Routine second-opinion cytopathology review of thyroid fine needle aspiration biopsies reduces diagnostic thyroidectomy

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Background. Follicular thyroid carcinoma cannot be distinguished reliably from benign follicular neoplasia by fine needle aspiration (FNA) biopsy. Given an estimated 20% risk of malignancy, many patients with indeterminate FNA biopsies require thyroidectomy for diagnosis. Some centers have shown significant discordance when a second pathologist evaluates the same FNA biopsy. We sought to determine whether routine second-opinion cytopathology reduces the need for diagnostic thyroidectomy, especially in patients with indeterminate FNA biopsies.

Methods. In all, 331 thyroid FNA biopsy specimens obtained from outside centers from 2004 to 2009 were reviewed at our institution. The FNA biopsy results were categorized into nondiagnostic (Bethesda I), benign (Bethesda II), indeterminate (follicular/Hurthle cell neoplasm, follicular/Hurthle cell lesion; Bethesda III & IV), and malignant (papillary or suspicious for papillary or other malignancy; Bethesda V and VI). Second-opinion cytology was compared with the initial opinion in 331 cases and with final operative pathology in the 250 patients who progressed to thyroidectomy.

Results. The average patient age was 51 with a predominant number of female (79%) participants. The overall cytology concordance for all 331 FNA biopsies was 66% (218/331). Concordance was highest at 86% (27/32) with malignant FNA biopsies. Concordance in the 129 patients with indeterminate FNA biopsies was only 37% (48/129). Indeterminate FNA biopsies were reread as nondiagnostic in 21% (27/129) of patients and as benign in 42% (54/129) of patients. Twenty-two patients with an indeterminate FNA biopsy reread as benign progressed to operative therapy for reasons other than cytology (eg, symptomatic nodule and radiation exposure/high risk) and were found to be benign in 95% (21/22) of patients on operative pathology for a 95% negative predictive value. An additional 11 patients with an indeterminate FNA reread as benign had follow-up FNA biopsies, each of which was benign. Indeterminate FNA biopsies on initial cytology had a malignancy rate of 13% (17/129) on operative pathology compared with 29% (14/48) for indeterminate FNA biopsies from second opinion. A second opinion improved FNA biopsy accuracy from 60% to 74%. Overall, second-opinion cytology of indeterminate FNA biopsies avoided diagnostic operation in 25% (32/129).

Conclusion. Routine second opinion review of indeterminate thyroid FNA biopsies can potentially obviate the need for diagnostic thyroidectomy in 25% of patients without increases in false negatives. (Surgery 2010;148:1294-301.)

From the Robert Wood Johnson Medical School, New Brunswick, NJ

Thyroid nodules are present in 19–67% of the population. Approximately 5–15% of thyroid nodules contain thyroid malignancy. Follicular thyroid carcinoma accounts for 10–25% of all thyroid malignancies. Fine needle aspiration biopsy (FNA) is the most accurate and cost-effective method for evaluating thyroid nodules. FNA cytology is useful for identifying features of papillary thyroid carcinoma, which is the most common form of thyroid cancer. It is also useful for the less common medullary and anaplastic thyroid carcinoma as well as other rare thyroid tumors. Unfortunately, follicular thyroid carcinoma (FTC) cannot be distinguished reliably from benign follicular neoplasia on cytology. This is because the diagnosis of follicular carcinoma requires evidence
of capsular or vascular invasions, necessitating tissue architecture and not directly observed with cytology.\textsuperscript{6}

Despite the limitations of FNA cytology, secondary cytology features on thyroid FNA can raise the suspicion for FTC. These features include a hypercellular, monomorphic specimen with little to no colloid.\textsuperscript{6} Such features suggest the diagnosis of follicular neoplasm, which is a cytologic diagnosis that carries a 20–30\% risk of malignancy.\textsuperscript{7} In 2007, the National Cancer Institute (National Institutes of Health) developed the Bethesda Thyroid Cytology 6-tiered classification for standardizing the reporting of thyroid FNA cytology (Fig).\textsuperscript{5} The risk of malignancy in each diagnostic category helps to guide the management. For example, patients with inadequate FNAs (Bethesda I) require repeat FNA, whereas patients with benign FNAs (Bethesda II) may be observed. The management of patients with papillary thyroid carcinoma (Bethesda VI) or suspicion for papillary thyroid carcinoma (Bethesda V) is typically total thyroidectomy for a high risk of malignancy (50–100\%), whereas the management of patients with follicular (or Hurthle cell) lesion (Bethesda III) or follicular (or Hurthle cell) neoplasm (Bethesda IV) is often thyroid lobectomy to obtain a diagnosis in the setting of a low risk of malignancy (5–50\%).\textsuperscript{5} Unfortunately, this practice results in most patients with Bethesda III and IV cytology undergoing unnecessary operation for benign disease.

