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Original Contribution

Processing the entire capsule in thyroid follicular lesions improves diagnostic accuracy

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ABSTRACT

Background: There is contradictory evidence in literature with respect to diagnosis and management of follicular lesions of the thyroid gland. From surgical pathology stand point, pathologists require submission and processing of entire capsule for microscopic evaluation. This can be extremely challenging especially in larger lesions.
Method: We studied the impact of submitting entire capsule on final pathologic diagnosis in cases on which only representative sections were submitted initially and entire capsule was submitted subsequently.
Results: A total of 80 specimens were identified. Mean size of the nodule in these cases was 4.4 ± 1.9 cm. Mean initial tissue sections submitted were 11.6 ± 3.6. Entire capsule was submitted subsequently in an additional 12.6 ± 13.3 sections. Submission of entire capsule contributed to final diagnosis in 3 (3.8%) cases whereby foci of capsular microinvasion were identified. There was no significant difference in the requirement of subsequent sections in specimens grossed by residents compared to those grossed by pathologist assistants (10.4 ± 10.8 vs. 14.4 ± 14.9, $p = 0.18$). The processing cost of additional sections of capsule was $ 4143 in these cases.
Conclusion: Processing of entire capsule in thyroid follicular lesions has a definitive yield that comes at a high cost. Thin slicing and looking for areas of gross abnormality such as mushrooming may be more practical especially in larger lesions.

1. Introduction

Follicular thyroid carcinoma (FTC) is the second most common malignancy of the thyroid gland, accounting for 10%–15% of all thyroid carcinomas [1,2]. The distinction of the follicular carcinoma from follicular adenoma primarily depends on either the identification of capsular invasion or the invasion of vascular spaces. Although capsular invasion seems to be a simple and straight-forward concept, there is no consensus as to the definition of capsular invasion. This has led to the grey zone category of minimally invasive thyroid follicular carcinoma (MI-FTC). The WHO classification now separates encapsulated angioinvasive follicular tumors into a distinct more aggressive category than minimally invasive carcinoma [3,4]. This leaves minimally invasive follicular carcinomas to be restricted to capsular invasion only.

The management guidelines for FTC and follicular adenomas are definite; however, for MI-FTC the management is controversial [5,6]. Accordingly from a pathologic stand point the handling of such specimens is controversial with respect to how much sampling is adequate.

We analyzed if the subsequent submission of entire capsule has an impact on the final pathologic diagnosis of follicular lesions of the thyroid gland in the cases on which only representative sections of the capsule were submitted initially.

2. Materials and methods

We did retrospective review of the thyroid gland surgical pathology specimens received in the pathology department of our institution, over a 5-year period from January 1, 2012, to December 31, 2016. Only those specimens on which additional tissue sections were submitted were included in the study.

Although there are standardized grossing manuals [7-9], different anatomic pathology laboratories have slightly different protocols for handling their specimens. It is prudent to clarify here that in our institution the pathologist assistants and residents are instructed to slice the thyroidectomy specimens at 2–3 mm intervals and to submit only representative sections for microscopic evaluation, however, if the pathologist thinks that the lesion represents a follicular adenoma, the standard protocol in our laboratory is to submit remainder of the entire capsule in blocks labelled “additional sections”.

We found 83 such cases in our database. Hematoxalin and eosin (H&E) stained glass slides for all the cases were retrieved and reviewed. No additional material or recut slides were submitted at the time of review.

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Additionally pathology reports were reviewed and data such as pathologic diagnosis, number of initial representative tissue sections, and number of subsequent tissue sections for processing entire capsule, grossing individual (resident versus pathologist assistant) and cost of processing tissue were collected.

While reviewing the glass slides of cases with diagnosis of MI-FTC, it was determined whether the foci of microinvasion were present on slides labelled with regular labels used in our laboratory or slides labelled with "additional section" label. If such foci were identified only on slides with additional section label, the subsequent sections of capsule were considered effective, as they resulted in changing the diagnosis from follicular adenoma to FTC or MI-FTC.

