# Minimally Invasive Follicular Thyroid Carcinoma

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## Abstract

Infiltration of the capsule, vascular invasion, and/or neoplastic extension into the adjacent parenchyma are regarded as prerequisites for the diagnosis of follicular carcinoma. In modern practice, most of these tumors fall into the category of minimally invasive follicular carcinoma (FCMI) characterized by evidence of limited capsular or vascular invasion with an excellent long-term prognosis and a good patient outcome. Notwithstanding the wide acceptance of the diagnostic criteria established by the World Health Organization for the classification of follicular carcinomas in particular, they have been difficult to apply and have led to a great deal of confusion. This confusion is compounded when applied to "low-grade" or "minimally invasive" follicular carcinoma because of the poor reproducibility of the classification and the variable results reported in the literature. Our surgical colleagues face a similar lack of a standardized treatment for low-grade follicular carcinomas, which leads to unnecessary surgical treatment. Standardization of histologic criteria is necessary to promote confidence and uniformity in the therapeutic approach of these tumors. We believe that an FCMI is defined as an encapsulated follicular tumor (not papillary), with only small to medium vessel invasion within or immediately adjacent to the tumor capsule and/or up to full-thickness capsular transgression without accompanying extension into the thyroid parenchyma (covered by fibrosis). By using these criteria, patients can be managed with conservative surgical excision to yield an excellent long-term patient outcome.

***Key Words:*** Follicular thyroid carcinoma; low grade, minimally invasive; thyroid neoplasm.

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*Endocrine Pathology,* vol. 12, no. 4, 01–06, December 2001

1046–3976/01/12:01–06/$0.00l

## Introduction

A follicular thyroid carcinoma (FTC) is epidemiologically, histologically, and clinically distinct from papillary thyroid carcinoma, yet it shares a few striking similarities, especially an indolent growth pattern, ability to concentrate iodine, and generally a good prognosis.

FTC accounts for approx 15% of all thyroid tumors and its frequency is increased in iodine-deficient regions of the world. FTCs occur in middle age to older individuals with some predominance in women, although they can occur at any time of life. These tumors usually present as a solitary encapsulated thyroid nodule with atrophy or compression of the adjacent parenchyma, but they can also develop in a thyroid gland with other preexisting conditions.

FTCs have been classified as either minimally invasive or widely invasive carcinoma. The histologic diagnosis of a widely invasive carcinoma is straightforward, although this type of tumor in modern practice is uncommon. However, the distinction between a low-grade follicular carcinoma and a follicular adenoma is often made with great difficulty, uncer-

tainty, and frank disagreement among experts in thyroid pathology.

At the Armed Forces Institute of Pathology (AFIP), we use the histologic criteria as defined by the World Health Organization classification as a guide in the diagnosis of FTC [1,2]. We do not intend herein to extend the arguments on histologic interpretation of thyroid carcinoma, except to say that all attempts at classifying a disease must at times be arbitrary.

The generally accepted diagnostic criteria for a minimally invasive follicular carcinoma (FCMI) include but are not limited to a neoplastic extension of follicular epithelial cells into the adjacent parenchyma, invasion by neoplastic follicular cells into blood vessels within or beyond the capsule, and capsular invasion. The latter is still controversial among pathologist. Specifically, there is disagreement on whether the tumor must merely extend into the capsule or whether it must entirely transgress the capsule to warrant a diagnosis of carcinoma. We hasten to add that the end point used to determine malignancy is not well defined in thyroid pathology either, since the presence of invasive activity sometimes is not a reliable indication of the degree of malignancy nor is it always a valid guide to prognosis. A follicular carcinoma showing minimal infiltration is occasionally associated with metastases, whereas patients in whom florid capsular and vascular invasion is demonstrated may live for years without ever developing metastases.

## Materials and Methods

Recently, members of the staff at the AFIP conducted a study of 95 cases of FCMI [3]. The detailed study of these tumors included size of the tumor, degree of cellularity, character of the capsule, degree of capsular penetration (more than half or less than half of the capsule thickness) and number of foci (single or multiple foci), type of vascular invasion (small to medium vessels) and number of vessels penetrated (single or multiple), parenchymal extension with or without intervening connective tissue, growth pattern (insular, trabecular, solid, follicular), presence or absence of oxyphilia, mitoses, and necrosis (Figs. 1–8).