Some centers have shown significant discordance when a second pathologist evaluates the same thyroid FNA. Interobserver variability is a well-established limitation of cytology.\textsuperscript{3} We sought to determine whether the second opinion for routine cytopathology reduces the need for diagnostic thyroidectomy, especially in patients with indeterminate thyroid FNAs.

**MATERIALS AND METHODS**

Thyroid FNA specimens from 331 consecutive patients that were performed at outside centers between 2004 and 2009 were obtained and reviewed at our institution. It has been our practice to obtain routinely all outside thyroid FNAs (not only challenging FNAs) for a second opinion at our institution. With rare exception, all the slides created from each thyroid FNA were obtained. One of three dedicated cytopathologists reviewed the cytology slides. The FNA results were categorized into 4 categories as listed in Table I: 1—nondiagnostic (ie, inadequate cellularity or preservation artifact; Bethesda I); 2—benign (eg, nodular goiter, lymphocytic thyroiditis, hyperplastic focus/adenomatous nodule; Bethesda II); indeterminate (ie, follicular or Hurthle cell lesion, follicular or Hurthle cell neoplasm, “suspicious for malignancy,” or “malignancy cannot be excluded”; Bethesda III or IV); and malignant (papillary or suspicious for papillary, medullary, and anaplastic thyroid carcinoma; Bethesda V or VI). Although the 6-tiered Bethesda system was employed in our study, we chose to combine Bethesda classes III and IV together in the same treatment category because these patients are typically treated the same with thyroidectomy for low risk (5–30\%) of malignancy. Likewise, Bethesda class V and VI were grouped together in the same treatment category because these patients are typically treated the same with thyroidectomy for high risk of malignancy (50–100\%).

Our cytologists used standard cytology criteria as defined by Kini and endorsed by the American Thyroid Association guidelines in their second-opinion interpretation of thyroid FNAs.\textsuperscript{1,6} Inadequate specimens (Bethesda I) were defined as the presence of less than 6–8 groups of well-preserved follicular cells, with less than 10–15 cells per group on at least 2 slides. Benign specimens (Bethesda II) were defined as those showing abundant colloid with follicular cells, even in the setting of hypercellularity, as long as the follicular cells were of mixed population showing some follicular and some hurthle cells without suspicious nuclear features. Follicular neoplasm (Bethesda IV) was defined as an aspirate that is hypercellular, monomorphic, with little to no colloid, typically arranged in a microfollicular pattern.\textsuperscript{6} A follicular lesion (Bethesda III) was defined as a specimen that demonstrated a suggestion of a microfollicular pattern or contained atypical nuclear features. Our cytologists avoided conferring the diagnosis of follicular lesion (Bethesda II); therefore, specimens that were felt to be a follicular lesion but contained a mixed cellularity of follicular and Hurthle cells (without true suspicious nuclear features) with abundant colloid would have been reinterpreted in the benign category (often as a hypercellular focus within a nodular goiter or adenomatous nodule). Finally, malignant FNAs (Bethesda VI) were those that demonstrated nuclear grooves and pseudonuclear inclusions to suggest papillary thyroid carcinoma. Specimens with nuclear grooves but questionable or no pseudonuclear inclusions that were deemed suspicious for papillary (Bethesda V) were included in the malignant category for treatment purposes. Features suggestive of medullary, anaplastic, and other rare thyroid tumors were included in the malignant category as well.
A cytology report reading, “nuclear grooves and pseudonuclear inclusions, suspicious for malignancy” was included as a Bethesda V (suspicious for papillary malignancy). In contrast, a cytology report reading, “hypercellular specimen with paucity of colloid, suspicious for malignancy” would have been included as Bethesda IV (follicular neoplasm). A cytology report reading “suspicous for malignancy but with poor or inadequate cellularity” would have been included in the Bethesda I (inadequate) category. Our cytologists were not blinded to the initial FNA report. Of note, our cytologists review nearly 1,000 thyroid FNAs annually.

