CASE REPORT

ANAPLASTIC THYROID CARCINOMA AND ITS OSTEOCLASTIC VARIANT

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ABSTRACT

Anaplastic thyroid carcinoma (ATC) is an uncommon highly malignant tumor. Osteoclastic type giant cell tumor of the thyroid is an extremely rare morphological variant of the undifferentiated carcinoma thyroid gland characterized by the presence of a large numbers of non-neoplastic multinucleated giant cells resembling osteoclasts, containing many small round to oval, uniform benign appearing nuclei. Frequent association with preexisting thyroid lesion is seen. We report here this unusual aggressive tumor in a 70 year old female who presented with dysphagia, dyspnea and a progressively increasing swelling over the anterior aspect of the neck. Histologically, many multinucleated osteoclast-like giant cells were seen accompanying the pleomorphic tumor cells and a diagnosis of anaplastic thyroid carcinoma with osteoclast like giant cells was made.

Key words: Anaplastic thyroid carcinoma, Osteoclasts, Thyroid gland, Giant cells

INTRODUCTION

Anaplastic thyroid carcinoma (ATC) is the undifferentiated tumor of the thyroid follicular epithelium.[1,2] It is the most aggressive thyroid gland neoplasm having a dismal prognosis.[1,3] It accounts for 5-10% of all the thyroid malignancies.[4,5,6] Microscopically, squamoid, giant cell and/or spindle cell variants are the usual patterns seen in the ATC.[1,3,7] However, association of this tumor with many multinucleated giant cells resembling osteoclast is very rare.[2,4,6] No evidence of osteoid formation is seen in these tumors.[4]

CASE REPORT

A 70 years female presented with a swelling of five years duration over the anterior aspect of the neck that had been progressively increasing in size. For the past two months, she had complaints of difficulty in breathing, hoarseness of voice, dysphagia and loss of appetite along with a rapid increase in the size of the neck mass. On examination, a diffuse, firm to hard, non-tender swelling, not moving with deglutition was noted over the anterior aspect of the neck, measuring 12 x 9 cm in size, extending into supraclavicular fossa. On routine investigations, low hemoglobin of 6gm% was noted. Thyroid function tests showed a minimal rise in the TSH levels. FNAC of the mass was first done 4 years back which was reported as multinodular goiter. Computed Tomography study revealed a diffusely enlarged and heterogeneously enhancing thyroid gland with superior mediastinal extention. Large nodular lesions with cystic degeneration, microcalcification and enhancing mural nodules were noted in both the lobes of the gland. Associated tracheal compression was seen (Fig.1). Patient underwent total thyroidectomy.

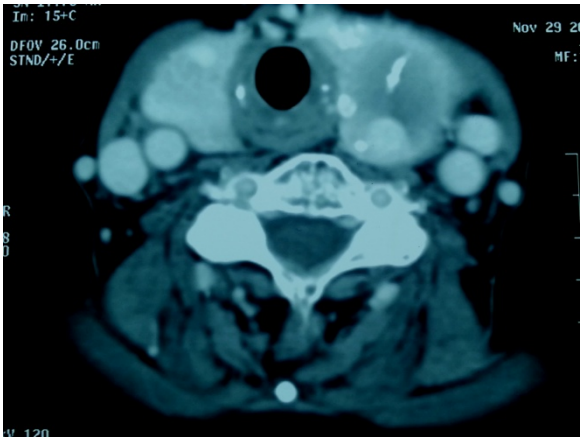

Fig.1: Axial Contrast enhanced CT scan showing presence of a cystic lesion with internal calcifications and intensely enchaning mural nodule in left lobe of thyroid gland.

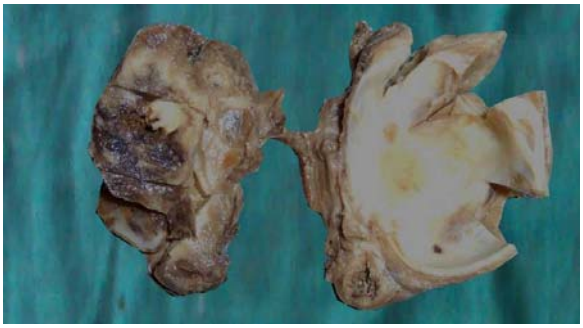

Fig. 2: Thyroidectomy specimen showing solid cystic tumor with extensive hemorrhage and necrosis.

Pathological Findings: Gross examination revealed a specimen of the thyroid gland with two lobes connected by the isthmus measuring 10 x 7 cm. On cut section, solid cystic areas with extensive hemorrhage and necrosis were seen (Fig.2). Microscopic examination of multiple sections from the specimen revealed a multifocal tumour composed of solid areas with pleomorphic, bizarre mononuclear cells and many osteoclast like giant cells (Fig.3A). Giant cells were large with 10 to 30 bland looking vesicular nuclei. Heavy lymphocytic infiltration and prominent vascularization was seen. Atypical mitosis, extensive areas of hemorrhage and necrosis and vascular invasion were also present (Fig.3B). Areas showing features of colloid goiter with cystic degeneration and focal calcification were also recognized in sections studied. A diagnosis of osteoclastic variant of undifferentiated carcinoma thyroid was made.