Most patients presented with a neck mass measuring on average about 3 cm in diameter. All tumors were encapsulated. As in most reported studies, females outnumbered males, with a mean age at presentation of 42 yr [3–7].

## Results and Discussion

It is our belief that the criteria we used for the diagnosis of FCMI are effective, reproducible, and useful. A generous sampling of the specimen was required, with multiple sections from the tumor-capsule-parenchymal interface. The neoplasms were arranged in follicles, trabeculae, or solid sheets, although the follicular pattern predominated. Nearly every tumor had both capsular and vascular invasion, with only a few tumors demonstrating capsular or vascular invasion alone. Careful consideration was given to the number of foci of invasion as well as to the size of the vessels invaded and to the extent of capsular penetration. Any tumors that had large-vessel invasion (muscular coat in the wall of the vessel) or had invasion of vessels distant from the tumor capsule were not considered to be FCMI. Likewise, if there were large protrusions of neoplastic cells out into the parenchyma without accompanying fibrous connective tissue from the capsule,

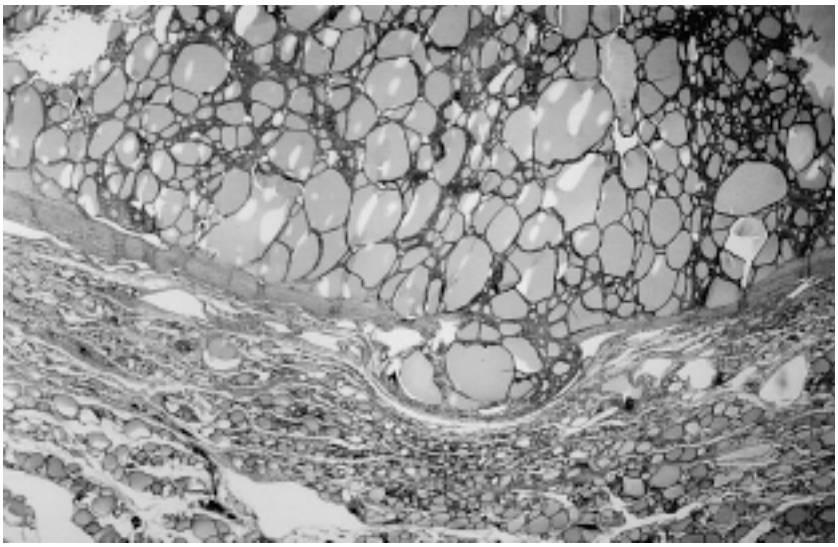

**Fig. 1.** FCMI showing encapsulated neoplasm with growth pattern of adenomatoid nodule extending into adjacent parenchyma (hematoxylin and easin [H & E] ×60).

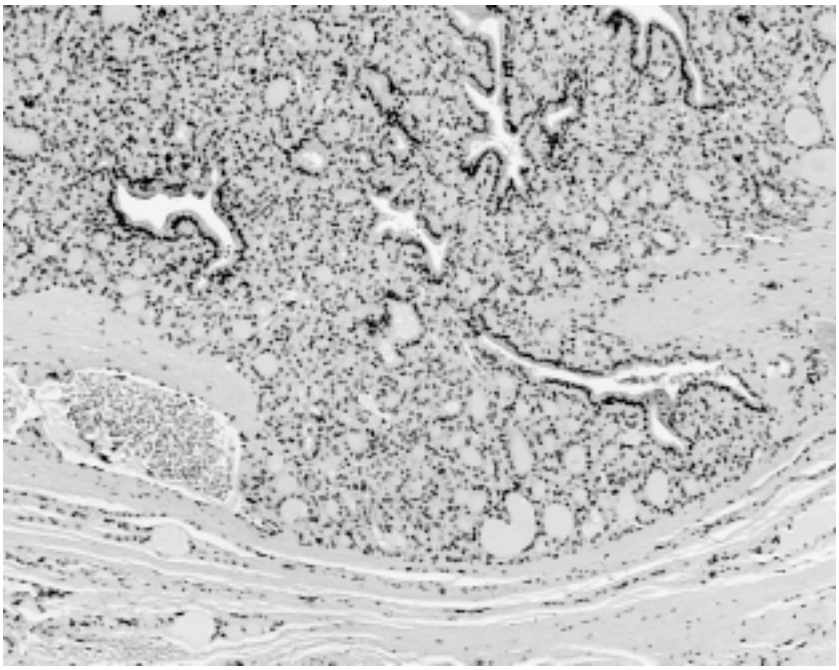

**Fig. 2.** FCMI showing moderately cellular tumor with full extent of invasion from main mass into its capsule (HE: ×100).

we did not call such neoplasms FCMI. The remaining histomorphologic criteria examined were not statistically significant in predicting patient outcome or long-term prognosis and thus were deemed useless for prognostic purposes.

