Role of imprint cytology in intra-operative diagnosis of thyroid lesions

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Abstract

Background:
Intra-operative imprint cytology is an important diagnostic modality in the diagnosis of thyroid lesions. A correct intra-operative diagnosis helps eliminate the need for second surgery.

Aim:
To study diagnostic accuracy of imprint cytology and to compare the imprint cytology results with that of the corresponding paraffin section diagnosis in thyroidectomy cases.

Materials and Methods:
This is a prospective study of 84 patients who have undergone thyroidectomies over a period of one year at the Department of Surgery, Thiruvananthapuram, Kerala, India. The intra-operative imprint cytology smears were stained by Papanicolaou method. The imprint cytology interpretation was later compared with the paraffin section diagnosis.

Results:
Of the 84 patients using haematoxylin and eosin stained histopathology sections as the gold standard, the diagnostic sensitivity of imprint cytology was 75% and specificity was 100%. Positive predictive value was 100%. Negative predictive value was 98.74%.

Conclusions:
Imprint cytology has high sensitivity and specificity in diagnosing lesions of the thyroid. The problems faced were in diagnosing follicular carcinomas and differentiating low grade lymphoma from lymphocytic thyroiditis.

Imprint cytology is a simple, reliable diagnostic technique. It has high sensitivity and specificity in intra-operative diagnosis of lesions of thyroid. In spite of the advent of newer diagnostic modalities like frozen sections, imprint cytology still holds its unique position in the current perspective.

Keywords:
Thyroid, imprint cytology, intra-operative diagnosis.

Introduction
Thyroidectomy specimens constitute a good number of cases received for histopathological examinations. Even though various investigative modalities are available for preoperative diagnosis like fine needle aspiration cytology, ultrasound scan etc., there are significant number of cases where these modalities fail to give an accurate diagnosis. Under such circumstances intra-operative diagnostic techniques like imprint cytology becomes useful. Imprint cytodiagnosis was recognized as a simple, rapid and reliable diagnostic method after pioneering work done by Dudgeon and Patrick as early as 1927(¹). After the pioneering work, this technique remained in oblivion for years. Later on the immense potential of intra-operative imprint cytodiagnosis was recognized and it came to be utilized in various diagnostic works. It can be used as an alternative to frozen sections since imprint cytology is a much cheaper, quicker and easier procedure. Frozen sections require expensive equipment and technical expertise. Imprint cytology on the other hand, can be done by trained personnel.

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with minimal expenditure \(^{(2)}\). The sensitivity and specificity of imprint cytology are comparable to that of frozen sections \(^{(3)}\).

Imprints of freshly resected surgical specimens give excellent cytomorphology and when used in conjunction with rapid pap staining, a fully accurate diagnosis can be offered within minutes. This helps in intra-operative decision making and eliminates the need for second surgery.

The purpose of this study is to assess the diagnostic accuracy of imprint cytology in thyroidectomies and to compare it with the corresponding paraffin section results.

Materials and Methods

The study was conducted on 84 patients who had undergone thyroidectomies over a period of one year. In each case, a record of complete history, clinical details along with clinical diagnosis was made. Immediately after surgical removal, the thyroidectomy specimen was thoroughly inspected and findings noted. The fresh thyroid specimen was cleaned with wet gauze to remove blood and other debris. Impressions were obtained on a glass slide from relevant areas of the cut surface. This was done by pressing firmly but gently by a “touch and withdraw” movement. This was followed by fixation in 95% isopropyl alcohol followed by conventional Papanicolaou stain.

The smears were carefully examined and a provisional cytodiagnosis of a basically benign or malignant lesion was offered. Sub-typing of lesion was done wherever possible. The specimens were subsequently fixed in formalin and embedded in paraffin for conventional histopathological diagnosis. The intra-operative cytodiagnosis and histopathological diagnosis were correlated.

Results

The distribution pattern of histopathology diagnosis is presented in Table 1 and comparison

<table>
<thead>
<tr>
<th>Case</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nodular colloid goitre</td>
<td>52</td>
</tr>
<tr>
<td>Hashimoto’s thyroiditis</td>
<td>4</td>
</tr>
<tr>
<td>Colloid Nodule</td>
<td>2</td>
</tr>
<tr>
<td>Adenoma</td>
<td>18</td>
</tr>
<tr>
<td>Papillary carcinoma</td>
<td>5</td>
</tr>
<tr>
<td>Follicular carcinoma</td>
<td>2</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>1</td>
</tr>
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</table>

Table 1. Case Distribution

<table>
<thead>
<tr>
<th>IMPRINT</th>
<th>MNG</th>
<th>HASHI</th>
<th>COLLOID NODULE</th>
<th>ADENOMA</th>
<th>PAP.CA</th>
<th>FOLL.CA</th>
<th>LYM</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>MNG</td>
<td>52</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>52</td>
</tr>
<tr>
<td>HASHI</td>
<td></td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>CN</td>
<td></td>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>ADENOMA</td>
<td></td>
<td></td>
<td></td>
<td>18</td>
<td></td>
<td></td>
<td></td>
<td>19</td>
</tr>
<tr>
<td>PAPILLARY CARCINOMA</td>
<td>5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>FOLLICULAR CARCINOMA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>LYMPHOMA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>TOTAL</td>
<td>52</td>
<td>4</td>
<td>2</td>
<td>18</td>
<td>5</td>
<td>2</td>
<td>1</td>
<td>84</td>
</tr>
</tbody>
</table>

Table 2. Imprint vs. Histopathology cross tabulation

*MNG-multi nodular goitre, HASHI-Hashimotos thyroiditis, CN-Colloid nodule
*Kappa value-0.958 measure of agreement
between imprint cytology and histopathology diagnosis is shown in Table 2.

In all 84 cases, cytology diagnosis was attempted and compared with paraffin sections. Imprint cytology was accurate in diagnosing all cases of nodular colloid goitre and Hashimoto’s thyroiditis. Imprints of benign lesions like colloid nodules were found to be hypo cellular with scanty clusters of benign follicular cells with abundant colloid in the background (Figure 1). In malignancies, papillary carcinoma thyroid was diagnosed with an accuracy of 100%. Imprints have the advantage that the pathologist can actually see the lesion and take appropriate samples. Imprint smears from cases of papillary carcinoma showed cellular smears with characteristic nuclear features like nuclear grooves and intra-nuclear inclusions. (Figure 2)

Cases of Hashimoto’s thyroiditis showed moderately cellular smears with large oncocytic cells with abundant cytoplasm and vesicular nucleus with lymphocytes in the background. (Figure 3)

The problem areas in using imprint cytology diagnosis were in diagnosing follicular carcinomas and low grade lymphoma. (Table 3) In one case of follicular carcinoma, nuclear features like large nucleus, prominent nucleoli, and coarse chromatin were evident; but in the other case these findings were not apparent and a wrong diagnosis of follicular adenoma was made. Thus, nuclear features can be subtle and histopathology is still the gold standard in the diagnosis of follicular carcinomas when a demonstration of capsular and vascular invasion is needed. Cases of follicular adenoma as well as follicular carcinoma can show atypia in cytology. One case of thyroiditis was misdiagnosed as low grade lymphoma. This may be because mixed population of cells in low grade lymphomas can simulate a florid reactive process.
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Discussion

Imprint cytology as a technique for rapid microscopical diagnosis was introduced as early as 1927\(^4\)\(^-\)\(^7\). Imprint cytology has been applied in the study of various tissues like lymph node, breast, thyroid, etc. \(^8\). In thyroid, a correct operative diagnosis is of utmost importance especially in malignancies. In case of pre-operative confirmation of malignancy by fine needle aspiration cytology the surgeon proceeds with total thyroidectomy were as if a conclusive diagnosis is not reached the patient is taken up for hemi or subtotal thyroidectomies and later if malignancy is confirmed, a second surgery is done. This is troublesome due to loss of time, cost of resurgery and increased morbidity. In our opinion, imprint cytology should be the procedure of choice in intra-operative evaluation for single time staging and cost effective management, especially in centres where frozen section facilities are not available. Even when frozen section facilities are available, in cases of thyroid malignancies like papillary carcinoma where nuclear features are important for diagnosis, imprint cytology is superior to frozen sections \(^9,\)\(^10,\)\(^11\).

FNAs are highly sensitive in case of lesions of thyroid. But there are occasions when FNAs can give false negative results \(^12,\)\(^13\). Examples are papillary carcinoma in multi nodular goitre or papillary carcinoma associated with Hashimoto’s thyroiditis. In imprint cytology multiple smears can the prepared from suspicious areas with the added advantage that the pathologist can see the lesion and make a morphological diagnosis.

In our study using imprint cytology, all 5 cases of papillary carcinoma could be diagnosed. The consistent features that helped in our diagnosis were nuclear features particularly the nuclear grooving \(^14,\)\(^15,\)\(^16\). In a study made by Rupp et. al. on nuclear grooving in cytological diagnosis of papillary carcinoma of thyroid, the importance of imprint cytology has been stressed upon.

The cases which were misdiagnosed in our study were that of low grade lymphoma and follicular carcinoma. Most thyroid lymphomas are of B-cell lineage and of MALT type, including low grade and high grade forms. The majority are associated with Hashimoto’s thyroiditis and can be difficult to separate clinically and cytologically from this disease. Low-grade lymphoma is especially difficult to diagnose because mixed cell population closely resembles a florid reactive process. In our study we had this problem of differentiating thyroiditis and MALToma. This diagnostic difficulty has been seen in other studies in the literature \(^17,\)\(^18,\)\(^19\). Follicular neoplasms are difficult diagnostic problems with imprint cytology \(^20\). We have one false negative case in this study. The other case was suggestive of carcinoma with nuclear enlargement, prominent nucleoli and a coarser chromatin. But in the false negative case the nuclear features were not that apparent. The application of dipeptidyl amino peptidase IV activity in cytological samples has been studied. The usefulness in differentiating follicular thyroid carcinoma from adenoma has been suggested in a study \(^21\). The dipeptidyl amino peptidase IV activity was found to be increased in follicular carcinomas than adenomas. Hence the gold standard in follicular neoplasm is histopathology, wherein we can demonstrate capsular and vascular invasion.

Conclusions

Imprint cytology has high sensitivity and specificity in diagnosing lesions of the thyroid.

- In case of neoplasm 100% sensitivity was

<table>
<thead>
<tr>
<th>Imprint cytology results</th>
<th>Diagnosis with histopathology</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Positive</td>
</tr>
<tr>
<td>Positive for malignancy</td>
<td>6 (true positive)</td>
</tr>
<tr>
<td>Negative for malignancy</td>
<td>2 (false negative)</td>
</tr>
<tr>
<td>Total</td>
<td>8</td>
</tr>
</tbody>
</table>

Table 3. Diagnostic sensitivity in cytology is 75%, specificity is 100%, positive predictive value is 100% and negative predictive value is 98.74%.
noted in diagnosing papillary carcinoma.

- Follicular neoplasms are cases where imprint cytology is problematic. A diagnosis of malignancy would require histopathology wherein capsular/vascular invasion can be demonstrated.

- Differentiating low grade lymphoma from lymphocytic thyroiditis can be difficult with imprint cytology.

In the future, the application of immunohistochemistry, special stains, and cytometric nuclear DNA analysis may improve the accuracy, sensitivity and speed of imprint cytological diagnosis \(^{(22, 23, 24)}\). The various publications on intra-operative imprint cytology of thyroid swellings conclude that being a rapid, simple, reliable and inexpensive procedure, intra-operative imprint cytology is a valuable tool in intra-operative tissue diagnosis.

**Acknowledgement**

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**References**