Second-opinion cytology reports were compared with the initial reports in 331 cases to determine interobserver variability. In addition, final pathology of the 250 patients who underwent thyroidectomy was compared with first- and second-opinion FNA results. Because FNAs of subcentimeter thyroid nodules were not performed routinely, papillary

<table>
<thead>
<tr>
<th>Bethesda Class</th>
<th>1st Opinion</th>
<th>2nd Opinion</th>
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<tr>
<td>Malig.</td>
<td>86</td>
<td>74</td>
</tr>
<tr>
<td>Benig.</td>
<td>129</td>
<td>5</td>
</tr>
<tr>
<td>Inde.</td>
<td>91</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>331</td>
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Fig. Diagram detailing the treatment of 331 patients with first- and second-opinion thyroid FNA cytology opinions and with final operative pathology in 250 patients progressing to operation. ATC, anaplastic thyroid carcinoma; bgn, benign (eg, nodular goiter, thyroiditis, follicular adenoma, hyperplastic nodule); FVP, follicular variant papillary thyroid carcinoma; mPTC, papillary microcarcinoma; MTC, medullary thyroid carcinoma; PTC, papillary thyroid carcinoma; surg, patient progressed to operation. (Color version of figure is available online.)

surg = patient progressed to surgery
PTC = papillary thyroid carcinoma
FVP = follicular variant papillary thyroid carcinoma
FTC = follicular (or hurthle cell) thyroid carcinoma
MTC = medullary thyroid carcinoma
ATC = anaplastic thyroid carcinoma
mPTC = papillary microcarcinoma

bgn = benign (e.g. nodular goiter, thyroiditis, follicular adenoma, hyperplastic nodule)
microcarcinomas on final pathology were considered an incidental finding and, therefore, were included in the benign category on final pathology. When the final pathology report was in question (n = 2), a second-opinion operative histology opinion was obtained from Dr. Juan Rosai, chairperson of operative pathology at the National Cancer Institute of Milan. A chi-square test and the Fisher exact test were used for significance testing and Cohan’s Kappa Coefficient was used to quantify interobserver variability.

RESULTS

A total of 331 consecutive outside FNAs underwent second-opinion cytology review at our institution. The mean patient age was 51 (range, 15–85 years) with a female predominance (79%). A diagram detailing the first-opinion cytology, second-opinion cytology in the 331 patients, and final pathology in the 250 patients who progressed to operation is listed in the Figure. The overall first- and second-opinion cytology concordance for all 331 FNAs was 66% (218/331; Cohan’s Kappa = 0.55; moderate agreement).

Cytology concordance was highest at 86% (74/86) with malignant FNAs. Concordance in the 129 patients with indeterminate FNAs (ie, follicular lesion and follicular neoplasm) by initial cytology review was only 37% (48/129) on second opinion (P < .0001).

Significant interobserver variability was noted with indeterminate FNAs. Indeterminate FNAs were reread as nondiagnostic in 21% (27/129) of patients and benign in 42% (54/129) of patients. These 81 patients (63%; 81/129) did not immediately progress to operation because of their second-opinion cytology review; 14 of 27 patients with indeterminate FNAs reread as nondiagnostic underwent operation with 10 revealing benign disease, 2 with micropapillary thyroid carcinoma, 1 with FTC, and 1 with follicular-variant papillary thyroid carcinoma (FVPTC). Another 8 of these 27 patients with indeterminate FNAs reread as nondiagnostic underwent repeat FNAs, and in each case, the FNA was found to be benign. Another 5 of 27 patients had clinical follow-up only.

In all, 22 of 54 patients with an indeterminate FNA reread as benign progressed to operation (for reasons other than suspicious cytology, eg, symptomatic nodule, growing nodule, nodule >4 cm, and other clinical suspicion for cancer such as a history of radiation exposure). These 22 were found to be benign in 95% (21/22) on final pathology for a 95% negative predictive value. The 1 patient with a false negative on second opinion had a FVPTC. Another 11 of 54 patients with indeterminate FNAs reread as benign had repeat FNAs. Each of these 11 FNAs showed benign disease. This amounts to 33 patients with indeterminate FNA reread as benign on second opinion with either operative or cytologic follow-up showing that 32 of 33 were benign, for a 97% (32/33) negative predictive value. The remaining 21 of these 54 patients had clinical follow-up only.

