International Journal of Medical Science and Applied Biosciences
ISSN: 2545-5893(Print) 2545-5877 (Online)
Volume 4, Number 4, December, 2019
http://www.casirmediapublishing.com

A Review of Important Limitations of Fine Needle Aspiration Cytology in the Investigation of Thyroid Masses

Obahiagbon Ikponmwosa* & Imasogie Dele Eradebamwen.**
*Department of Anatomic Pathology, University of Benin Teaching Hospital, Benin City, Nigeria
**Department of Anatomic Pathology, University of Benin Teaching Hospital, Benin City, Nigeria
Email: ikflex@yahoo.com; Corresponding Author: Obahiagbon Ikponmwosa

ABSTRACT
Thyroid masses are frequently encountered in clinical practice and are readily accessible for fine needle aspiration cytology (FNAC), either directly or via image guidance, for rapid diagnosis in the hope of avoiding unnecessary surgery. FNAC of the thyroid is attractive because it is a relatively simple technique, non-invasive, minimally painful, relatively cheap, and offers the possibility of arriving at definitive morphological diagnoses of thyroid masses without first surgically obtaining a specimen. It is important to develop, ensure and maintain expertise in this proven investigative modality while recognizing its important limitations, some of which this article highlights.
Keywords: Thyroid, Fine needle aspiration cytology (FNAC), Limitations.

INTRODUCTION
Thyroid enlargement is a relatively common clinical presentation, and the superficial and accessible location of the thyroid gland makes it one of the most readily investigable by fine needle aspiration cytology (FNAC). Thyroid nodules have a reported prevalence of 4 – 7% in the general population, with the incidence rising with increasing age, prior radiation exposure and ingestion of goitrogens. Most causes of thyroid enlargement are non-neoplastic conditions or benign neoplasms, and modalities like FNAC are required for rapid diagnosis of patients and selection of those requiring surgical intervention, with the potential of avoiding unnecessary surgery.[1] However, despite its current global status as a powerful screening tool that saves many needless thyroidectomies,[2] thyroid FNAC has some important limitations which are briefly highlighted in this article.

IMPORTANT LIMITATIONS OF THYROID FNAC
There are increasing concerns that like any other test, thyroid FNAC has its limitations, especially when compared to histolopathological examination following surgical biopsy, which it is often intended to replace. The reported pitfalls are those related to specimen adequacy, sampling techniques, the skill of the aspirator performing the aspirations, the experience of the cytopathologist interpreting the aspirate and overlapping cytological features between benign and malignant follicular neoplasms.[3] Inadequate specimens, indeterminate FNA, and false positive and false negative diagnosis, are the major limitations of thyroid FNAC.[4] FNAC has in recent decades emerged as an investigative modality widely reported to be sensitive in diagnosing papillary, medullary, poorly differentiated follicular and anaplastic carcinomas. However, its value is limited by its inability to distinguish among follicular lesions, which exist on both the benign and malignant sides of the divide. This is due to overlapping cytological criteria among benign lesions like hyperplastic adenomatoid nodules in goitres and follicular adenomas and malignant lesions like well-differentiated follicular carcinomas and follicular variants of papillary carcinomas.[5] The distinction between follicular adenoma and follicular

International Journal of Medical Science and Applied Biosciences
ISSN: 2545-5893(Print) 2545-5877 (Online)
Volume 4, Number 4, December, 2019
http://www.casirmediapublishing.com

carcinoma, even on histology, is based strictly on the demonstration of capsular and/or vascular invasion by the tumour cells,[6] meaning that architectural detail that cannot be provided by thyroid FNAC is required here. Clinicians, pathologists, and even patients must bear this in mind, so that expectations are kept modest.