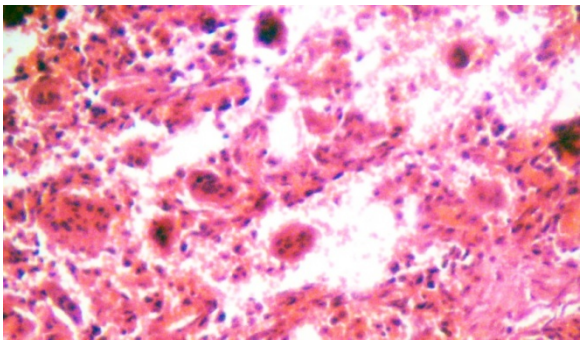

Fig.3A: Numerous osteoclasts-like multinucleated giant cells embedded in a stroma of pleomorphic monomorphic tumor cells. (H&E Stain, X400)

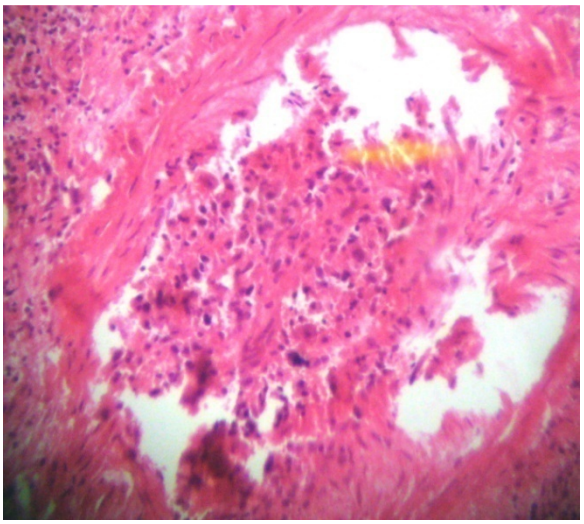

Fig.3B: Tumor cells invading the vessel wall. (H&E Stain, X400)

DISCUSSION

Anaplastic carcinoma of the thyroid gland is a rare swiftly growing extremely aggressive tumor.[1,2] The peak incidence is in late adulthood with slight female preponderance.[2,6] Clinically, the patient usually presents with a rapidly increasing bulky neck mass associated with dysphonia, dysphagia and dyspnea. Compression of the adjacent vital structures of the neck and extension into the ribbon muscles, esophagus, trachea, skin and adjoining bones is generally present at the time of initial presentation in most of the cases.[2,3,7] Most are fatal within 6 to 12 months of the initial diagnosis.

Origin of these tumors has been investigated by many authors.[2] For many years, most of these anaplastic giant cell tumors of the thyroid were considered as sarcomas.[2,4,6] However, Ewing in 1928, expressed doubt regarding the sarcomatous nature of these tumors. In 1930, Smith proposed an epithelial origin. The osteoclastic variant of ATC was first reported as a tumor of unknown histogenesis by Nadal in 1910. In 1940, Hebbel classified them as giant cell tumors of epithelial origin. Ultrastructural studies done by Jao and Gould, in 1974, supported this theory suggesting a follicular epithelial origin for these tumors.[2,4,5,6] Since then, based on cumulative evidence from electron microscopic, immunohistochemical and cell culture studies, most pathologists agree that ATC with all its heterologous tumor elements arise from follicular epithelial cells.[1,2,6]

Histologically, anaplastic carcinoma of the thyroid gland is broadly classified into squamoid and sarcomatoid subtypes. The sarcomatoid variant commonly shows two patterns – spindle cell and giant cell.[3] These three major subtypes can sometime coexist and they are not predictive of the patient's outcome.[1] The unusual variant of the usual anaplastic giant cell carcinoma associated with many bland looking multinucleated giant cells resembling the osteoclasts is the so called osteoclastic type and is extremely uncommon with only a few immunohistochemical and cytological well documented cases in the literature.[1,4,6] Microscopically, the osteoclastic variant of ATC characteristically reveals a solid proliferation of undifferentiated pleomorphic mononuclear stromal cells intermingled with many multinucleated osteoclast-like giant cells (MOGC).[1,2,5,6] These MOGCs are packed with several uniform sized, round to oval, benign nuclei, often centrally placed. The cytoplasm is abundant and dense eosinophilic.[1,2,5] Many researchers believe that these cells are non neoplastic, reactive cells of monocytic/histiocytic lineage that are derived as a result of mononuclear cell fusion.[1,3,4,7] Immunohistochemically, this theory is supported by the fact that the MOGC express CD68 and cathepsin K with colocalisation of cathepsin B and its endogenous inhibitor cystatin C. These also show cellular staining for lysozyme.[1,4]

Common microscopic diagnostically useful features of ATC are high mitotic activity, large areas of necrosis with palisading at necrotic edges and tendency for tumor cells to invade the walls of the veins replacing normal smooth muscle.[3,5]

Most of these tumors arise as a result of dedifferentiation of preexisting differentiated thyroid tumor.[2,3,6,7] Anaplastic transformation mostly develops in papillary carcinoma or its variants but may also take place in follicular, Hurthle cell or insular carcinomas or in a metas-

tatic focus.[3,6,7] Association of giant cell ATC with preexisting goiter has also been documented in literature by some investigators.[2,4,6,7]

Immunohistochemically, in 50-100% of the cases, these undifferentiated tumors are positive for low molecular weight keratins (CK7+ve, CK20-ve), thus, confirming their epithelial origin.[3,4] Vimentin positivity is present in spindle cell component.[3,4,7] Anaplastic carcinomas in 79% of the cases express PAX8. TTF-1 is usually negative except in few cases with a squamoid component.[3] Thyroglobulin is generally undetected.[3,7]

At molecular level, the major genetic alteration present in majority of ATC is the presence of inactivating TP53 mutations which is not present in residual differentiated tumor. Other common mutations are RAS and BRAF mutations which are seen in both differentiated and dedifferentiated cancers.[3,7]

To conclude ATC with osteoclast- like giant cells is a rare, aggressive undifferentiated tumor having a very poor prognosis. Similar tumors have been described in breast, pancreas, skin, ovary, soft parts and heart.[3,4,6]

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