

The Use of Fine Needle Aspiration Biopsy in the Management of Thyroid Disease

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Nadira Mamoon, Sajid Mushtaq, Muhammad Muzaffar (Departments of Cytopathology, Armed Forces Institute of Pathology, Rawalpindi.)

Amir Hussain Khan (Department of Pathology, Army Medical College, Rawalpindi.)

Abstract

Fine needle aspiration biopsy is now a first line investigation in thyroid disease. The purpose of this study was to evaluate the results of this technique in comparison with routine histopathology. A total of 593 aspirations over a four year period were included. There were 390 (65.7%) solitary nodules, 124 (20.9%) multinodular goiters, 66 (11.1%) diffuse goitres and 13 (2.2%) recurrent post thyroidectomy nodules. Radioisotope scanning in 386 cases showed 325(84.2%) cold nodules, 54(14.0%) warm nodules and 7(1.8%) hot nodules. There were 458 (77.2%) colloid goitres and cysts, 14 cases of thyroiditis (2.2%) and 30 malignancies diagnosed on fine needle aspiration biopsy. In 19 cases (3.2%) a diagnosis of follicular neoplasm and in 29 cases (4.9%) a diagnosis of suspicious aspirate was made. Histological results were available in 176 cases. In 108 cases findings of histology and FNAB were compared with radioisotope scanning. A sensitivity of 92.8% and 42.8%, a specificity of 90.1% and 98.7% and accuracy index of 90.3% and 94.3% was found, when considering suspicious cases alternately as positives and negatives. Surgery was recommended in all suspicious cases to prevent reduction in sensitivity of the technique. Fine needle aspiration biopsy was found to be a highly effective procedure which can obviate a lot of unnecessary surgery in thyroid lesions (JPMA 47:255,1997).

Introduction

Fine needle aspiration biopsy (FNAB) has become established the world over as a first line investigation in thyroid lesions¹⁻³. Its primary use is in the management of a solitary thyroid nodule although it can also be of help in diffuse goiters^{4,5}. FNAB is a safe and inexpensive tool in the study of thyroid lesions provided that adequate cytopathology services are available⁴. The main aim of FNAB in nodular thyroid enlargement is differentiating benign from malignant lesions^{6,7}. This study was undertaken to evaluate the results of FNAB in comparison with histology findings and also to document the pattern of thyroid disease in our population as diagnosed on cytology.

Patients and Methods

This study included 593 aspirations reported at the Armed Forces Institute of Pathology (AFIP) from January, 1992 to December, 1995. The patients were mostly referred from civil and military hospitals in the Rawalpindi -Islamabad region to the Cytopathology department at AFIP for FNAB. Aspirations were also performed by the surgeons at these hospitals and the smears were sent for interpretation. FNA was done with a 21-23 gauge needle and 5-10 ml disposable syringe without local anaesthesia. In patients with small nodules up to 3 cm, a single aspiration and in larger nodules aspiration from more than one site was done. Several passes were made on each aspiration. In cystic nodules the cyst was completely emptied and then FNAB was done from any residual swelling. In cases of inadequate aspiration, repeat aspiration was performed after two weeks interval. Two to four smears were made in

each case. In case of cysts, fluid aspirated was also centrifuged and examined. Cytospin and cell block preparations were not made routinely. Smears with at least six fragments of follicular epithelial cells were considered to be adequate. The smears were alcohol fixed and stained with H&E and Papanicolaou stains. The histology results were obtained from the records of Histopathology department at AFIP and Army Medical College Rawalpindi. Colloid goiter, thyroiditis and colloid cysts were considered to be negative smears. Papillary carcinoma, medullary carcinoma and anaplastic carcinoma were considered to be positive. High colloid content and abundant cellularity with monolayered plaques formed by cohesive and standard sized follicular cells were the cytological criteria for non-malignant follicular proliferations (hyperplastic colloid nodules). Criteria for labelling an aspirate as follicular neoplasm were absent or low colloid content and abundant cellularity with variable arrangements of follicular cells as well as scattered scarcely cohesive cells. The cells were slightly larger than in non-malignant follicular proliferations. An aspirate was labelled as suspicious if it showed low cellularity but marked lack of cohesion or cytological atypia.