Furthermore, even where lesions reliably diagnosable by FNAC are concerned, there remains the lingering challenge of the possibility of false positives and false negatives. According to the Papanicolaou Society of Cytopathology Task Force on Standards of Practice, a false negative rate not exceeding 2% and a false positive rate of no more than 3% are the benchmarks for FNAC of the thyroid.[7] Obviously, most practitioners have not yet seen their practice reach the level of sensitivity and specificity proposed by the Task Force.[2] Therefore, there is much need for improvement in the standards of the practice of thyroid FNAC before the promise of its potential can be fully achieved. False negatives could result when the needle misses a nodule. In a study by Mokhtar et al two cases were interpreted cytologically as goiter and on the histology, in addition to the goiter, one case contained papillary carcinoma and the other contained minimally invasive follicular carcinoma, which were missed by inadequate FNAC sampling technique. It is presumed in these cases that the needle was not introduced within the thyroid nodule and what was received in FNA was the thyroid tissue adjacent to the nodule.[8] This is a very likely pitfall when a nodule within an enlarged thyroid cannot be identified by palpation on neck examination prior to needle insertion. Sclabas and colleagues have mentioned that the routine use of ultrasound-guided FNAC is likely to minimize false negative results, and if an FNAC is obtained under ultrasound guidance by an experienced radiologist and interpreted by an experienced thyroid cytopathologist, one should expect false negative rates of < 4%.[9] However, while that may be a useful and practicable suggestion, it should be remembered that one of the main reasons why thyroid FNAC has received such huge acclaim is because it is inexpensive; and so bringing in the additional expense of ultrasonography and the need for expert/experienced radiologists/sonologists (reliable thyroid FNAC already requires not just any pathologist but an experienced cytopathologist) will result in a loss of that much desired advantage of cost-effectiveness, so important in resource-poor settings. Furthermore, some studies have even suggested that ultrasound guided thyroid FNAC is profitable only to the extent that it reduces the frequency of inadequate or insufficient aspirate specimens whilst increasing the frequency of satisfactory smears, but however does not result in increased cytodiagnostic accuracy in comparison to freehand FNAC.[10] Inadequate FNA specimen can occur as a result of sampling error, faulty technique and highly vascular or focal lesions. Thyroid nodules that are sclerotic or calcified and those with large areas of cystic degeneration or necrosis are extremely difficult to aspirate.[4]

False positives are encountered in the situations of overlap of diagnostic criteria between benign and malignant lesions, already highlighted above. Hurthle cell lesions present yet another challenge in diagnostic thyroid cytopathology, because a hyperplastic Hurthle cell nodule in Hashimoto thyroiditis or in a multinodular colloid goitre, and a Hurthle cell neoplasm (benign or malignant), display similar cytological findings.[11] The diagnosis of

International Journal of Medical Science and Applied Biosciences
ISSN: 2545-5893(Print) 2545-5877 (Online)
Volume 4, Number 4, December, 2019
http://www.casirmediapublishing.com

Hashimoto thyroiditis on FNAC is based on the presence of adequate proportions of lymphoid and Hurthle cells, but when there's a marked deviation in the proportions of these cell types, diagnostic confusion ensues.[2] It is well known that Hurthle cells on a background of lymphocytic thyroiditis, have been found to exhibit nuclear elongation, intranuclear grooves, and even intranuclear inclusions, all of which can lead to a wrongful (false positive) diagnosis of papillary thyroid carcinoma.[12] In hyperplastic lesions, increased cellularity and overlapping criteria can also lead to false positive diagnosis of thyroid carcinoma.[2] Both false positive and false negative diagnoses are significant and potentially litigious diagnostic errors. The indeterminate thyroid FNAC is about the most confusing diagnosis in thyroid cytology, and includes the use of terms like 'atypical', 'suspicious for malignancy' and 'follicular lesion.'[8] The reported percentages of such diagnoses in published studies ranges from 5 – 42%.[13,14,15] A lot of these cases still end up requiring surgical resection due to the limitedness of thyroid FNAC, and this amounts to time wasting.

CONCLUSION

Although FNAC of the thyroid proves to be a very useful investigative modality, its many limitations must however be borne in mind by the clinicians and patients, as well as the cytopathologists, who must familiarise themselves with the numerous diagnostic pitfalls and work to increase expertise. A vital part of the expertise required in diagnostic thyroid cytopathology is to be conversant with the limitations thereof. Moreover, there is still much need to raise the standards of the practice of thyroid FNAC before the promise of its full potential can be fully achieved.

