Follicular Lesions of the Thyroid

Aarti Mathur, MD[a], Matthew T. Olson, MD[b], Martha A. Zeiger, MD[a,*]

KEYWORDS

• Follicular • Cancer • Thyroid • Neoplasms

KEY POINTS

- Follicular lesions of the thyroid gland include benign follicular adenoma, minimally invasive follicular carcinoma, widely invasive follicular carcinoma, and encapsulated and infiltrative follicular variant of papillary thyroid cancer.
- Fine-needle aspiration (FNA) biopsy is the best diagnostic test to diagnose a thyroid nodule but is indeterminate in 15% to 20% of cases, especially when follicular lesions are involved; capsular invasion, the hallmark that distinguishes benign from malignant, cannot be assessed with FNA.
- Molecular markers are a recent promising area of research to differentiate thyroid neoplasms; however, none has proved adequate in differentiating benign from malignant follicular tumors.
- At a minimum, a diagnostic thyroid lobectomy is required to assess the histologic architecture and obtain a definitive diagnosis. However, gray zones exist within the diagnostic spectrum of follicular neoplasms.
- Widely invasive and infiltrative follicular variant of papillary thyroid cancers have higher recurrence rates and metastatic potential; a total thyroidectomy is therefore indicated.
- Controversy exists for small, minimally invasive carcinomas and well-encapsulated follicular variant of papillary cancer in patients younger than 45 years; some consider a lobectomy sufficient treatment.

INTRODUCTION

Follicular lesions of the thyroid encompass a wide range of diseases, including benign follicular adenoma, malignant follicular carcinoma, and follicular variant of papillary cancer. Follicular adenoma is defined as an encapsulated, benign neoplastic proliferation of thyroid follicles.[1] Follicular carcinoma represents 10% to 15% of all thyroid

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[a] Department of Surgery, Johns Hopkins University School of Medicine, 600 North Wolfe Street, Baltimore, MD 21287, USA; [b] Department of Pathology, Johns Hopkins University School of Medicine, 600 North Wolfe Street, Baltimore, MD 21287, USA
* Corresponding author. Department of Surgery, The Johns Hopkins Hospital, 600 North Wolfe Street, Blalock 606, Baltimore, MD 21287.
E-mail address: mzeiger@jhmi.edu

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cancers, and has been classified by the World Health Organization as minimally invasive follicular carcinoma (MIFC) or widely invasive follicular carcinoma (WIFC).[2] Follicular variant of papillary thyroid cancer (FVPTC) is the second most common variant of papillary carcinoma after the classic variety. Because, follicular neoplasms also represent a spectrum of disease with considerable morphologic overlap rather than discreet entities, controversy exists regarding diagnoses of these histologic subtypes. These lesions have subsequently been referred to as "the bane of the pathologist."[3] Furthermore, the specific diagnosis has an impact on patient treatment and prognosis. This review addresses the clinical presentation, preoperative diagnosis in the era of molecular markers, pathologic diagnosis, treatment, and prognosis of follicular lesions, taking into account the frequent controversy about definitive histologic diagnoses.

CLINICAL PRESENTATION

Thyroid nodules are present in 60% to 70% of the US population; most are benign, and only 5% are malignant.[4] Most patients with a follicular adenoma or carcinoma present with a solitary thyroid nodule, which is either palpable or incidentally discovered on imaging in an otherwise asymptomatic patient. The nodule may also occur in association with thyroiditis or nodular hyperplasia. Patients with large tumors may complain of compressive symptoms such as dyspnea, coughing, choking sensation, dysphagia, inability to lie flat, or hoarseness. Rarely, patients may present with hyperthyroidism. Most patients with an adenoma are clinically and biochemically euthyroid. Approximately 1% of follicular adenomas are toxic adenomas, causing symptomatic hyperthyroidism, and nearly all of these lesions are benign.[5] However, hyperthyroidism usually does not occur until an adenoma is larger than 3 cm.

Follicular carcinoma typically presents as a solitary mass, usually greater than 2 cm, and is more prevalent in iodine-deficient regions.[6] It occurs most often in women. MIFC resembles a follicular adenoma with an indolent course; it tends to present in younger patients, and some have proposed that it may be a precursor to its WIFC counterpart. Conversely, WIFC is clinically recognizable as a cancer. It tends to present in older patients, with a median age of 60 years. Follicular carcinoma has a tendency for hematogeneous spread, but the patient rarely has lung or bone metastases at initial presentation.

FVPTC is a unique intermediate clinical entity, with histologic and clinical features that span the cytologic features of classic papillary thyroid cancer (PTC) and the architectural features of follicular thyroid cancer. According to a large population-based study of more than 10,000 cases,[7] the mean tumor size was larger than that of classic PTC, but smaller than follicular cancer. Extrathyroidal extension and lymph node metastases in FVPTC are seen more commonly than with follicular cancer, but less commonly than with classic PTC. Distant metastases were present in 2%, compared with 1% in patients with PTC and 4% with follicular cancer.[7]

PREOPERATIVE DIAGNOSIS

Ultrasonography

Certain sonographic features of a thyroid nodule can be used as predictors of the presence of a malignancy. Characteristics of a suspicious nodule include the following: unifocal, hypoechoic, solid, a discontinued halo, irregular margins, microcalcifications, and predominantly intranodular color flow.[8,9] Recent studies using duplex ultrasonography showed that the absence of blood flow in a follicular