The patients with indeterminate FNAs confirmed to be indeterminate or malignant on second opinion cytology underwent operation and were found to be malignant in 29% (14/48) on final pathology compared with only 13% (17/129) of the indeterminate FNAs from initial opinion (P < .01). Overall, routine cytopathology second opinion of indeterminate thyroid FNAs (Bethesda III and IV; follicular lesion and follicular neoplasm) showed discordance in as many as 63% (81/129) of patients and potentially avoided unnecessary diagnostic thyroidectomy in 25% (32/129).

The accuracy of thyroid FNAs at referring institutions compared with our institution is listed in Table II. The accuracy of FNA (when considering malignant and indeterminate FNAs as a positive test that require thyroidectomy) was improved from 60% to 74% with cytology second opinion.
DISCUSSION

FNA cytology is the most accurate and cost-effective method for evaluating thyroid nodules. Unfortunately, thyroid cytology has its shortcomings. First, up to 7% of thyroid nodules will continue to yield an inadequate specimen and necessitate thyroid lobectomy for diagnosis. Another 15–30% of patients will have an indeterminate cytology diagnosis (follicular or Hurthle cell neoplasm, or follicular or Hurthle cell lesion; Bethesda III or IV cytology) and will often require thyroid lobectomy for diagnosis.

Some large centers obtain second opinion cytopathology review of thyroid FNAs routinely or selectively, and 3 centers have published their series. The overall concordance rates range from 40% to 82%, with the highest rates for malignant FNAs. Concordance rates for indeterminate (Bethesda III and IV) thyroid FNAs range from 36% to 68%. In a series of 97 thyroid FNAs from the University of Pennsylvania, a second opinion changed management strategies in 28 patients (29%, 28/97) and improved the accuracy of FNA from 73% to 85%. In 12 patients, the diagnosis was changed from malignant to benign (5 of these progressed to operation and 4 were benign; I had a Hurthle cell carcinoma). Interestingly, in another 16 patients, the diagnosis was changed from benign to malignant (and 13 of these turned out to be malignant on final pathology). This was not the case in our series, as none of 91 specimens thought to be benign on initial cytology review were thought to be suspicious or frankly malignant on second opinion. It is known that even on operative pathology, interobserver discordance can be as high as 18%.

In another series from University California, San Francisco, routine second opinion of 147 FNAs changed management in 8 patients (5%, 8/147) and improved the accuracy of FNA from 84% to 90%. Interestingly, in this series as in our series, not a single initial FNA opinion was changed from benign to indeterminate or malignant.

Thyroid cytology is known to have diagnostic limitations. The data suggest that referring cytologists in New Jersey are cautious about conferring a benign diagnosis to avoid the risk of a false-negative FNA. This may be an example of cytologic defensive medicine. However, this practice leaves many patients potentially undergoing unnecessary diagnostic thyroid operation for benign disease. Our series represents the largest published series of thyroid FNA second opinions with 331 patients and final pathology in 250 patients. In our study, 129 patients were referred to us with indeterminate thyroid FNA diagnosis (Bethesda III or IV) warranting diagnostic thyroidectomy. A second-opinion review suggested that of these 129 FNA, 54 of these were benign and another 27 non-diagnostic, prompting a repeat FNA. These 81 (63%, 81/129) patients had their management changed. Of the 54 patients with a benign second opinion, 22 progressed to operation (either for a symptomatic goiter, a nodule >4 cm, an enlarging nodule, or other clinical suspicion for cancer), and 21 were found to have benign disease for a reassuring 95% negative predictive value on second opinion of indeterminate FNAs. Another 11 of 54 patients with indeterminate FNAs reread as benign had repeat FNAs, and each of these 11 FNAs was found to be benign. This result amounts to 33 patients with indeterminate FNA reread as benign on second opinion with either operative or cytologic follow-up showing that 32 of 33 were benign. This finding suggested that second-opinion cytology review of indeterminate thyroid FNAs can potentially obviate the need for diagnostic thyroidectomy in 25% of patients without increases in false negatives.

