Follicular Neoplasm: Evaluation of the Risk of Malignancy Using the Modified Bethesda Classification

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ABSTRACT

Background: The Bethesda 2007 Thyroid Cytology Classification defines Follicular Neoplasm as a category of cases with cellular specimens showing abundant follicular cells arranged in a microfollicular pattern with little or no colloid. The current recommendation for the management of these cases is lobectomy. There has been great difficulty and variability in triaging and reporting follicular neoplasm. In our institution, this category is further subclassified into two: 1) Microfollicular patterned neoplasm (FN1) and 2) Follicular lesion with some features suggestive of but not diagnostic of follicular variant of papillary thyroid carcinoma (FN2). We reviewed the cases of follicular neoplasm seen over a period of three years to document the follow-up trend using this two-tier classification.

Design: A search of the cytology records was performed for the period between January 2008 and December 2010. All thyroid FNA cases were reviewed and the ones with the diagnosis of follicular neoplasm (including Hurthle cell neoplasm) were identified. Correlating follow-up surgical pathology reports were reviewed. The percentage of cases showing a malignancy was calculated.

Results: Two hundred and forty six cases of follicular neoplasm with surgical follow-up were identified (217 FN1 and 29 FN2). Malignancy was identified in 32% of all FN cases. This was disproportionately higher in the FN2 (72%) compared to the FN1 (27%) cases. In the FN1 category, malignancy rate for Hurthle cell neoplasm and FN, NOS were 28% and 26%, respectively. The malignant cases are largely follicular variant of papillary carcinoma. When the benign cases are further classified into neoplastic vs. non-neoplastic, 57% are neoplastic and are predominantly follicular adenoma and Hurthle cell adenoma, while 43% are non-neoplastic and are predominantly nodular goiter.

Conclusion: The FN2 category requires a more aggressive follow-up than the FN1 category and justifies an immediate referral for lobectomy. The FN1 category may require further triage using other ancillary methods. The rate of malignancy in the present study is 32%, a higher end of previously reported values in the literature.

BACKGROUND

Diagnosis of follicular lesions of the thyroid in cytologic preparations has long been considered a diagnostic gray area and there has been so much variability to how these cases are triaged and reported. Follicular lesions of the thyroid, or follicular proliferation, include entities such as nodular hyperplasia, follicular adenoma, follicular carcinoma and follicular variant of papillary carcinoma (FVPTC), and these different entities have overlapping cytomorphologic features. As a result of this, FNA cannot precisely distinguish follicular carcinoma from follicular hyperplasia or follicular adenoma. Even after applying strict criteria, majority of the cases diagnosed as follicular neoplasm are benign lesions which do not require surgery. In this respect the significance of making a diagnosis of follicular neoplasm on fine needle aspiration (FNA) biopsy remains a controversial issue.

The incidence of follicular carcinoma in the general population is significantly decreasing with a reported incidence of 2%. Since the prevalence of follicular carcinoma is so low, the predictive value of thyroid cytology in detecting follicular carcinoma is expected to be low. Not surprisingly, the chance of a cytologic diagnosis of follicular lesion as a predictor of follicular carcinoma is minuscule. A significant number of cases that are malignant on follow-up of follicular patterned lesions are FVPTC.

DESIGN

We performed a retrospective analysis of follicular neoplasm data by reviewing the cytology diagnosis cases (by using the Modified 2007 Bethesda reporting guidelines) and the surgical outcomes from 2008 to 2010 at Yale Hospital. All FNA cases had a cytologic diagnosis of follicular neoplasm with a further subclassification into one of three subgroups: Microfollicular patterned neoplasm, Hurthle cell neoplasm, and follicular lesion with some features suggestive but not diagnostic for follicular variant of papillary carcinoma. Correlating surgical pathology follow-up reports were reviewed. The percentage of cases showing malignancy was calculated for each category.

RESULTS

We identified a total of 246 FNA samples from 235 patients who underwent thyroid resection. Of the 246 FNAs, 153 specimens were processed in-house at the Yale Hospital; 93 FNA specimens were prepared at outside institutions and received as consult cases.