In assessing the processing cost we used the cost of reagents and consumables including cassette, glass slide, coverslip, and label. We also included the compensation for the histotechnologists and laboratory technicians but did not include the compensation for pathologist assistants, residents and the pathologists.

Data were analyzed using Student's *t*-test, and $\chi 2$ analysis. All data were analyzed using SPSS v. 24.0, and a p value of 0.05 or less denoted statistical significance.

3. Results

A total of 83 thyroid gland resection specimens were identified on which additional tissue sections were ordered. Of these, 80 were for the submission of entire capsule. Mean size of the nodule in these cases was 4.4 ± 1.9 cm. Mean initial sections submitted in these 80 cases were 11.6 ± 3.6. Entire capsule was submitted subsequently in an additional 12.6 ± 13.3 sections increasing the total number of sections per case to 24.2 ± 14.3 sections. The submission of entire capsule contributed to final diagnosis in 3 (3.8%) cases, whereby foci of microinvasion of the capsule were identified modifying the diagnosis from follicular adenoma to minimally invasive follicular thyroid carcinoma (MI-FTC) [Table 1]. Foci of vascular invasion were not identified in any of the additional tissue sections. There was no significant difference in the requirement of subsequent sections in specimens grossed by residents compared to those grossed by pathologist assistants [Table 2]. Subsequent processing added an additional cost of $ 4143 in these 80 cases.

4. Discussion

The nature and management of minimally invasive follicular thyroid carcinoma (MI-FTC) is controversial. A benign and indolent course is reported by many studies owing to low risk of recurrence and distant metastasis [10,11]. A recent study found 100% disease-free survival with up to 16 years of follow-up [12]. On the contrary, some authors do not consider MI-FTC to be purely an indolent disease [13,14]. The controversy is not limited to the management but has roots extending to the surgical pathology. From a pathologic stand point, the MI-FTC is defined by minimal to focal invasion of the fibrous capsule (as opposed to unequivocal frank invasion in FTC) by the tumor. Although seemingly a simple concept, there is no consensus on what constitutes capsule invasion, let alone the minimal invasion. Some pathologists require complete transgression of the capsule, while others do not; some consider mushroom-shaped tumor in the capsule as invasion while others order deeper recuts to exclude invasion. The situation is even more complicated in cases where such areas are adjacent to a previous biopsy site and may represent capsular rupture related to prior fine-needle aspiration [15,16].

Table 2
Mean number of additional sections of capsule submitted by residents and pathologist assistants.

	Residents	Pathologist assistants	p-Value
Mean (± sd)	10.4 ± 10.8	14.4 ± 14.9	0.18
Median (Range)	8 (1–64)	9.5 (2–73)	0.17

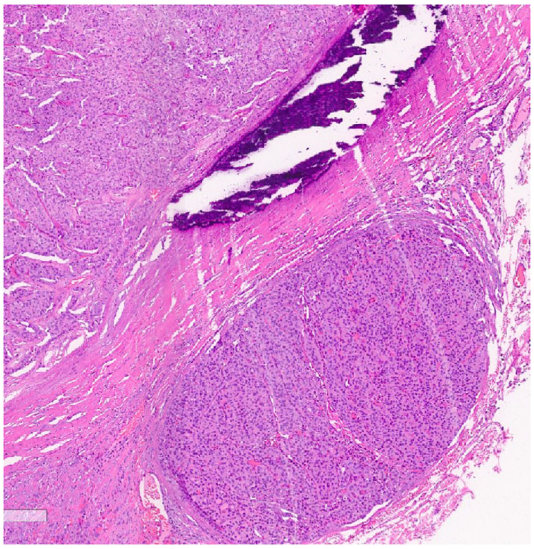

Fig. 1. Photomicrograph depicting unequivocal capsular invasion (H&E, 50×).

