

Dilemma in the Cytodiagnosis of Sarcomatoid Variant of Anaplastic Carcinoma Thyroid- a Case Report

Dr Sonali Datar¹, Dr Rasika Gadkari², Dr Pradip Umap³

Assistant Professor^{1,2,3}, Department of pathology, Indira Gandhi Government Medical College, Nagpur, Maharashtra, India

Abstract

Anaplastic thyroid carcinoma (ATC) is the most aggressive form of thyroid cancer. Although less than 5% of thyroid cancers, it is responsible for more than half of deaths attributed to thyroid cancer, with a mortality rate over 90% and a mean survival of six months. The diagnosis of ATC is usually based on clinical examination, cytology, histology, imaging study and immunohistochemistry. FNAC is reported to be 90% accurate in diagnosing ATC. A preoperative cytological diagnosis helps to determine the treatment plan in these patients. ATC needs to be differentiated from high grade tumors with the microscopic features originating from adjacent structures and at times immunohistochemistry is essential for establishing the correct diagnosis.

The problems in sarcomatoid variant of ATC are compounded when cellularity is low and epithelial cells are sparse. In such cases diagnosis of malignancy and differentiation from other soft tissue tumors presents major dilemma.

Key words; Anaplastic thyroid carcinoma, cytological diagnosis, immunohistochemistry.

I. INTRODUCTION

Anaplastic thyroid carcinomas (ATC) are rare, aggressive undifferentiated tumors with a very high mortality. It usually affects elderly people with a mean age in mid 60's.^[1] We report a case of young female with lung metastasis with fatal outcome in just one month. In sarcomatoid anaplastic carcinoma thyroid, a variant with low cellularity is a diagnostic challenge. With differential diagnosis, diagnoses ranging from Riedel's thyroiditis on one hand, other soft tissue tumors and low grade sarcomas on other, a preoperative recognition of this tumor helps to plan treatment for these patients.^[2] Immunohistochemical markers have definite role to differentiate between anaplastic thyroid carcinomas from soft tissue tumors.^[3]

II. CASE REPORT

A 40 years old female patient presented with swelling in midline of neck since last three months with complaint of severe breathlessness since one month in

ENT OPD. She also complained of change in voice and difficulty in swallowing since last fifteen days. On physical examination, well defined swelling was noted measuring 12×8cm extending from hyoid bone above to sternal notch below more on right side. Lower limit of the swelling could not be palpated. It was hard, fixed to underlying structure, did not move with swallowing. Overlying skin was shiny. Her thyroid function tests were within normal limits. No concomitant or past H₂O benign thyroid disease was reported by patient. No regional lymphadenopathy was found. Ultrasonography revealed ill defined heterogeneously hyperechoic lesion arising from right lobe of the thyroid probably of neoplastic etiology.



Figure 1 (a): Photograph of patient showing thyroid swelling

CT scan revealed large moderate heterogeneously enhancing necrotic mass arising from right lobe of thyroid with retrosternal extension s/o primary neoplastic lesion showing heterogenous necrotic areas suggestive of metastasis.

With clinical diagnosis of malignant thyroid neoplasm, guided FNAC of thyroid mass was done. Multiple aspirations were tried showed low cellularity of loosely cohesive oval to spindle cells with scanty myxoid stroma in haemorrhagic background. Spindle cells showed mostly uniform nuclei with mild nucleomegaly. The cellular cohesion was lost and many isolated spindle cells were seen. On vigorous searching, few spindle cells with nuclear

pleomorphism, hyperchromasia, prominent nucleoli and occasional tumor giant cell were found with sparse inflammatory cells and necrosis.

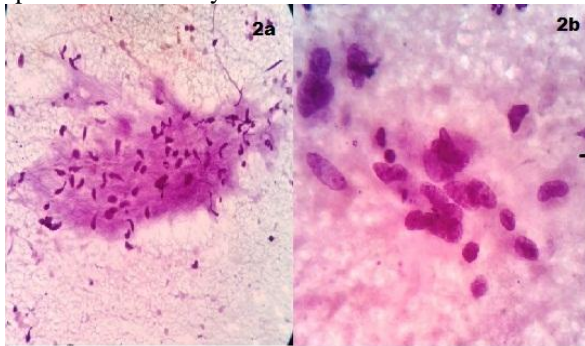


Figure 2(a) and 2(b): FNAC smears showing myxoid stroma and pleomorphic hyperchromatic spindle cells with prominent nucleoli at places (H&E x200)