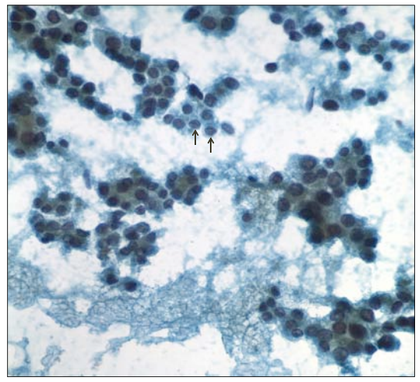

Figure 1. Follicular lesion with some features (i.e. slight membrane irregularity, nuclear grooves) suggestive of but not diagnostic for papillary carcinoma follicular variant (FN2)

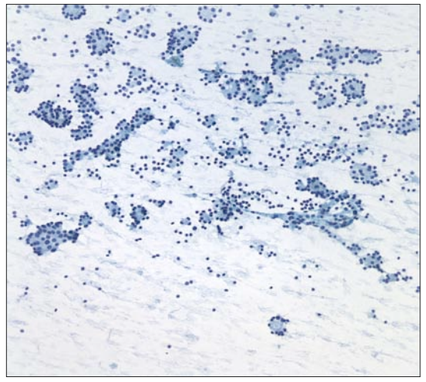

Figure 2. Microfollicular patterned neoplasm (FN1a)

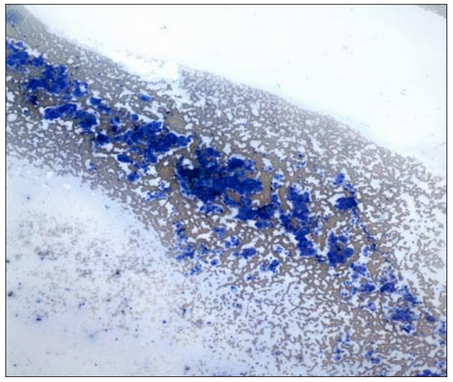

Figure 3. Hurthle cell neoplasm (FN1b)

TABLE 1. Correlating surgical outcomes of Microfollicular patterned neoplasm (FN1a), Hurthle cell neoplasm (FN1b), and Follicular lesion with some features suggestive of but not diagnostic for papillary carcinoma follicular variant (FN2).

	Cytologic Diagnosis			
Surgical Outcome:	**FN1a**	**FN1b**	**FN2**	All cases
Malignant	31 (26%)	27 (28%)	21 (72%)	79 (32%)
Benign neoplastic	52 (44%)	42 (43%)	1 (4%)	95 (39%)
Benign non-neoplastic	36 (30%)	29 (30%)	7 (24%)	72 (29%)
All cases	**119 (100%)**	**98 (100%)**	**29 (100%)**	**246 (100%)**

TABLE 2. Final Surgical Diagnosis for the 79 malignant cases

	Cytologic Diagnosis			
Surgical Diagnosis:	**FN1a**	**FN1b**	**FN2**	All cases
Papillary thyroid carcinoma	17 (22%)	20 (25%)	19 (24%)	56 (71%)
Follicular carcinoma	12 (15%)	1 (1%)	2 (3%)	15 (19%)
Hurthle Cell carcinoma	1 (1%)	6 (8%)	—	7 (9%)
Poorly diff. carcinoma	1 (1%)	—	—	1 (1%)
Grand Total	**31 (39%)**	**27 (34%)**	**21 (27%)**	**79 (100%)**

Cytologic diagnosis of follicular neoplasm was classified as follows: Microfollicular patterned neoplasm, FN1a – 119/246 (48%), Hurthle cell neoplasm, FN1b – 98/246 (40%), follicular lesion with some features suggestive but not diagnostic for papillary carcinoma follicular variant, FN2 – 29/246 (12%). All patients had undergone either lobectomy or total thyroidectomy. The final surgical diagnostic categories were as follows: Malignant – 79/246 (32%), Benign neoplastic – 95/246 (39%), and Benign non-neoplastic – 72/246 (29%). Malignant cases were predominantly FVPTC across all the three initial cytologic diagnoses: FN1a (17 of 31), FN1b (20 of 27), FN2 (19 of 21). Non neoplastic cases were mostly hyperplastic thyroid nodules (goiter).

CONCLUSIONS

- The main diagnostic dilemma in follicular patterned lesions is to differentiate follicular variant of papillary carcinoma (FVPTC) from other follicular lesions. A significant proportion of cases with surgical intervention of total thyroidectomy had benign (neoplastic and non-neoplastic) histology, thus making surgery unnecessary in these patients.
- In our study, follicular lesion with some features of papillary thyroid carcinoma (FN2) has significantly higher rate of malignancy, and justifies immediate referral for lobectomy. On the other hand, microfollicular patterned neoplasm (FN1a) and Hurthle cell neoplasm (FN1b) have much lower rate of malignancy and may require non-surgical management.
- Overall malignancy rate of follicular neoplasm in this study was 32% which represents the higher end of the reported literature.
- Goal of the diagnosis of follicular pattern lesion should be to identify FVPTC and manage those cases more aggressively.

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