Based only on the presence of capsular and/or vascular invasion of the degree already cited (irrespective of the number of foci), we believe that the diagnosis of FCMI will correctly predict the biologic behavior of the tumors in these patients; that is, they will not die from their disease nor will they develop metastatic disease with any appreciable degree of frequency. It can be argued that these tumors may then be considered benign if they do not develop metastases or cause the patient's death. This brings us back to the definition of malignancy in the thyroid gland, or in other organs for that matter, and it is our position that infiltrative behavior is diagnostic of a carcinoma but should not imply a poor biologic outcome. Therefore, even though patients do not die from their disease or develop metastatic disease, we still believe that the term *FCMI* when applied strictly will allow the treating surgeon and endocrinologist to realize the low probability of disseminated disease and permit them to tailor the patients' treatment to a lobectomy alone without additional surgery or adjuvant therapy. If the neoplasm does not meet these strict criteria, then the treatment modalities employed may need to be more aggressive and include completion thyroidectomy with ablative radioactive iodine therapy.

In support of this assertion, most patients were treated surgically with a lobectomy or lobectomy and isthmusectomy. The prognosis of these tumors was very favorable with an excellent long-term survival rate. An exceedingly low number of patients developed recurrent or secondary tumors, and when they did, surgery was again used to managed the recurrence. Of the 95 patients in the study, 94 were alive and well without evidence of disease (mean:

**Fig. 3.** FCMI showing cellular tumor that infiltrates its capsule without invading vessel (HE: ×80).

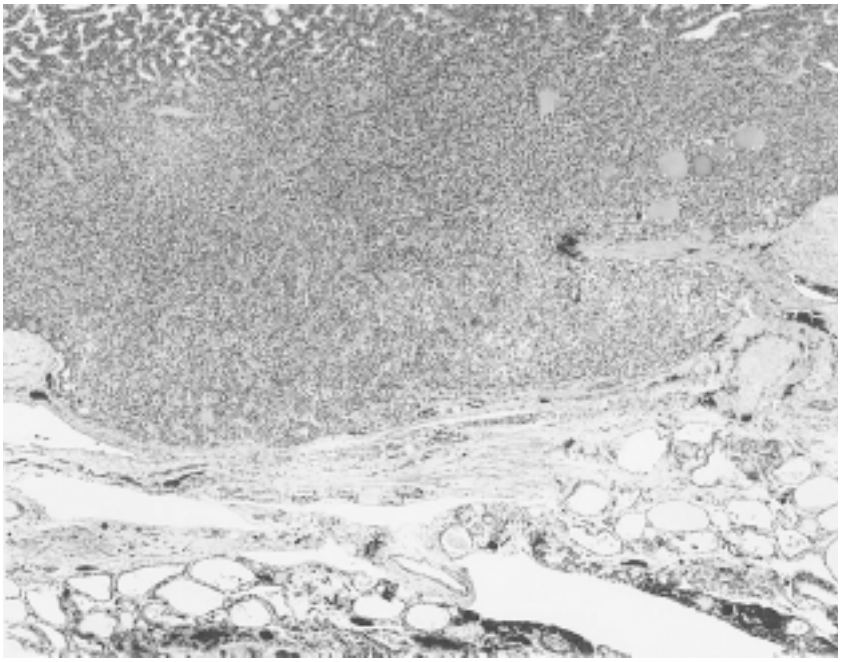

**Fig. 4.** FCMI showing marked neoplastic protrusion into adjacent thyroid parenchyma surrounded by connective tissue (HE: ×40).

16.8 yr of follow-up). Four patients had developed a recurrence during the follow-up period, and one patient had died with disease. There was an excellent prognosis associated with surgical excision with no difference in outcome based on the type of surgical treatment [3,8–15]. The beneficial effects of $^{131}$I ablation in terms of recurrence and mortality rate are not particularly convincing, except in patients who have undergone total thyroidectomy or near total thyroidectomy for a follicular carcinoma, rather than using $^{131}$I in patients who have only had lobectomy or lobectomy-isthmusectomy.

