Journal of the American Society of Cytopathology (2016) 5, 107–115

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ORIGINAL ARTICLE

Undifferentiated (anaplastic) thyroid carcinoma and its mimics: a report of 59 cases

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Received 17 June 2015; accepted 12 August 2015

KEYWORDS
Anaplastic thyroid carcinoma;
Undifferentiated thyroid carcinoma;
Thyroid;
Fine needle aspiration;
Cytomorphology

Background Anaplastic thyroid carcinoma (ATC) is relatively rare. A correct pathologic diagnosis is mandatory to exclude less aggressive entities, and guide management. We describe our experience with the fine needle aspiration (FNA) cytomorphology of ATC and potential mimics.

Materials and methods Cytology files were searched to recover all cases of ATC/suspicious for ATC. Surgical pathology files were searched for ATC cases having corresponding cytology. FNA was performed using standard technique.

Results Of 59 FNA cases, 34 were correctly diagnosed as ATC (or possible ATC); 22 were false negative, and 3 false positive. All but 2 patients were confirmed by tissue biopsy or clinical course. Of 56 true ATC cases [51 patients (mean age: 69 years) (F:M ratio: 1.24:1)], 40 were primary, 11 metastatic, 4 recurrent, and 1 indeterminate. Carcinoma not otherwise specified (6), malignant not otherwise specified (5), differentiated thyroid cancer (3), atypical (2), suspicious for neoplasm/malignancy (2), and unsatisfactory (4) constituted the false negative diagnoses. Smear cellularity and cell distribution were variable. Malignant cells were mostly epithelioid, but accompanied by pleomorphic, spindle, and multinucleated forms. Differentiated thyroid carcinoma was diagnosed in 5 cases. Background necrosis and/or inflammation were common (80%). Three false positive cases included 1 example each of melanoma, Hürthle cell carcinoma, and metastatic squamous carcinoma. Where follow-up was possible, 91% of patients were dead of disease.

Conclusion A FNA diagnosis of ATC/probable ATC was made in 34 out of 56 cases (sensitivity: 61%). Problematic cases were associated with incomplete sampling, lack of cell block immunostaining, uncertainty of anatomic site, and overlapping morphologic features with non-ATC malignancies.

Introduction

Undifferentiated (anaplastic) thyroid carcinoma (ATC) is a rare variant (<2%) of thyroid carcinoma.[1,2] Patients typically present with a rapidly growing thyroid or neck mass.

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2213-2945/$36
http://dx.doi.org/10.1016/j.jasc.2015.08.001

Associated signs and symptoms are commonly those of tracheal compression including dysphonia, stridor, and hoarseness, along with neck pain and even dysphagia. A history of long-standing goitrous thyroid enlargement, prior neck irradiation, or even a differentiated thyroid carcinoma is not unusual. The disease course is both rapid and fatal with a median survival of five months; fewer than 20% of patients survive 1 year.

Although clinical presentation is usually typical, other treatable entities may mimic ATC. In many instances, because of impending airway compromise, clinical management frequently demands a rapid response. Recommended guidelines recently published by the American Thyroid Association (ATA) state that morphologic diagnosis is mandatory, and whenever possible, a definitive pathologic diagnosis should be obtained prior to surgery. These guidelines also affirm that fine needle aspiration (FNA) cytology should play a role in the preoperative diagnosis of ATC, but in those cases where cytology yields nondiagnostic material because of limited sampling, open biopsy should be performed.[2] As FNA biopsy is currently the de facto diagnostic test initially applied to evaluate any type of thyroid nodule/mass lesion, our aim was to review our FNA biopsy experience with this uncommon thyroid malignancy.

Materials and methods

Case selection

We searched the cytology files for the past 15 years for cases diagnosed as ATC at The Ohio State University Wexner Medical Center and Virginia Commonwealth University. In addition, we searched the surgical pathology files for cases diagnosed as ATC having corresponding cytopathology. Demographic information, clinical history, as well as detailed cytomorphologic data were collected.

Technique

Ultrasound-guided percutaneous FNA biopsy was performed using standard techniques with 21-25 gauge needles. FNA was performed by various practitioners including cytopathologists, endocrinologists, and surgeons. Conventional direct smears were available in all cases. A minimum of 2 smears (often more) per case were examined. Slides were stained using Romanowsky (Diff-Quik) and/or Papanicolaou (Pap) stains. Slides prepared for Pap staining often underwent rehydration of air-dried slides prior to staining. Liquid based slides were made from aspirated material also. Cell blocks (when available) were prepared using the plasma-thrombin method. Formalin-fixed paraffin-embedded tissue sections from a cell block were stained with hematoxylin and eosin.

Results

A total of 56 ATC cases and 3 incorrectly diagnosed (false positive) as such constituted the 59 examples in this series. These were obtained from 51 patients with 5 individuals having two separate FNAs. Of the ATC cases, 31 were women and 25 men (F:M ratio: 1.24:1) ranging from 44-98 years of age (mean age: 69 years) (Table 1). Aspirates were acquired from the thyroid gland (33 cases), neck mass not otherwise specified (NOS) (16), neck lymph node (6), and lung (1). Forty aspirates were from primary neoplasms, 11 from metastatic deposits, 4 from recurrent neck masses, and in 1 case the status of the neoplasm was unknown. Most patients had an FNA biopsy of a single anatomic site. The 5 patients having biopsies at two separate sites included lung and thyroid gland (1 case), bilateral neck masses (2 cases), and thyroid gland plus neck mass (2 cases). All patients (excluding the one with a lung lesion) had some form of typical clinical presentation for ATC, including an obvious (often very large) thyroid mass, history of a rapidly developing neck/thyroid mass, dysphagia, shortness of breath, stridor, and/or hoarseness. Forty-five cases (80%) were confirmed by a subsequent tissue diagnosis, and 9 cases were confirmed by clinical follow-up only. Of 34 individuals having clinical follow-up, 31 (91%) were dead of disease. Seventeen patients had no known clinical follow-up, but of these only 2 did not have a confirmatory tissue diagnosis of ATC. Therefore, only 2 patients (4%) (patient 17 and patient 28) had no tissue verification, or confirmatory clinical outcome.

A total of 34 of 56 FNA biopsies were diagnosed correctly (true positives). (Fig. 1) These diagnostic phrases included “ATC/consistent with, likely, or favor ATC” for a sensitivity of 61% for an ATC diagnosis. A specific diagnosis of ATC or probable ATC was made in 26 of 40 (65%) primary neoplasms, but only 8 out of 15 (53%) metastatic/recurrent ones. Among the 22 false negative (FN) diagnoses, 14 (64%) were still diagnosed as malignant entities, but not as ATC specifically. These interpretations included a differentiated form of thyroid cancer (2 cases papillary thyroid carcinoma [PTC], and 1 Hürthle cell carcinoma [HCC]), carcinoma/poorly differentiated carcinoma (6 cases), and malignant neoplasm NOS (5 cases). Eight of these latter 11 malignant aspirates were from sites designated as “neck”, not specifically as thyroid. Thus, a malignant diagnosis (combining ATC, carcinoma NOS, differentiated thyroid carcinoma, and malignant neoplasm NOS interpretations) was made in 48 out of 56 (86%) of ATC cases. Four aspirates were designated as unsatisfactory for interpretation, 2 as suspicious for neoplasm/malignancy, and 2 as atypical cells only. Of the 4 cases deemed unsatisfactory due to the absence of cellular material, review of subsequent tissue pathology showed extensive sclerosis/hyalinization in 2 of them consistent with the paucicellular variant of ATC.