Liver Mass as First-Time Diagnosis of Sarcomatoid Anaplastic Thyroid Carcinoma: A Rare Malignancy Presenting at an Unexpected Body Site

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Patient: Female, 66-year-old
Final Diagnosis: Sarcomatoid anaplastic thyroid carcinoma
Symptoms: Abdominal pain • dysphagia • dyspnea • fatigue • hemoptysis • jaundice • lymphadenopathy • neck mass
Clinical Procedure: US-guided FNA and core needle biopsy of the liver
Specialty: Pathology

Objective: Challenging differential diagnosis
Background: Anaplastic thyroid carcinomas are aggressive malignancies associated with poor clinical outcomes and challenges in diagnosis. While local/regional disease in the neck is the most usual site of biopsy, in some cases, distant metastases may be the site of initial investigation.

Case Report: A 66-year-old woman with a clinical concern for diffuse metastatic malignancy of unknown primary presented to the Emergency Department (ED) with jaundice and shortness of breath. Recent laboratory test results revealed an elevated CA 19-9. Urinalysis revealed hematuria, proteinuria, and hyperbilirubinemia. She had a computed tomography (CT) scan of the chest, abdomen, and pelvis revealing diffuse involvement of the liver, lungs, adrenals, kidneys, thyroid, pancreas, gallbladder, and brain, but had not yet had a biopsy for definitive diagnosis. An ultrasound-guided liver biopsy was evaluated for cytological features, histological features, and pattern of immunostaining. The cytomorphological histological features were concerning for a high-grade malignancy. Immunohistochemical evaluation revealed that the lesion was positive for CK-AE1/AE3, BRAF, CK7, GATA3, SATB2, PAX8, and TTF-1, but the lesion was not reactive to the following stains: napsin, CK20, CDX2, PCEA, calcitonin, ER and thyroglobulin. The patient was diagnosed with a sarcomatoid anaplastic thyroid carcinoma and died within a few days after diagnosis.

Conclusions: This case illustrates that unanticipated specific diagnoses of widely metastatic anaplastic thyroid carcinoma are feasible when integration of patient history, clinical setting, imaging findings, clinical laboratory results, cytomorphology, histomorphology, and results of ancillary immunohistochemical testing are thoughtfully pursued and synthesized.

Keywords: Biopsy, Fine-Needle • Carcinoma • Image-Guided Biopsy • Neoplasms, Unknown Primary • Thyroid Neoplasms

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Background

Anaplastic thyroid carcinoma (ATC) is an aggressive and usually fatal malignancy, classically presenting as a rapidly enlarging lower anterior neck mass in an elderly patient. It comprises 1.3-9.8% of all thyroid carcinomas [1]. While some patients with ATC have metastatic disease at the time of their original presentations, diagnoses of ATC are often based upon clinical, radiologic, and pathologic correlations centered on the workup of the primary disease in the neck. Metastases from primary ATC at the time of initial evaluation have been reported at various body sites, including but not limited to regional lymph nodes, lungs, liver, bone, GI tract, and brain [2]. We report an unusual case of a patient with ATC whose chief concern and clinical history were listed by the clinical team as “jaundice and liver mass” without mention of disease in the neck. Cytology slides were initially reviewed with only that information.

Case Report

Two days later, after core biopsy and the first round of IHC studies had been received, the pathology team discovered evidence of disease in the neck by performing review of the electronic medical record. A 66-year-old woman presented to the ED with concerns regarding jaundice. Her “yellow-green skin discoloration” had been worsening for a few weeks. She also reported worsening dyspnea and recent dysphagia with solid foods, in addition to fatigue, abdominal pain, and recent hemoptysis. Physical examination revealed conjunctival icterus, jaundice, a tender neck mass, right upper chest wall tenderness, and palpable lymphadenopathy in the lower neck. Assessment notes indicated inability to carry out self-care and being bedridden, even though she reported having been active, swimming and cycling, up to 1 month before her presentation. Imaging studies and clinical laboratory tests were performed.