This study contains several limitations. First, our cytologists were not blinded to the initial FNA interpretation, potentially leading to bias. Second, of 54 patients whose FNA result was changed from follicular neoplasm/lesion to benign, we only have operative pathology on 22. Therefore, there is no way to be sure that the remaining 32 patients did not unequivocally develop a thyroid malignancy.

Table II. Accuracy of thyroid FNAs from referring institutions versus RWJMS

<table>
<thead>
<tr>
<th>Referring institution</th>
<th>RWJMS</th>
<th>P value (chi square)</th>
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<tbody>
<tr>
<td>True positives</td>
<td>70</td>
<td>66</td>
</tr>
<tr>
<td>False positives</td>
<td>86</td>
<td>47</td>
</tr>
<tr>
<td>True negatives</td>
<td>67</td>
<td>84</td>
</tr>
<tr>
<td>False negatives</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>93%</td>
<td>93%</td>
</tr>
<tr>
<td>Specificity</td>
<td>44%</td>
<td>64%</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>45%</td>
<td>58%</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>93%</td>
<td>94%</td>
</tr>
<tr>
<td>Accuracy</td>
<td>60%</td>
<td>74%</td>
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RWJMS, Robert Wood Johnson Medical School.

Only patients progressing to operative resection with final pathology were included in this analysis. A positive test was a malignant or indeterminate FNA (ie, necessitating operation). A negative test was a benign FNA. Nondiagnostic FNAs were excluded from accuracy analysis.
We did have repeat interval FNAs on 11 of these 32 patients (revealing benign disease in all 11), and the remaining 21 patients had clinical follow-up with examinations and thyroid ultrasonographies.

A final problem with our study is that follicular (and Hurthle cell) lesion (Bethesda III) was grouped together with follicular (and Hurthle cell) neoplasm (Bethesda IV) in the “indeterminate” category. A recent series has shown that stratifying these diagnoses aids in identifying higher risk patients as the follicular neoplasm diagnosis carries a 21% risk of malignancy (and as much as 38% when nodule size is >4 cm), whereas follicular lesions carry only a 7% risk of malignancy and perhaps may be followed. Unfortunately, some have also shown that false negatives in patients with indeterminate cytology might result in treatment delay and worse clinical outcomes. Moreover, a 7% risk of malignancy in the follicular lesion category (Bethesda III) for many of the patients in our practice (and given our medical-legal system) is often enough to warrant diagnostic operation with follicular lesion as with follicular neoplasm (Bethesda IV).

In conclusion, significance interobserver variability exists in the interpretation of thyroid FNA. Cytology discordance can be as high as 63% with Bethesda III and IV thyroid FNAs (follicular lesion and follicular neoplasm). Strong consideration should be given to obtaining a cytopathology second opinion of Bethesda III and IV thyroid FNAs in asymptomatic, low-risk patients because a second opinion might obviate the need for diagnostic thyroidectomy in approximately 25% of patients.

REFERENCES

DISCUSSION

Dr Ashok R. Shaha (New York, NY): Excellent presentation. Really nice study; this is a very appropriate clinical study. A couple of points and 1 question.

Whenever you rereview the slides from outside, it is extremely important that you have reviewed all the slides. That information is not conveyed many times. The previous cytologies might have 10 slides, and they might have forwarded you three slides, so several slides are missing. And I think that is very important.
The second point is, if you are going to negate the previous suspicious needle biopsy and not operate on that patient, then be careful that all other parameters are suspicious for benign pathology: The size, the sonographic findings, age, and sex. Otherwise, you are going to be in trouble sometimes.

Now, the trouble may not occur, your accuracy is 95% correct. But that last 1 patient, where you miss the diagnosis, is going to haunt you. So, if you are going to take the responsibility on cytology, it is not only on cytology, you must take the responsibility of the entire patient in follow-up. Otherwise, you are going to have a problem.

Dr Janice Pasieka (Calgary, Alberta, Canada): Where does the clinical aspect of the patient come in? It is
1 thing you have a fine needle aspiration, you get a second opinion. But when do you then override that with the clinical features and what you see in front of you? Try to be Oslerian about it. The second thing is to challenge you and think that you may want to take this 1 step further and have all of your surgical permanent sections with a second opinion, because we have found that the intraobserver variation, even on the final pathology, can change. I think that this is a difficult area for our pathologists. We had a 25% change in the final diagnosis when a blinded pathologist read everything. I think it would be interesting if you did that with your patients.