An aspirate was also considered suspicious if it showed some but not all features of papillary carcinoma that is papillary architecture of fragments, psammoma bodies and nuclear pseudo-inclusions. The following parameters⁸ were analyzed; (1) sensitivity: the proportion of patients with malignant thyroid disease and positive cytology findings; (2) specificity: the proportion of patients without malignant thyroid disease and negative cytology findings; (3) positive predictive value: the probability of having malignant thyroid disease and positive cytologic findings (4) negative predictive value: the probability that a patient did not have malignant thyroid disease in the presence of negative cytologic findings and (5) accuracy index: the proportion of correct results (true positives and true negatives) in relation to all cases studied. Cytologically suspicious cases were considered alternately as positive and negative.

Results

The total number of aspirations was 593. There were 405 (68.3%) females and 188 (31.7%) males. Their ages ranged from 6 to 92 years. The majority of these lesions were solitary nodules numbering 390 (65.7%). There were 124 (20.9%) multinodular goiters suspected of harbouring malignancy. Sixty-six (11.1%) were diffuse goiters and 13 (2.2%) were recurrent post-thyroidectomy nodules. Aspiration proved 207 (39.1%) of these lesions to be cystic. Radio-isotope scanning had been done in 386 cases. Out of these 325 (84.2%) were cold nodules, 54 (14.0%) warm nodules and only 7 (1.8%) were hot. No major complications (seeding of tumour, palsy of the laryngeal nerves and hematoma) were recorded. Only slight local pain was found after FNAB.

Table I. Results of Fine Needle Aspiration biopsy in 593 patients.

| Cytology findings | No. of patients | (%) |
|--------------------------------|-----------------|--------|
| Colloid goiter | 251 | (42.3) |
| Colloid cyst | 207 | (34.9) |
| Acute thyroiditis | 7 | (1.1) |
| Granulomatous thyroiditis | 4 | (0.6) |
| Hashimoto's thyroiditis | 3 | (0.5) |
| Suspicious (cellular) aspirate | 29 | (4.9) |
| Follicular neoplasm | 19 | (3.2) |
| Papillary carcinoma | 6 | (1.0) |
| Medullary carcinoma | 2 | (0.3) |
| Anaplastic carcinoma | 21 | (3.5) |
| Lymphoma | 1 | (0.1) |
| Inadequate | 43 | (7.2) |

Table I shows the results of FNAB in 593 patients. Colloid goiters and cysts added up to 458(77.2%) of our cases. Fourteen cases were of thyroiditis including 3 cases of Hashimoto's thyroiditis. There were 29 (4.9%) suspicious cellular aspirates and 19(3.2%) cases of follicular neoplasms.

Table II. Results of FNAB in 386 cases who underwent radioisotope scanning.

| Radioisotope scan Results | No. | Fine Needle Aspiration Biopsy | | | | |
|---------------------------|-----|-------------------------------|--------------|---------------------|------------|------------------|
| | | Colloid goiter | Colloid cyst | Follicular neoplasm | Suspicious | Malignant |
| Cold nodule | 325 | 182 | 129 | 8 | 5 | 1 (papillary Ca) |
| Warm nodule | 54 | 53 | . | . | 1 | . |
| Hot nodule | 7 | 7 | . | . | . | . |

Table II shows the results of FNAB in 386 cases who underwent radioisotope scanning. Majority of the warm and all the hot nodules proved to be colloid nodules. One warm nodule was labelled as suspicious. Most of the cold nodules were benign (95.6%), however on aspiration there were 8 (2.5%) follicular neoplasms, 5 (1.5%) suspicious aspirates and 1(0.3%) papillary carcinoma. The post-operative histological findings in 176 patients were correlated with previous FNAB findings (Table III).