No stromal fragments with sclerosis or hyalinization and no epithelioid cells seen. In view of rapidly growing thyroid mass, CT findings, with spindle cell morphology and nuclear atypia a diagnosis of spindle cell variant of Anaplastic thyroid carcinoma favoring paucicellular variant was suggested. Histopathology was advised for confirmation with immunohistochemistry as cell block showed mostly blood. Section from thyroid mass showed interlacing bundles of spindle cells with collagen with myxoid areas. Individual spindle cells showed mild nuclear pleomorphism, occasional mitotic figures and anaplastic large cells. Areas of necrosis was seen. No epithelial elements were seen

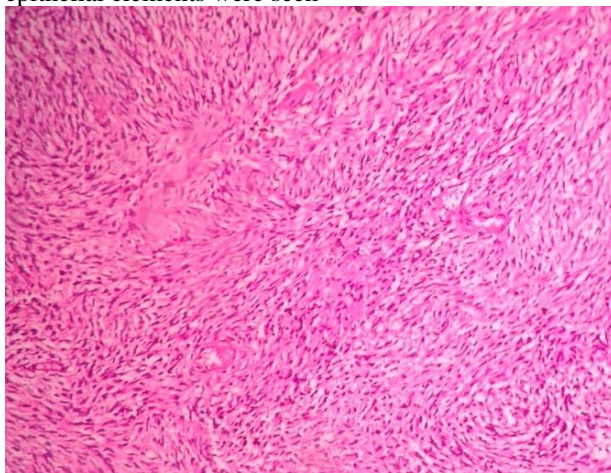


Figure 3: Biopsy showing interlacing bundles of spindle cells with collagen with myxoid areas (H&E x200)

On immunohistochemistry tumor cells exhibited focal immunopositivity for pancytokeratin and TTF-1. Immunonegativity for thyroglobulin/EMA/CEA/Pax 8/synaptophysin/chromogranin and strong and diffuse immunopositivity for vimentin was seen [Figure 4a, 4b, 4c].

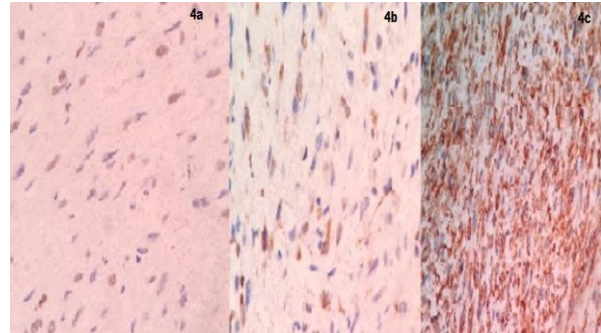


Figure 4(a) 4(b) 4(c): Immunohistochemistry TTF-1 positivity, Cytokeratin positivity and vimentin positivity respectively

Pancytokeratin positivity confirms epithelial origin. Vimentin positivity confirms spindle cell nature. Synaptophysin and chromogranin negativity rules out medullary carcinoma thyroid. EMA and CEA negativity ruled out sarcomatoid squamoid differentiation. Thus diagnosis of Anaplastic carcinoma thyroid spindle cell variant was confirmed. Patient was referred to the oncology unit for palliative treatment-radiotherapy and chemotherapy however succumbed to her condition in just one month.

III. DISCUSSION

ATC is an aggressive form of cancer of thyroid gland and represents less than 5% of all thyroid cancers.^[4,5] It usually presents in people in their 60 and 70s and has about 55-77% female preponderance. Patients presents with a rapidly growing mass that frequently have extra thyroid extension. Regional nodal metastases and vocal cord paralysis are seen in up to 40% and 30% respectively.^[2] Systemic metastases occur in up to 75% of patients, with lung being the most common site. There are three patterns of ATC-Spindle cell, giant cell and squamoid. All of them carries same prognosis.^[6]

There are two etiopathogenetic theories 1) One is development due to anaplastic transformation of an accompanying well differentiated tumor. 2) other is de novo development theory. FNAC is reported to be 90% accurate in diagnosing ATC.^[7]

On cytology spindle cell variant of ATC needs to be differentiated from varied conditions ranging from nonneoplastic, benign and malignant tumors. The fragments of spindle cells in this case showed minimal atypia and need to be differentiated from Reidel's thyroiditis which is a rare chronic fibro inflammatory process with favorable prognosis. Riedel's thyroiditis can mimic ATC as the sclerosis causes breathlessness due to compression. On microscopy it shows fibrous stroma which is hyalinised and never myxoid, and there is no atypia, no necrosis, no vascular invasion and are negative for epithelial markers.^[8] On cytology uniform spindly fibroblastic cells are seen in these tumors with insignificant atypia. Benign nerve sheath tumors like Schwannomas and Neurofibromas shows

single or wavy bundles of elongated spindle cells with pointed ends with bland chromatin with moderate degree of nuclear pleomorphism. Benign neoplasms like solitary fibrous tumor and benign nerve sheath tumors never present clinically with huge swelling with compressive symptoms.

