Anaplastic Transformation of Differentiated Thyroid Carcinoma

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Abstract: Anaplastic thyroid cancer (ATC) is one of the most aggressive malignancies that arise from transformation of pre-existing differentiated thyroid cancer (DTC). However, the carcinogenic mechanism of anaplastic transformation remains unclear. We describe a case for huge goiter diagnosed as papillary thyroid carcinoma, which underwent thyroidectomy. The final histology showed anaplastic transformation. The clinical and possible etiological aspects are discussed.

Keywords: anaplastic, thyroid cancer, transformation

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Introduction

Anaplastic thyroid cancer (ATC) ranks among the most lethal of all human malignancies[1-3]. The majority of patients diagnosed with ATC have evidence of distant metastatic disease at presentation, and despite aggressive treatment that includes surgery, chemotherapy, and radiotherapy, almost all affected individuals eventually die of their disease[4-5]. The fatal disease course in patients with ATC represents a dramatic contrast compared to the excellent prognosis of individuals diagnosed with differentiated thyroid cancer (DTC). Fortunately, ATC is a rare type of thyroid cancer representing less than 2% of newly diagnosed malignant thyroid tumours[6]. Considerable clinical, pathological, and experimental evidence supports the hypothesis that ATC transforms, or evolves from pre-existing DTC[7] . Nonetheless, the etiology of anaplastic transformation as a step in thyroid tumorigenesis currently remains unclear.

We describe here a case of huge goiter in an old lady who presented with pressure symptoms, diagnosed as papillary carcinoma thyroid, who underwent thyroidectomy and the final histological diagnosis was confirmed as anaplastic transformation.

Case Scenario

90-year-old female patient was admitted through the Accident and Emergency, with huge neck swelling of 10 years duration, stridor attacks, shortness of breath, difficulty of swallowing, change in voice and loss of weight. She had no previous medical illness. On admission, she was very ill, tachypnoeic. Neck examination revealed huge swelling of the thyroid gland more on the left side, with lobulated surface. The neck veins were severely engorged with dilated superficial veins on the chest wall (Fig 1).

Laboratory investigations were within normal limits, chest x-ray showed compression of the trachea and multiple nodules in both lungs. Fine needle aspiration (FNA) showed papillary carcinoma. At surgery, the patient was intubated with difficulty as the trachea was kinked. The tumor was invading the strap muscles and the carotid vessels. Subtotal thyroidectomy was performed. Postoperatively, the patient was shifted to the surgical intensive care. On extubation on next day, the patient was doing well and there were no more pressure symptoms. The serum calcium was 2.2 mmol/L in the first post-operative day. On the 6th day postop the patient developed severe drop in O_2 saturation, due to the extensive lung metastasis, reintubated and transferred to surgical intensive care. She expired on the 10th postop day.

Fig. (1). Huge goiter in a 90-year old lady during anesthesia.

Discussion

In thyroid tumours the co-existence of well and poorly differentiated tumour has led to the hypothesis that poorly differentiated thyroid tumours develop from well-differentiated type. Currently there is no generally acceptable technique for predicting which thyroid neoplasms will undergo anaplastic transformation. In the past investigators believed in that thyroid stimulating hormone (TSH) played an important role in this process [8]. There is also clinical evidence that irradiation has an etiological role in anaplastic tumour development [9], and the suggestion was raised that both TSH and irradiation may act as co-factors in the transformation process. However, Abe et al [10] have demonstrated that growth and metabolic activity of undifferentiated thyroid tumours is independent of TSH function. Also minority of individuals with ATC was found to have a history of radiation exposure [3].

Our patient was a 90 year-old lady with a long standing thyroid swelling is of some interest. It was observed that anaplastic tumour evolution occurs in older individuals, often with longer standing history of a thyroid tumour or history of incomplete resected thyroid tumour [2-4,11]. This is taken as the basis for the occurrence of anaplastic transformation. The histopathological

examination of the patient's specimen showed association of anaplastic tumour with DTC with a transitional zone (Fig. 2). The pathological association of anaplastic tumour with DTC component led to emergence of the anaplastic transformation concept, which can be considered as a form of post-malignant transformation progression [12,13].

Anaplastic tumour cell lines, grown in culture or as xenografts in athymic mice, have provided investigators with an experimental model to study both the biology of the disease and the effects of various treatment regimens [14,15]. Some authors presented molecular evidence that suggests ATC arises from a pre-existing DTC [16]. Others described mutation of the Tp53 gene to be commonly present in anaplastic tumours but rarely present in DTC [17,18].

A recent report showed that derangement of the E-Cadherin/Catenin Complex is associated with the transformation of DTC into ATC [19]. There is also a suggestion that loss of TCEAL4 expression, might be associated with development of ATC from DTC [20]. It is clear, therefore, that debate still continues on the exact aetiology in the transformation of DTC into anaplastic type as the mechanisms that underline the transformation of DTC into anaplastic are complex and still awaits further clarification.

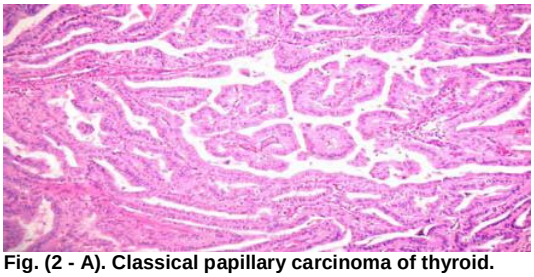

Fig. (2 - A). Classical papillary carcinoma of thyroid.

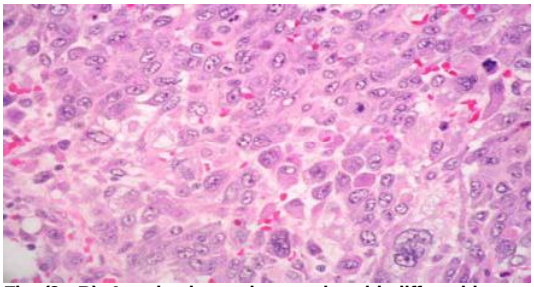

Fig. (2 - B). Anaplastic carcinoma, thyroid, diffuse bizarre, anaplastic cells, with enlarged, pleomorphic nuclei, frequent mitosis, neither papillary nor follicular differentiation seen.

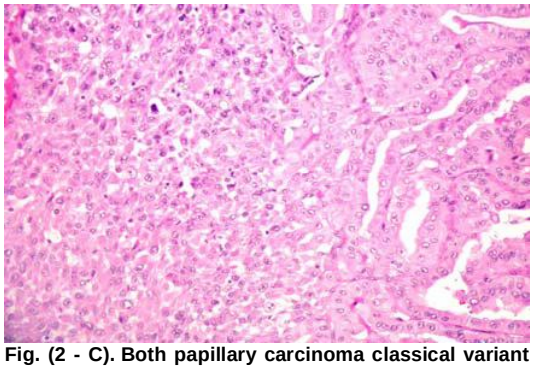

Fig. (2 - C). Both papillary carcinoma classical variant in the left side of the picture transforming into anaplastic carcinoma in the right side of the picture (arrows denote the classical papillary carcinoma).

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