Table III. Correlation between FNAB diagnosis and histological diagnosis.

| Cytological diagnosis | No. of cases (n=176) | | Post-operative Histology | | | | | |
|-----------------------|-------------------------|--------|--------------------------|--------|------------|--------|-----------|-------|
| | | | Colloid goiter | | F. adenoma | | Malignant | |
| | No. | (%) | No. | (%) | No. | (%) | No. | (%) |
| Negative | 147 | (83.5) | 146 | (82.9) | 0 | (0.0) | 1 | (0.5) |
| Suspicious | 11 | (6.2) | 5 | (2.8) | 1 | (0.55) | 5 | (2.8) |
| Foll. neoplasm | 10 | (5.7) | 5 | (2.8) | 3 | (1.7) | 2 | (1.1) |
| Positives | 8 | (4.5) | 2 | (1.1) | 0 | (0.0) | 6 | (3.4) |

Many of the remaining patients were followed up regularly and did not undergo surgery. Histopathology results of patients operated upon at other centres could not be recorded. In the group with negative cytological findings, one patient had a papillary carcinoma on histology. This was reported as colloid goiter on FNAB. Review of the case showed hypocellular smears showing some cells with nuclear inclusions. However, definite papillary fragments were not seen most likely due to sampling error. Of the 8 positive cases, there were 3 papillary, 2 anaplastic and 1 medullary carcinoma. On FNAB one of the anaplastic carcinomas had been diagnosed as papillary as some of the fragments showed papillary fronds, the remaining diagnoses being the same. Two false positive cases proved to be of colloid goiters. Review of the cases showed hypercellular aspirates with singly dispersed cells and small groups of cells forming a follicular pattern. The cells showed anisonucleosis and nuclear pleomorphism. Of the eleven suspicious aspirates, five proved to be hyperplastic colloid goiters. There was one follicular adenoma and five malignant lesions. The malignant lesions comprised two papillary carcinomas, one malignant lymphoma, one anaplastic carcinoma and one follicular-parafollicular (intermediate type) carcinoma. Out of the ten aspirates reported as follicular neoplasms, five were found to be hyperplastic colloid goiters, three follicular adenomas and two were follicular carcinomas. Histopathology results in 108 patients with cold nodules who underwent surgery are given in Table IV.

Table IV. Comparison of histopathology and FNAB results in 108 cases of cold thyroid nodules.

| Fine needle aspiration biopsy | No. | Histopathology | | |
|---------------------------------|-----|----------------|--------------------|----------------|
| | | Colloid goiter | Follicular adenoma | Malignant |
| Colloid goiter/cyst | 94 | 93 | 1 | - |
| Follicular neoplasm | 5 | 1 | 3 | 1 |
| Suspicious | 3 | 1 | 1 | 1 |
| Malignant (Papillary carcinoma) | 1 | - | - | 1 |
| | | | | (Papillary Ca) |

Majority of the benign reports were confirmed. One nodule reported as colloid nodule was found to be a follicular adenoma. Of the five aspirates reported as follicular neoplasms, three were confirmed to be

follicular adenomata and one proved to be a follicular carcinoma. Out of the three suspicious aspirates, one was malignant (follicular carcinoma) and one was found to be a follicular adenoma. The papillary carcinoma reported on aspiration was also confirmed on histology. On the whole, 8 (7.4%) out of 108 cold nodules were neoplastic and 3 (2.8%) were malignant.

Histopathology results of the warm nodule reported as suspicious on FNAB were not available.

Evaluation of the results considering suspicious cases alternately as positives and negatives showed (1) sensitivity of 92.8% and 42.8%, (2) specificity of 90.1% and 98.7%, (3) positive predictive value of 44.8% and 75%, (4) negative predictive value of 99.3% and 95.2%, (5) Accuracy index of 90.3% and 94.3%.