Based on our criteria, the 10-yr survival rate is \>95% for patients with FCMI. Cancer mortality is extremely low, with few recurrences and no distant metastases. FCMI has demonstrated an excellent patient survival with conservative therapy. Additional surgical therapy is not recommended and should be used only in the presence of recurrent disease or secondary tumor development.

We found no difference in the patient outcome based on gender, tumor size, presence of mitoses, tumor cellularity, cytoplasmic oxyphilia, necrosis, thickness of the tumor capsule, frequency (single or multiple areas of invasion), or type of invasion (either vascular or capsular) [3]. Oxyphilic cell carcinomas, considered by some investigators as a subtype of FTC, have a similar outcome to other types of differentiated thyroid cancers. It has been our experience that tumors with cytoplasmic oxyphilia have a prognosis similar to that for nonoxyphilic tumors of similar stage [3].

The recognition of FCMI based on their characteristic microscopic appearance

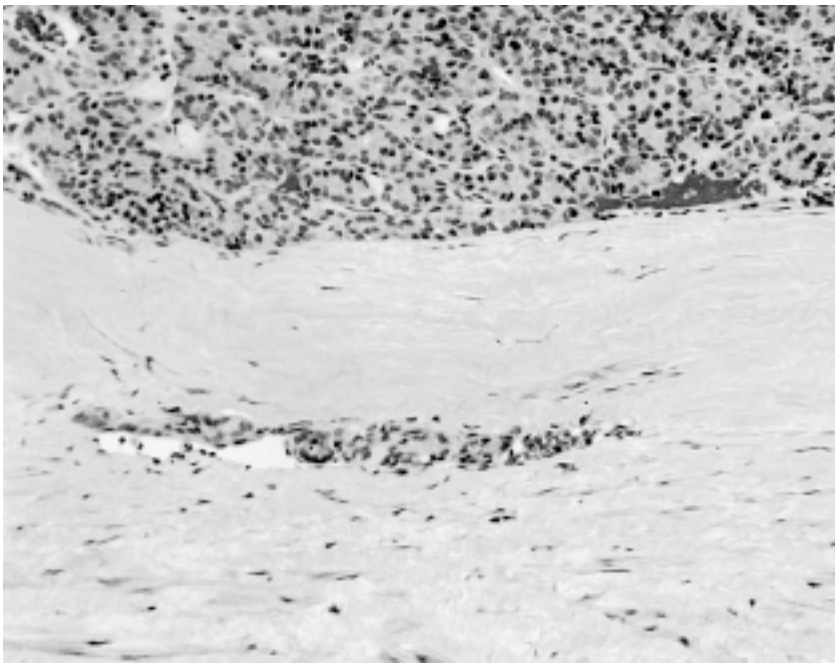

**Fig. 5.** FCMI showing tumor with thickened capsule. A small intracapsular vessel lacking continuity with the main mass is invaded by tumor (HE: ×135).