Fig. 1 demonstrates an unequivocal capsule invasion while Fig. 2a to d demonstrate representative images of our cases demonstrating minimally invasive disease. These controversies bring us to the issue of gross sampling of the follicular lesions as to what constitutes adequate sampling. Histologic examination of at least ten tissue sections is recommend by NCCN guidelines [6]; however, most pathologists require submission of entire capsule for microscopic evaluation in order to rule out capsular invasion and thus minimally invasive follicular carcinoma (MI-FTC). If only representative tissue sections are initially processed, they usually order processing of the remainder of the tissue or at least the capsule before signing out the case. Processing of additional tissue sections has been shown to have a definite yield [17-21]. Diagnoses were modified in 2 to 22.5% of cases in these studies [17-22]. In our study subsequent processing of the entire capsule resulted in diagnostic modification in 3 (3.8%) cases. In a cohort of 14 cases, Yamashina et al. [23] demonstrated that circumferential evaluation of the fibrous capsule identified intracapsular angioinvasion in seven cases, and minimal capsular invasion in two cases. However, in this study entire capsule was submitted from the beginning. On evaluation of entire capsule, we found minimal capsular invasion in three of our cases, however, none of the cases demonstrated intracapsular angioinvasion.

In their review of MI-FTC, Thompson LD [24] came to the conclusion that multiple sections were needed to demonstrate capsular or vascular invasion, with an average of 18.0 sections examined per tumor. Additionally, they [24] showed that 4.2% patients with MI-FTC

Table 1
Breakdown of number of cases with initial and final diagnoses.

Initial diagnosis	Number of cases	Final diagnosis after submission of entire capsule	Number of cases
Follicular adenoma	80	Follicular adenoma	77
MI-FTC	0	MI-FTC	3