Discussion

Thyroid disease is common in Pakistan and is seen at all ages, Fine needle aspiration biopsy provides a safe, economical and accurate method to diagnose thyroid disorders. This is basically a technique that helps in differentiating lesions that require surgery from those that can be managed otherwise. Many centres in Pakistan are now using this technique as a routine first line investigation^{9,10}. In this study thyroiditis was diagnosed in 14 cases. Those with acute thyroiditis underwent incision drainage if required. Acute thyroiditis is more frequent in this study (7 cases) as compared to Hashimoto's thyroiditis (3 cases) and granulomatous thyroiditis (4 cases). However, the overall frequency of 1.1% among all aspirates is comparable to other reports¹¹. Granulomatous thyroiditis had to be differentiated from tuberculosis both on morphological and clinical grounds. Hashimoto's thyroiditis showed typical features of an abundant polymorphous lymphoid population along with Hurthie cells¹¹. Papillary, medullary and anaplastic carcinomata were easily detected when characteristic features were seen as mentioned by other workers^{12,13}. A diagnosis of suspicious or cellular aspirate was made when all the criteria were not fulfilled. A diagnosis of follicular neoplasm was made using criteria suggested by Lowhagen⁴ and others¹⁴. It is not possible to differentiate follicular adenoma from follicular carcinoma on FNAB as capsular and vascular invasion cannot be assessed. Most of the aspirates reported as positive for malignancy were confirmed on histology. Out of those reported as suspicious, only 33% were confirmed to be malignant, the remaining being adenomatous goitres or follicular adenomas. As compared to other reports³ where the percentage of suspicious cytological findings that proved benign or malignant on histology were similar. In our study the proportion of benign lesions was higher than malignant. This suggests that some unnecessary surgery was carried out on the basis of FNAB diagnosis.

The sensitivity, specificity, accuracy and predictive values in the study also reflected this trend.

Hawkins et al³ including cytologically suspicious specimens alternately as positives or negatives gave the following results. A sensitivity of 86.3% and 67.7%, specificity of 95.3% and 99.4%, positive predictive value of 79.7% and 94.1%, negative predictive value of 97.0% and 93.1% and accuracy index 93.7% and 93.2%. In our study the results show a markedly lower positive predictive value and a higher negative predictive value. These results are most likely due to our tendency to report as suspicious the slightest degree of atypical cytological features. With more experience and confidence in the technique, this tendency is likely to be reduced. This study also shows that the sensitivity of the cytological results is much greater when suspicious findings are considered as positive. This is at the expense of a fall in positive predictive value. Similar results have been reported in other studies^{3,4}. Surgery is advocated therefore, when the aspiration biopsy results are suspicious as well as when they are malignant. Although, this tends to increase the false positive rate from 1.1% to 9% indicating that some benign lesions are being removed, this is necessary to prevent reduction in the sensitivity of the technique. The overall frequency of malignancy among thyroidectomy patients in this study is 7.9%.

In other series it varies from between⁹ to 78% with a median of 23%¹. The lower rate in this study is most likely due to the increased frequency of benign thyroid disease in the northern parts of Pakistan. The frequency of malignancy in cold nodules after thyroidectomy (Table IV) in this study is 2.7%. This is also much lower than the reported incidence of 10-20%¹⁵. If surgery had been restricted to cases with a positive or suspicious FNAB report the frequency would have risen to 33%. In solitary cold nodules where many patients are asymptomatic, follow up with repeat FNAB, and thymidine suppressive therapy¹⁶ could possibly have avoided some unnecessary surgery. To conclude, FNAB has been found to be a valuable and safe diagnostic technique in the management of thyroid lesions. Patients with benign FNAB findings can be managed with medical treatment, avoiding unnecessary surgery. It is necessary for reliable results that FNAB be performed and reported by people with experience in this technique. Needless to say, in a third world country like ours, FNAB is a technique that can reduce expenditure on unnecessary surgical procedures.

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