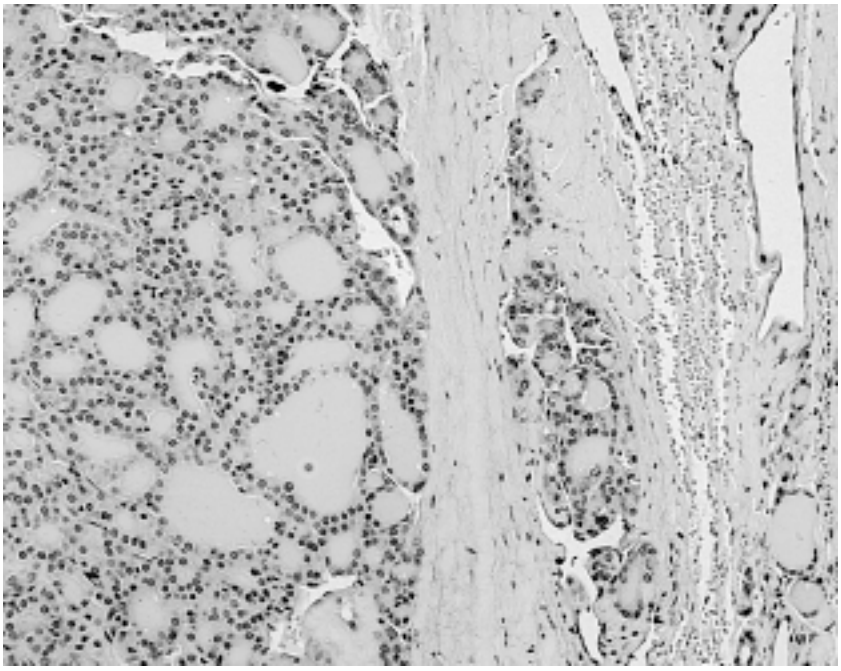

**Fig. 6.** FCMI showing endothelial-lined medium size vessel occluded by tumor thrombus (HE: ×135).

and the strict criteria established is extremely important in allowing the treating clinician to apply the appropriate conservative patient management, preventing excessive and unnecessary surgery.

## Acknowledgments

The opinions or assertions contained herein are the private views of the author and are not to be construed as official or reflecting the views of the Department of Defense. The article was presented in part at the Endocrine Pathology Society Session at the USCAP Meeting, Atlanta, GA, March 3, 2001.

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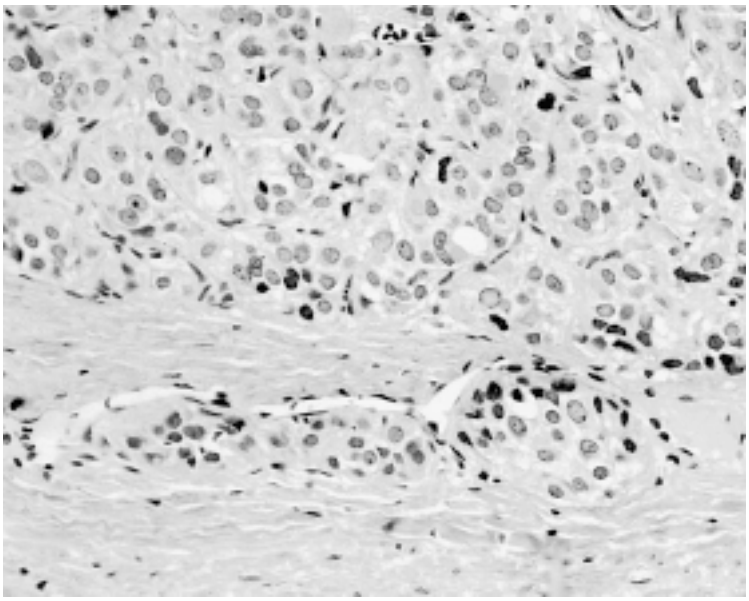

**Fig. 7.** FCMI. Although closed to the tumor mass, this endothelial-lined space shows unequivocal invasion by tumor (HE: ×135).

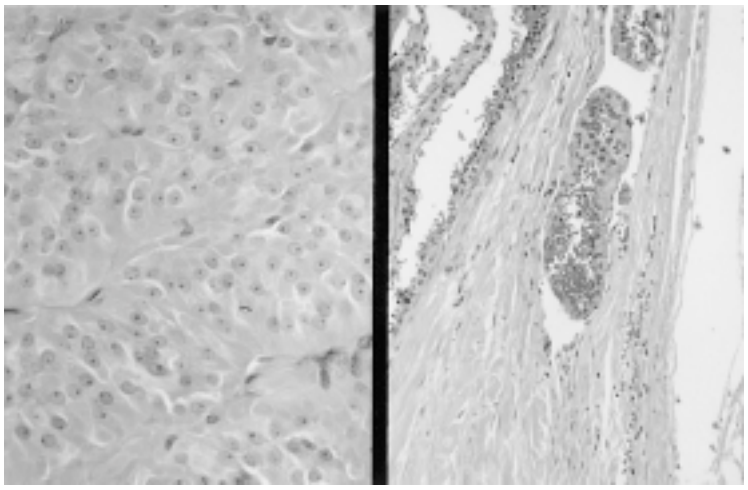

**Fig. 8.** FCMI with oxyphilic cells. **(Left)** A characteristic trabecular pattern of growth, cells with abundant cytoplasm, prominent central nucleoli, and a mitotic figure; **(right)** at a lower magnification, same tumor showing vascular invasion (HE: ×135).


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