CT scans confirmed findings compatible with widespread malignancy with mass lesions in her liver (Figure 1), lungs, adrenals, kidneys, neck (Figure 2), pancreas, gallbladder, and brain. Mild anemia, hemoglobin 10.5 g/dL, mild leukocytosis, and leukocytes 17,000/mm³ were confirmed. Bilirubin was 15 µmol/L and hepatic enzymes were elevated. An ultrasound-guided liver biopsy was performed and was evaluated for cytologic features (Figure 3), histologic features (Figure 4), and pattern of immunoreactivity (Figure 5). The combined cytomorphologic and histologic features were those of a pleomorphic sarcomatoid high-grade malignancy with variably spindled-to-epithelioid morphology and associated necrosis. Immunohistochemical studies performed on sections from the accompanying core biopsy confirmed the malignant cells to be positive with CK-AE1/AE3, CK 7, TTF-1, GATA3, PAX8, SATB2, and BRAF V600E.

The malignant cells were nonreactive with CK 20, thyroglobulin, calcitonin, napsin, CDX2, PCEA, and ER.

The combined clinical setting, imaging findings, cytomorphic-ology, histomorphology, and ancillary testing results together allowed for a specific diagnosis of metastatic anaplastic thyroid carcinoma. The patient was referred for palliative care services and died within a few days after diagnosis.

Figure 1. CT scan of abdomen confirming numerous mass lesions in the liver, radiologically compatible with diffuse metastatic disease.

Figure 2. CT scan of neck confirming a large heterogenous mass involving the left thyroid lobe with surrounding soft tissue extension, associated stenosis of the trachea, and cervical lymph node involvement.
Figure 3. Cytomorphology from fine-needle aspiration of the liver specimen received with requisition stating a history of “jaundice and liver mass” without mention of disease elsewhere in the body. (A) Loosely cohesive population of overtly cytologically malignant cells with anisocytosis and varied morphologic features (Papanicolaou stain, 400×). (B) Some malignant cells with rounded-to-oval nuclei and open chromatin and others with spindled hyperchromatic nuclei (Papanicolaou stain, 600×). (C) Sarcomatoid cells with tapering cytoplasmic extensions, nuclear pleomorphism, and coarse chromatin readily identified (Papanicolaou stain, 600×).

Figure 4. Histomorphology from liver core biopsy also received with requisition giving history of “jaundice and liver mass” without mention of disease elsewhere in body. (A) Geographic necrosis comprising much of the core biopsy with viable malignant cells at tips of cores (hematoxylin and eosin, 200×). (B) Pleomorphic malignant cells with predominantly spindled and focally epithelioid morphologies, nucleomegaly and hyperchromasia, compatible with a sarcomatoid morphology (hematoxylin and eosin, 400×).
Discussion

ATC is the most undifferentiated form of high-grade follicular cell-derived thyroid neoplasm [3]. The classic presentation of ATC is that of a rapidly enlarging anterior lower neck mass in a person in the sixth or latter decades of life. This malignancy often invades adjacent structures, causing hoarseness, dysphagia, and dyspnea. These carcinomas are amongst the most aggressive primary thyroid malignancies and sometimes present with metastatic disease at the time of diagnosis, with involvement of regional lymph nodes and the lungs seen with greatest frequency at the time of presentation [3,4]. The median survival of patients with ATC is 4 months, and the disease is associated with a low (10-20%) median 1-year survival rate. Some genetic alterations found in ATCs are mutations in PS3, BRAF V600E, RAS family, and TERT [5]. ATCs may develop in patients with goiter in regions of the world in which endemic goiter is more prevalent [3]. ATCs arise in backgrounds of pre-existing differentiated thyroid carcinomas. Current evidence does not support the theory that ATCs arise de novo [6].

