

UNIVERSITY OF
CALGARY

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- Least common form of thyroid carcinoma, accounting for less than 5% of cases¹
- Female predominance, mean age of 65 years^{1,2}
- Very poor prognosis (mortality rate reaching 100%) with a mean survival of less than 6 months^{1,2}
- No known risk factors³
- Greater than 25% of cases exhibit coexisting well-differentiated thyroid carcinoma^{1,2}
- Arise *de novo* or dedifferentiate from well-differentiated carcinoma (commonly papillary or follicular thyroid carcinoma)^{1,4}
- Clinical symptoms include^{1,3}:
 - Firm, painful, rapidly growing low anterior neck mass
 - Dyspnea, dysphonia, dysphagia due to compression of neck structures
- Extrathyroidal extension and distant metastasis at time of presentation is common^{1,2}

- Male; 6th decade; presented with a 4.3 x 2.5 cm right neck mass
- Fine needle aspiration (FNA) revealed papillary thyroid carcinoma
- Histological examination post-thyroidectomy revealed ATC (70%) arising within a tall cell variant of papillary thyroid carcinoma (30%)
- Ancillary tests showed a *BRAF V600E* mutation
- Positive lymph nodes and positive margins prompted an extended right neck dissection
- Biopsies obtained one year after the initial diagnosis confirmed recurrent/residual malignancy and progression into laryngeal skeleton, trachea, soft tissue, and right carotid artery
- Repeat imaging indicated an enlarging right ventricular mass and a defect on the pulmonary valve

- Chemotherapy, immunotherapy, and radiotherapy
- As the disease progressed, goals of care changed from palliative to symptom management to comfort
- Surgeries throughout the course of the disease included:
 - Thyroidectomy
 - Extended right neck dissection
 - Tracheostomy
 - Salvage total laryngopharyngectomy with esophageal reconstruction

- Neck: extensive scar tissue and tumor surrounding nerves, vessels, and muscle was observed
- Lungs: multiple white-tan nodules were present and several pulmonary vessels contained tumor emboli (Fig 1D)
- Heart: a white hemorrhagic mass was observed penetrating the epicardium (Fig 1A). Sectioning the heart revealed the mass to almost completely replace the right ventricular wall (Fig 1B). The mass nearly filled the right ventricular chamber and extended into the pulmonary artery (Fig 1C).

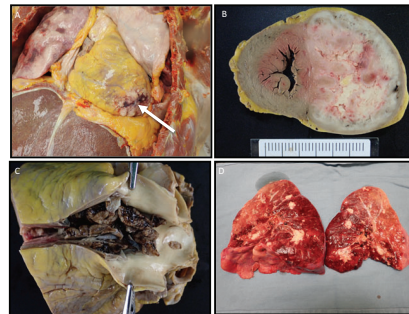


Fig. 1.

- A. Heart *in situ* showing mass invading through the epicardium (arrow)
- B. Transverse section of the heart showing massive tumor infiltration
- C. Pulmonary artery opened showing mass extending through pulmonary valve
- D. Sections of lungs showing multiple white-tan nodules throughout the parenchyma

- Neck contained fibrotic tissue in absence of malignant cells; residual/recurrent malignancy could not be ruled out due to limited size of tissue sample
- Pulmonary and cardiac masses were confirmed to be ATC morphologically resembling that found in the neck on initial diagnosis (Fig 2).

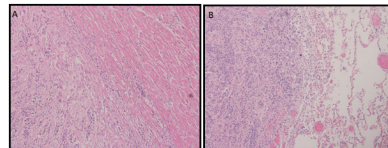


Fig. 2.

A. Cardiac mass, showing malignant cells adjacent to and invading into the myocardium (H&E, 100x magnification)

B. Pulmonary mass, showing malignant cells adjacent to lung parenchyma (H&E, 100x magnification)

- Complications of extensively metastatic anaplastic thyroid carcinoma
 - Massive hemorrhage through tracheostomy likely secondary to abscess erosion into neck vessels and/or tumor erosion into lung vasculature

- FNA is approximately 90% accurate in diagnosing ATC⁴
- Core biopsy should be performed when FNA is nondiagnostic and ATC is clinically suspected⁴

- ATC may be misdiagnosed using FNA due to⁴:
 - Fibrosis
 - Necrosis, hemorrhage, leukocyte infiltration
 - Areas of well-differentiated thyroid carcinoma within the same mass
- CT and PET scans are useful for finding metastatic disease and determining extent of spread⁴
- No standard treatment for ATC exists; an approach combining surgery, chemotherapy, and radiotherapy should be utilized²

- ATC uses the same T stage parameters as differentiated thyroid carcinomas (previously ATC were always assigned T4) as outlined by AJCC⁵
- ATC is always stage IV due to its severe prognosis and tendency for rapid progression⁴
- Subgrouped into IVA, IVB, and IVC based on AJCC TNM parameters (Fig 3)^{5,6}:
 - IVA: intrathyroidal disease
 - IVB: gross extrathyroidal extension or lymph node metastasis
 - IVC: distant metastasis

T	N	M	Stage
T1a-T3a	N0	M0	IVA
T1a-T3a	N1	M0	IVB
T3-T4	Any N	M0	IVB
Any T	Any N	M1	IVC

Fig. 3. TNM parameters for staging of ATC according to AJCC 8th Edition, adapted from Tuttle *et al.* 2017

- Majority of ATC arise from a well-differentiated thyroid carcinoma suggesting that well-differentiated carcinomas may be precursor lesions^{4,7}
- Chromosomal gains, deletions, and genetic mutations such as *RAS*, *BRAF*, and *p53* may be responsible for the transformation from tall cell papillary to ATC⁴

- Lungs are the most common location for distant metastasis, followed by cervical and intrathoracic lymph nodes^{4,7}
- Other locations include, but are not limited to, pleura, adrenal glands, liver, and brain⁷
- Cardiac metastasis from primary ATC is rare, occurring only in 1-2% of cases^{8,9}
- ATC metastasizes to areas in the heart not frequently involved by metastasis from other tumors; likely due to the aggressive nature of ATC⁹

- ATC is a rare, aggressive tumor associated with rapid metastasis and a poor prognosis
- ATC is often found arising within a differentiated thyroid carcinoma
- Thorough sampling and accurate, timely histological diagnosis is crucial in providing optimal patient care as well as understanding the clinical course and prognosis of the disease
- Further research into this disease is required to develop effective therapies

- [illegible]