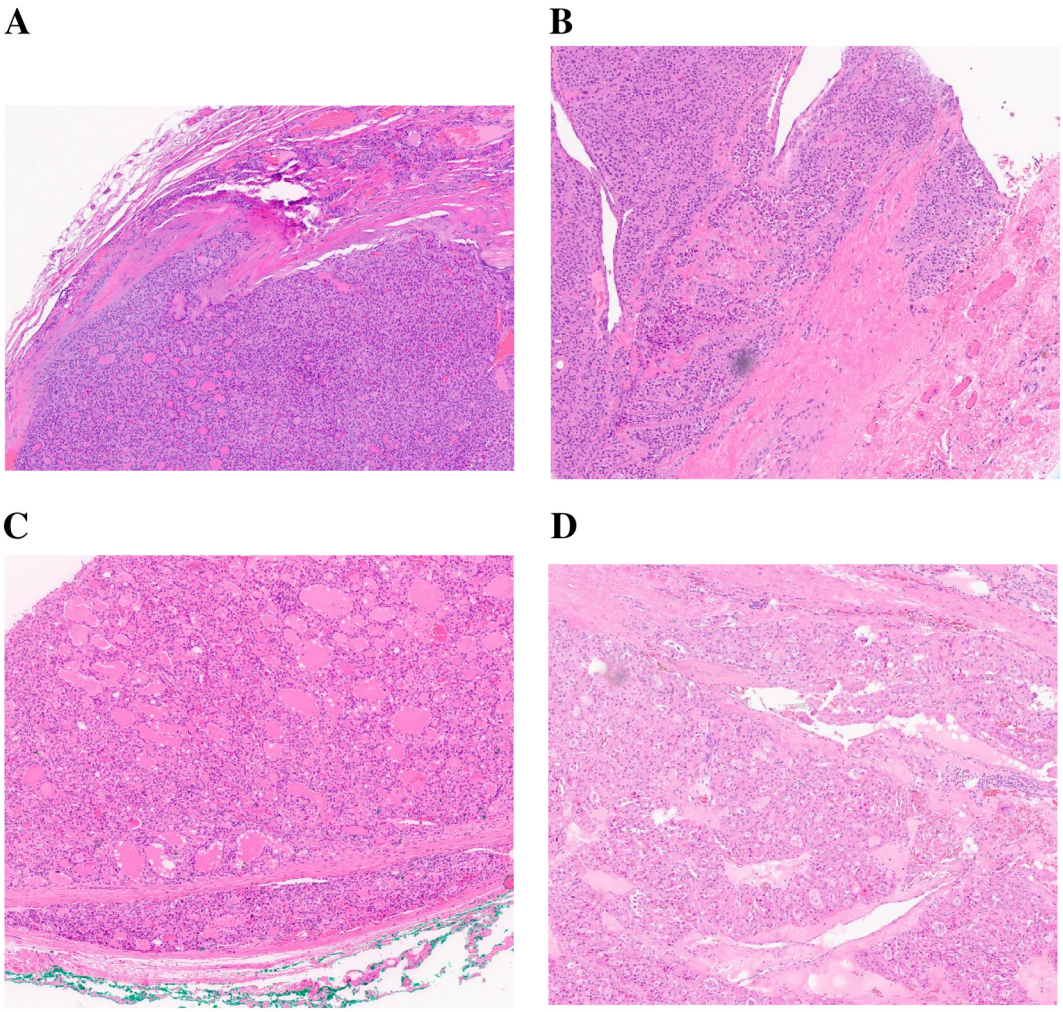

Fig. 2. a–d: Photomicrographs demonstrating areas of microinvasion in MI-FTC (H&E, 50×).

Table 3
Demographic and follow up data of patients with MI-FTC.

Age (years)	Gender	Treatment received	Vital status
33	Female	Total thyroidectomy followed by radioactive iodine therapy.	Alive without evidence of disease, 38 months after surgery.
41	Male	Total thyroidectomy	Alive without evidence of disease, 63 months after surgery.
44	Female	Total thyroidectomy	Alive without evidence of disease, 54 months after surgery.

developed recurrent disease and average survival was 18.1 years. The demographic and follow up data of our three patients with MI-FTC are summarized in Table 3.

Considering patient care, there is absolutely no way this diagnostic discrepancy can be over looked. From a pathologic and specimen grossing standpoint; however, the argument in favor of representative sections is that even if the entire capsule is submitted; the glass slides are still representative, constituting 4 to 5 μm of an average tissue thickness of 3 mm. Moreover, although the precise management differences are dependent on different factors and are beyond the scope of this discussion, the generalized principles for management of thyroid follicular adenoma versus minimally invasive thyroid follicular carcinoma are the same [5,6]. Thin slicing of the specimen with careful examination of the cut surfaces for suspicious areas such as areas of mushrooming may have comparable yield to processing the entire capsule, although this hypothesis needs to be verified by a future study.

From grossing perspective, pathologists tend to trust pathologist assistants more than residents. Galvis et al. [25] found that cases grossed by pathologist assistants had a significantly decreased re-submission rate compared to those grossed by residents. Others, however, found no significant difference in grossing quality of specimens grossed by residents versus those grossed by pathologist assistants [17,26]. In our study residents were able to submit the capsule in lesser number of sections as compared pathologist assistants; however, the difference was not statistically significant.

With decreased compensation and strict reimbursement criteria the laboratories are trying to come up with ways to cut expenses. In such a scenario, the processing of additional tissue adds additional costs for an anatomic pathology laboratory. The cost of processing one tissue section in our laboratory is estimated to be $4.11. This includes the cost of the reagents, cassettes, glass slides, coverslips, and the labor costs of preparing the slides. This is certainly not inconsequential since the mean number of subsequent sections for submission of entire capsule was 12.6 which equates to an average additional cost of $51.80 for each specimen.

5. Conclusion

Processing of entire capsule in thyroid follicular lesions has a definitive yield that comes at a relatively high cost. Whether or not this diagnostic yield makes a difference in patient management is unclear, so is the amount of effort and expense that should be exercised in this regard. Thin slicing and looking for areas of gross abnormality such as mushrooming may be more practical and cost effective, especially in larger lesions.

Compliance with ethical standards

Funding

None.

Conflict of interest

All Authors declare that they have no conflict of interest.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee.

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Informed consent

Informed consent was obtained from all individual participants included in the study.

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All authors have contributed significantly, and are in agreement with the content of the manuscript.

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