The microscopic appearance of ATCs is highly variable in growth pattern and cytologic appearance. ATCs may show sarcomatoid, giant cell, and epithelioid morphologies. These morphologic appearances may occur singly or in admixed combinations. The sarcomatoid pattern is most common and is composed of malignant spindle cells, which resemble those in high-grade pleomorphic sarcomas. The giant cell pattern consists of highly pleomorphic large cells, some of which are multinucleated. Epithelial pattern ATCs show cohesive cell nests with moderately abundant cytoplasm that is often eosinophilic and may impart a squamoid appearance. True squamous differentiation with keratinization may be observed. Rare morphologies of ATC have also been described, including a paucicellular variant (which can mimic fibrosing Hashimoto’s), a rhabdoid variant, and a small cell carcinoma variant [3,7]. The diversity of histomorphologic appearances should be kept in mind when interpreting cytologic specimens, as mirroring features can be seen in cytologic preparations of the various major patterns and variant types.

PAX8 and TTF-1 are transcription factors that play a role in thyroid organogenesis. PAX8 IHC is variably positive in up to 79% of cases of ATC, but its sensitivity differs among histologic subtypes. Thus, ruling out other primary malignancies and correlating PAX8 positivity with clinical, radiological, and morphological pictures is necessary for optimizing the use of this IHC marker in confirming diagnoses of metastatic ATC [1]. TTF-1 and thyroglobulin are often negative in IHC testing of ATCs. TTF-1 is retained in only 18% of ATC cases, a significantly lower percentage than for PAX8 [8]. TTF-1-positivity is expected in some metastatic lung carcinomas, an important differential to consider in the work up of ATC. BRAF V600E is frequently positive in anaplastic and differentiated thyroid carcinomas. When
positive in conjunction with TTF-1 and PAX8, as in our case, it supports a diagnosis of ATC that likely arose from a differentiated cancer [9]. While positive GATA3 testing results may be of value in supporting a diagnosis of metastatic ATC from an unconfirmed primary, other diseases such as breast carcinomas, urothelial carcinomas, and mesotheliomas are also commonly GATA3-positive. It is prudent to include pankeratin IHC and calcitonin IHC in the workup of potential ATCs. It has been reported that 80% of ATCs are positive for keratins. A negative calcitonin is also useful in terms of ruling out medullary carcinoma of the thyroid, especially in conjunction with a negative result with CEA [1,10].

Histologically, ATCs often show necrosis, increased mitotic activity, and infiltrative patterns of growth. Vascular invasion is commonly present. In a recent study comparing cytomorphological features of ATC with differentiated thyroid carcinoma, the following features were statistically significant in confirming diagnoses of ATC: nuclear pleomorphism, coarse/clumped chromatin, macronucleoli, apoptosis, and necrosis [4]. Considering morphologic features in concert is important, as some less poorly-differentiated thyroid carcinomas and even some benign lesions of the thyroid can show moderate to even marked areas of “endocrine atypia” [4].

Because our patient died shortly after diagnosis, she did not undergo thyroidectomy. Sadly, this is not an uncommon clinical course for ATC, and the disease is almost always fatal, with short survival periods. It is interesting that our patient did not present for medical care until she became jaundiced from metastatic disease, and the clinical care group chose to biopsy a large liver mass, providing the cytopathology team evaluating the case with a history of “jaundice and liver mass”. A drawback in this report is that an autopsy was not performed.

Conclusions

Metastatic disease from a sarcomatoid ATC, as diagnosed in this case, is an important differential diagnosis to keep in mind when an elderly patient presents with multisite metastases from an undefined primary source. Clinical, radiological, and laboratory correlations are of paramount importance in correlating with cytomorphology/histomorphology and in helping to determine the best panel of IHC studies to consider.

Statement

This case will be presented as an abstract poster at the ASCP Annual meeting of 2023.

Declaration of Figures’ Authenticity

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References: