsies in 16 cases with a yield of 56%. These authors and others¹⁰ have suggested that at least three attempts should be made before a lesion is considered to be benign, although no details of their false negative rates from repeat attempts were given. In our series the false negative rate of first and second attempts was fairly similar and we would suggest that, if adequate material has been obtained, other forms of investigation should be considered if there is clinical suspicion of malignancy

in the presence of a negative needle biopsy result.

In summary, our results suggest that, if a positive diagnosis of malignancy or of a specific benign condition is made cytologically from a percutaneous needle biopsy specimen of a pulmonary nodule, the result is reliable. A non-specific negative result, however, cannot be relied on.

The second role for needle biopsy in the investigation of pulmonary nodules is to provide a histological diagnosis on the basis of which a decision can be made about palliative treatment in those patients with cancer for whom surgery is not an option. Payne *et al*⁶ showed that needle biopsy material is not as accurate at predicting cell type as other biopsy material. In their large study there was agreement of needle biopsy cytology with histology in 62%, similar to the 61% in the present series (the patients in the present series seen during 1976-79 are included in the series of Payne *et al*). Only 150 of the 473 cases with a needle biopsy cytology report of malignancy, however, had histological material available for comparison in the present series, 32% of the group. There is obviously room for error if the distribution of cell type in this subgroup is not representative of the group as a whole. Table 3 shows the distribution of the cell type of tumour diagnosed at cytology in the whole group of 473 patients and the subgroup of 150 who later had surgery or necropsy. In the latter group there is a higher percentage of squamous cell carcinoma and a lower percentage of adenocarcinoma than in the group as a whole. One major error of cytology compared with histology was the misdiagnosis of adenocarcinoma as squamous cell carcinoma. The other error was in misdiagnosis of squamous cell carcinoma or adenocarcinoma as undifferentiated tumour. The proportion of undifferentiated tumours and small cell tumours diagnosed cytologically was relatively constant in the two groups. Rudd *et al*¹⁰ compared the accuracy of diagnosis of small cell tumours by needle and bronchial biopsy techniques and found that it was reliable by both methods. We have found, however, that needle biopsy cytology is not accurate in the diagnosis of small cell carcinoma, although our group with this cell type was extremely small.

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