Dr Tomer Davidov (New Brunswick, NJ): Thank you for your comment. Actually, I did talk to our chief of surgical pathology. She pointed out that what they are calling cancer now, they would have never called cancer 25 years ago. So, it is interesting that even on final operative pathology, opinions may differ. That is a great idea, and I will certainly look into that.

To answer the first question, you are absolutely right. Cytology is 1 key piece of information for managing these patients with thyroid nodules. But we do use other factors in our decision making. For example, if the patient has radiation exposure, certainly that raises the level of suspicion. A male patient with nodules is more suspicious. A suspicious feature on ultrasound or a growing nodule, to us, that’s suspicious, even though there is literature to suggest that benign nodules grow just as much as malignant nodules. Finally, anything that resembles symptoms—dysphagia, neck pressure—although it is not necessarily suspicious for cancer, it does push us more toward surgery. So, yes, we do use other clinical factors other than cytology in our decision making.

Dr Scott Wilhelm (Cleveland, OH): A question I had for you, when you brought up your own potential limitations to your study, you mentioned you had 20 patients who did not wind up undergoing any operation and underwent clinical follow-up alone. So, if you take 20 over your denominator of 250, then you have about 8%.

Number one, I am just curious. I know this is an outside read. So do you have any potential follow-up? Did those patients get follow-up ultrasounds? Any other repeat biopsies that may or may not have come back to you?

Then my other question would be, you initially started out with 331 patients and dropped to 250, so you have another 81 patients who underwent clinical follow-up. Again, that would take your denominator now to 101 patients of 331, which is getting closer to 30% of your patients who would then have clinical follow-up, versus 8% that you did in your particular portion. Do you have any information on that 30% or the 8% number?

I know it is hard; I am just curious.

Dr Tomer Davidov (New Brunswick, NJ): That is a great question. That is a major limitation of the study, of course. Follow-up was especially important in that subset of patients: the 54 patients where initial opinion was suspicious for follicular lesion or neoplasm and our pathologist said it was benign. Those patients were really referred to us for surgery and we took our cytologist’s opinion and said this FNA does not really look that suspicious. That was the whole point—we were trying to avoid unnecessary surgery. Even so, 22 of those patients did progress to surgery, and these were high-risk patients—those with enlarging nodules, radiation exposure, or other risk factors. And, 21 of 22 showed benign disease. We did repeat FNAs in 11 other patients—this amounts to 33 patients with either operative or cytological follow-up showing 32 of 33 benign. The remaining 21 patients who did not have surgery or repeat FNA did have some form of clinical follow-up—physical examination or ultrasound. Some were followed by us and others by their referring endocrinologists. Unfortunately, we do not have all that information such as repeat ultrasounds or other FNA from those patients who chose to follow-up only with the referring endocrinologists.

Dr Antonio Stephen (Boston, MA): This is related to Dr. Wilhelm’s question, but specifically, I am wondering about the 12 patients who had papillary or suspicious for papillary from the outside cytopathologist who were interpreted as either nondiagnostic or benign at your institution. How did you approach those patients? Did they have repeat biopsies? How comfortable were you not operating on those patients?

And finally, were there any specific cytologic characteristics that were found by the first cytopathologist that were interpreted as different or wrong by yours?

Dr Tomer Davidov (New Brunswick, NJ): Actually, if any cytopathologist was telling us there were nuclear features of papillary thyroid cancer, we were really hard pressed not offer operative therapy to those patients. So, why do we even get second opinion on those patients with a diagnosis of papillary or suspicion for papillary? If our cytopathologists interpreted a papillary or suspicious for papillary FNA as nondiagnostic or benign, then we would have a discussion with the patient and might offer a lobectomy with frozen section for diagnosis instead of total thyroidectomy up front. It might affect our management. We would also consider a repeat FNA and discuss that with the patient—although if 1 cytopathologist says papillary, views some grooves or an inclusion, and embraces that suspicion, then we usually would want to offer at least lobectomy for diagnosis with frozen section.

About the second point. The main complaint our cytopathologists had was that they felt outside smears were too thick, and therefore, nuclear features could not be reliably interpreted. In term of specific cytologic features, it seemed that the hypercellular specimens thought to be follicular lesion or neoplasm, but that contained abundant colloid with a mixed cellularity and without suspicious nuclear features—those were often reinterpreted by our pathologists as benign.

Dr Peter Mazzaglia (Providence, RI): I am wondering if you have access to or information about the prevalence of Hashimoto’s thyroiditis in the patients who had the follicular neoplasms, because we found that in patients with Hashimoto’s, if we alert the cytologist to that diagnosis, then it may change the initial interpretation of the cytology. And it does seem to have an effect.
on increasing the number of false positives in that group.

Dr Tomer Davidov (New Brunswick, NJ): We did not do that, but we should look into it. I think thyroiditis is fairly easy to diagnose on FNA, so I imagine that if the pathologist would find many lymphocytes on the smear they would figure out there is underlying thyroiditis. As I understand from our cytopathologists, occasionally you could get a nuclear groove or even pseudonuclear inclusion that is the result of thyroiditis. But the quick answer is, no, we did not alert them to the presence of thyroiditis. I will look into it; I appreciate it.

Dr Douglas Evans (Milwaukee, WI): I wanted to follow up on Ashok’s point because it is really a good one. To my knowledge, there is no mechanism to reimburse the sending institution for collating the slides, the report, and sending it to your pathologist, even though your pathologist can then bill for the second review. To what degree does that impact your inability to obtain some slides? I assume that there were some patients for whom you could not obtain their outside biopsy slides.

Number two, whose job is that at your institution? Having a cancer practice, this is a big deal.

And then last, is your inside review of the outside pathology a templated report? Getting at Ashok’s point, ie, there were 5 slides prepared, and 3 were sent; on those 3 slides, I think this is a real opportunity, because this paper will be published, for you to make some recommendation in an area that we all struggle with. Because errors occur every week in medicine because biopsy slides are not accurately reviewed.

Dr Tomer Davidov (New Brunswick, NJ): Thank you for all those points. The first point is we are actually pretty meticulous about making sure that every patient that had an outside biopsy brings their slides, and that job belongs with our nurse. And she is very meticulous about calling and harassing the patients to go pick up the slides themselves and to make sure that they come in with those slides, regardless of what the diagnosis was. I would say only a handful of patients could not make it happen, or the outside institution gave them a hard time, but we put the responsibility for obtaining the slides it on the patient, and our nurse really goes after them to make sure that they bring their slides in. I would say that of 331, perhaps 3 or 4 patients came without we are pretty meticulous about that.

The second question, with regard to making sure we obtain all the slides, that is an important point. There is 1 referring institution that is notorious for giving us approximately a third of the slides that they actually have. They do not give us everything, and we often have to send the patient back to get the remaining slides. Yes, they give the patients a hard time about it—I guess it is a reimbursement issue.

In terms of whether we have a template of how many slides were done the first time around and how many were sent to us, we do not have a formal template. Our pathologists report the number of slides that were given to us. We do ask patients to bring all slides and sometimes send them back for remaining slides, especially when there is a discrepant diagnosis.

Dr Douglas Evans (Milwaukee, WI): Does your pathology report reference the previous pathology report and alert the clinician that there is a difference of opinion?

Dr Tomer Davidov (New Brunswick, NJ): The second-opinion report does not reference the diagnosis from the other report, even though the cytologist usually observes the initial report. We always have it. So, the pathologist does not, per se, indicate “this is a discrepant report.” We know there is a discrepant report that when we get the second opinion report and compare it ourselves with the original report.

Dr Douglas Evans (Milwaukee, WI): I think the important point and this is done at many places, if not everywhere. That pathologist does not reference the previous report. Now, most pathologists will not review slides without the prior report, but that does not mean that the clinician gets the report.

So, it is an important point to remember that as a clinician, it is up to us to look at both the previous report and the current one, because the current pathology report oftentimes, if it is discrepant, will not reference that previous report.

Dr Stanley Trooskin (New Brunswick, NJ): Just a point of clarification. Our pathologists do denote how many slides they get. The initial report has how many slides they were sent to us, we do not have a formal template. Our pathologists report the number of slides that were given to us. They do not give us everything, and we often have approximately a third of the slides that they actually have. They do not give us everything, and we often have to send the patient back to get the remaining slides. Yes, they give the patients a hard time about it—I guess it is a reimbursement issue.

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