Most common malignant tumors of thyroid like Papillary carcinoma of thyroid presents with characteristic nuclear features such as finely granular, powdery nuclear chromatin, nuclear grooves, intranuclear cytoplasmic inclusions and presence of psammoma bodies infrequently and dense cytoplasm with well defined borders. Immunohistochemically it is TTF-1, Vimentin, Cytokeratin, Thyroglobulin, Pax 8 positive.^[3,6]

Spindle cell variant of Medullary thyroid carcinoma is characterized by eccentrically placed nuclei, neuroendocrine type chromatin, inconspicuous nucleoli, binucleated and multinucleated cells, ill defined cell border and a clean background and presence of amorphous amyloid material sometimes.^[9] On immunohistochemistry synaptophysin and chromogranin positivity is noted.

Spindle cell variant of ATC show neoplastic cells arranged in loose clusters as well as dispersed singly in haemorrhagic background. Individual cells showed malignant cytologic features including large pleomorphic nuclei with irregular nuclear membrane, coarse clumped chromatin and prominent nucleoli. Immunohistochemistry shows a variable immunophenotype. Immunoreactivity for cytokeratin is present in 40% to 100% of cases. Vimentin is consistently present in the spindle cell component, whereas EMA and CEA are particularly expressed in the squamoid cells.

Typically, ATC cells are not immunoreactive for thyroglobulin, calcitonin, TTF-1, PAX8 positivity found in 79% of ATCs and in up to 92% of ATCs showing squamoid features.^[3,6] Treatment of ATC is controversial and nonspecific. Patient often present at an advanced stage making curative resection unfeasible so multimodal treatment is needed.^[10]

REFERENCES

- [1] Sze-How NG, Imisairi AH. The Aggressive Anaplastic Thyroid Carcinoma: A case Report and Institutional Review. *World J Endocr Surgery* 2012; 4(1):20-22.
- [2] Alwani Mobeen, Rathod Gunvanti B. :Diagnosis of anaplastic thyroid carcinoma on fine needle aspiration cytology-A rare case report. *International Archives of Integrated Medicine* 2015; 2(3):183-187.
- [3] Ragazzi M, Ciarroochi A, Sancisi V, Gandolfi G, Bisagni A, Piana S. Update on anaplastic thyroid carcinoma; Morphological, molecular, and genetic features of the most aggressive thyroid cancer. *Int J of Endocrinol* 2014; 790834.
- [4] Mehadi G, Ansari H.A, Siddiqui, S.A. Cytology of anaplastic giant cell carcinoma of the thyroid with osteoclast-like giant cells-A case report. *Diagn. Cytopathol* 2007; 35(2):111-112.
- [5] P. Piromchai, T. Ratanaanekchai and P. Kasemsiri. Diagnosis and Treatment of anaplastic thyroid carcinoma. *International Journal of Clinical Medicine* 2012; 3(1): 69-73.
- [6] Huang JC, Huang SC, Chou FF, Wang PW. Papillary Thyroid Carcinoma with Anaplastic Transformation: A case report. *J Intern Med Taiwan* 2009; 20:167-170.
- [7] Gunes P, Aker FV, Erkan M, Demirturk P, Dulundu E. Incidental anaplastic thyroid carcinoma: A case report. *Turk J Pathol* 2008; 24(1):54-58.
- [8] Juan Rosai. In Rosai and Ackerman's Surgical pathology. Vol 1, 9th ed. Mosby: Elsevier; 2004. pg 515-568.
- [9] Orell SR, Sterret GF, Whitaker D. In Fine needle aspiration cytology. Orell SR editor. 4th edition Elsevier; 2005. 125-158.
- [10] S. Ursino, F. Fiorica, A. Stefanelli, M. Pedriali, C. Colosimo, P. Cocuzza et al. Anaplastic Thyroid Cancer: a case report of a long term survival patient and review of literature data. *European Review for Medical and Pharmacological sciences* 2014; 18:1368-1372.