ACKNOWLEDGEMENT

We sincerely acknowledge the various authors and works cited in this article.

REFERENCES

1. Mojghan A, Ramzy I, Rubenfeld S, Wheeler T M. Accuracy of Fine-Needle Aspiration of Thyroid. A Review of 6226 Cases and Correlation with Surgical or Clinical Outcome. Arch Pathol Lab Med. 2001; 125:484–488.
2. Haberal AN, Toru S, Özen Ö, Arat Z, Bilezikçi B. Diagnostic pitfalls in the evaluation of fine needle aspiration cytology of the thyroid: correlation with histopathology in 260 cases. Cytopathology. 2009 Apr 1; 20(2):103-8.
3. Caraway NP, Sneige N, Samaan NA. Diagnostic pitfalls in thyroid fine-needle aspiration: A review of 394 cases. Diagn Cytopathol 1993; 9:345-50.
4. Pandey P, Dixit A, Mahajan N C. Fine-needle aspiration of the thyroid: A cytohistologic correlation with critical evaluation of discordant cases. Thyroid Res Pract 2012; 9:32-9.
5. Sidawy MK, Del Vecchio DM, Knoll SM. Fine-needle aspiration of thyroid nodules. Cancer (Cancer Cytopathol) 1997;81:253–9
6. Bagga P K, Mahajan N C. Fine needle aspiration cytology of thyroid swellings: How useful and accurate is it? Indian J Cance 2010; 47:437-42.
7. Suen K. Guidelines of the Papanicolaou Society of Cytopathology for the

International Journal of Medical Science and Applied Biosciences
ISSN: 2545-5893(Print) 2545-5877 (Online)
Volume 4, Number 4, December, 2019
http://www.casirmediapublishing.com

Examination of Fine-Needle Aspiration Specimens from Thyroid Nodules: The Papanicolaou Society of Cytopathology Task Force on Standards of Practice. Diagn Cytopathol 1996; 15(1): 84-89.

8. Mokhtar GA, Bokhary RY. Cytohistologic Correlation Study of Thyroid Lesions with Emphasis on the Diagnostic Pitfalls. Journal of King Abdulaziz University-Medical Sciences. 2011; 18(4):53-67.
9. Ylagan LR, Farkas T, Dehner LP. Fine-needle aspiration of the thyroid: a cytohistologic correlation and study of discrepant cases. Thyroid 2004; 14:35–41.
10. Mehrotra P, Viswanathan H, Johnson S J, Wadehra V, Richardson D L, Lennard T W J. Ultrasound guidance improves the adequacy of our preoperative thyroid cytology but not its accuracy. Cytopathology 2006; 17: 137–144.
11. Nguyen GK, Ginsberg J, Crockford PM, Villanueva RR. Hashimoto's thyroiditis: cytodiagnostic accuracy and pitfalls. Diagn Cytopathol 1997; 16:531–6.
12. Giorgadze T, Rossi ED, Fadda G. Does the fine-needle aspiration diagnosis of "Hurthle-cell neoplasm/follicular neoplasm with oncocytic features" denote increased risk of malignancy? Diagn Cytopathol 2004; 31:307–12.
13. Baloch ZW, Sack MJ, Yu GH, Li Volsi VA, Gupta PK. Fine-needle aspiration of Thyroid: an institutional experience. Thyroid 1998; 8(7): 565-569.
14. Gharib H, Goellner JR, Johnson DA. Fine needle aspiration cytology of the thyroid. A 12-year experience with 11,000 biopsies. Clin Lab Med 1993; 13(3): 699-709.
15. Goldstein RE, Netterville JL, Burkey B. Implication of follicular neoplasm, atypia, and lesions suspicious for malignancy diagnosed by fine-needle aspiration of thyroid nodules. Ann Surg 2002; 235(5): 656-664.