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RESEARCH ARTICLE

ANAPLASTIC TRANSFORMATION OF PAPILLARY THYROID CARCINOMA: A RARE BUT FATAL SITUATION(CASE REPORT)

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Abstract

Anaplastic thyroid cancers are the final dedifferentiation form of follicular thyroid tumors. They are one of the most serious cancers with a survival average of 6 months after diagnosis. Many studies suggest that anaplastic thyroid cancers are a form of a pre-existing differentiated thyroid carcinoma, but only a few cases have been reported in the literature. We report the case of a 64-year-old patient, with a 30-year history of a thyroid nodule. He presented a latero cervical swelling with compression signs, evolving for 2 months in a context of general state alteration. The tomodensitometry objectified a malignant process of the right thyroid compartment with repression of the upper airways. This process is associated with a large necrotic right jugulocarotid adenopathy, multiple lymph nodes, and secondary pulmonary parenchymal lesions (balloon release). The patient underwent a total thyroidectomy with lymph node dissection. The anatomopathological study revealed an anaplastic carcinoma of the thyroid developed on a papillary thyroid carcinoma (PTC). Thus supporting anaplastic transformation of PTC. Subsequently, the patient received radiochemotherapy but died from the disease 3 months after diagnosis. The case reports highlight that although rare, the transformation of a differentiated thyroid carinoma into anaplastic carcinoma can occur on the initial lesion or on metastases. This transformation radically changes the patient's prognosis. Early management and rigorous long-term follow-up are therefore necessary.

Introduction:-

Papillary thyroid carcinoma is the most common malignant tumor of the thyroid with a relatively favorable prognosis. Studies support the concept that anaplastic thyroid carcinoma arises from a pre-existing differentiated thyroid carcinoma.(Kim et al. 2016) This transformation is rare, and the anaplastic carcinoma is one of the most aggressive cancers. It is responsible for more than half of the deaths attributed to thyroid cancer, with a survival

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average of 6 months after diagnosis.(Ragazzi et al. 2014) We report the case of an anaplastic carcinoma developed on a pre-existing papillary thyroid carcinoma with lymph node and lung metastases.

Case Report:

We report the case of a 64 years old patient, with a history of balanced type 2 diabetes and a 30 years neglected thyroid nodule. The size of the nodule has been increased slowly. Recently, two months before hospitalisation, the evolution was marked by the appearance of a swelling in the right cervical region rapidly increasing with signs of compressions such as dysphonia and swallowing difficulties. All of this evolving against a background of fever and general condition deterioration with significant weight loss. Cervical ultrasound revealed an hypoechoic right toto-lobar thyroid nodule classified Ti-Rads 5, with an upper right heterogeneous jugulocarotid lymphadenopathy containing a tissue look like the thyroid gland measuring 44 mm short axis.

The tomodensitometry objectified a malignant process of the right thyroid compartment of 3x6x7 cm plunging in endothoracic (laterotracheal) with repression of the upper airways and the trachea on the left, without vascular invasion. This process is associated with a large necrotic right jugulocarotid adenopathy measuring 6.5x3.6 cm with multiple lymph node and secondary pulmonary parenchymal lesions (balloon release) (**Figure 1**). Thyroglobulin was greater than 1500 ng / ml suggesting the differentiated origin of tumor proliferation, other tumor markers were negative.

The patient underwent a total thyroidectomy with lymph node dissection. The anatomopathological study of the surgical specimen revealed an anaplastic carcinoma of the thyroid developed on a papillary carcinoma in its vesicular variant measuring 7 cm in long axis, infiltrating the tumor capsule, without breaking the thyroid capsule. Presence of images of vascular emboli. With central lymph node metastases and right jugulocarotid arteries from the anaplastic process with capsular invasion (**Figure 2**).

A multidisciplinary consultation meeting indicated concomitant radiochemotherapy for the anaplastic component with ARI therapy with I131 and braking treatment with L-Thyroxine for the differentiated component. The evolution was marked by a deterioration of the general condition, with anorexia, vomiting and cachexia (weight loss of 10 kg in 1 month). Control of cervical lesions, but rapid progression of lung metastases in favor of the latter anaplastic origin (**Figure 3**). The patient died three months after surgery from respiratory distress.

Discussion:-

Anaplastic thyroid carcinoma is the most aggressive thyroid cancer (50% of all thyroid cancer-related mortalities). Although it represents only 1 to 2% of all thyroid tumors. The average age of diagnosis is 60 years (64 years for our patient), with a survival average of six months after diagnosis.(Gentile et al. 2020) The pathogenesis of anaplastic thyroid cancer remains unclear, the association with pre-existing differentiated thyroid carcinoma has been described in several cohorts.(Lam et al. 2000) This anaplastic transformation is a post-malignant progression of a differentiated thyroid process after several years of evolution.(Wiseman et al. 2003)

This concept has been confirmed by molecular studies. A recent next-generation sequencing study reported that anaplastic carcinoma contains a higher number of mutations than papillary carcinoma suggesting a gradual build-up of somatic mutations during progression from papillary to anaplastic carcinoma.(Landa et al. 2016) Another study demonstrated the involvement of the BRAF gene mutation and the TERT promoter gene as predisposing factors for this transformation.(Oishi et al. 2017) Anaplastic transformation occurs in the thyroid gland, regional lymph nodes, or in distant metastases from papillary thyroid carcinoma (pleural, pulmonary, mandibular, etc.). (Abe et al. 2014; Ambelil et al. 2016; Kim et al. 2016; Wiseman et al. 2003)

In our case, anaplastic carcinoma appeared after 30 years evolution of a thyroid nodule, while evolution duration of the papillary carcinoma is undetermined. Anaplastic transformation is probably produced in the thyroid carcinomatous focus as suggested by the presence of anaplastic foci within the papillary proliferation, with an exclusively anaplastic nature of lymph node metastases. Altough, the thyroglobulin level suggests the presence of papillary carcinoma metastases, the dramatic development of lung metastases is more in favor of an undifferentiated process.

Therapeutic management requires a multidisciplinary approach. According to recent guidelines from the American Thyroid Association, surgery, radiotherapy and / or chemotherapy should be considered for the anaplastic

component.(Molinaro et al. 2017) Braking therapy with L-thyroxine and therapy with I131 are also indicated for the differentiated component. In our case, this therapeutic approach allowed control of the cervical site, but was ineffective on pulmonary metastases whose progression was fatal for our patient.

Finally, new molecular targeted therapies are an emerging promising treatments. These drugs are often multiple receptor tyrosine kinase inhibitors, several have been tested in clinical trials with encouraging results so far and which may, in the near future, improve the prognosis of one of the most common carcinomas.(Molinaro et al. 2017)

Figure 1:- Initial CT images of the patient showing the tumour process with lymph node and lung metastases.

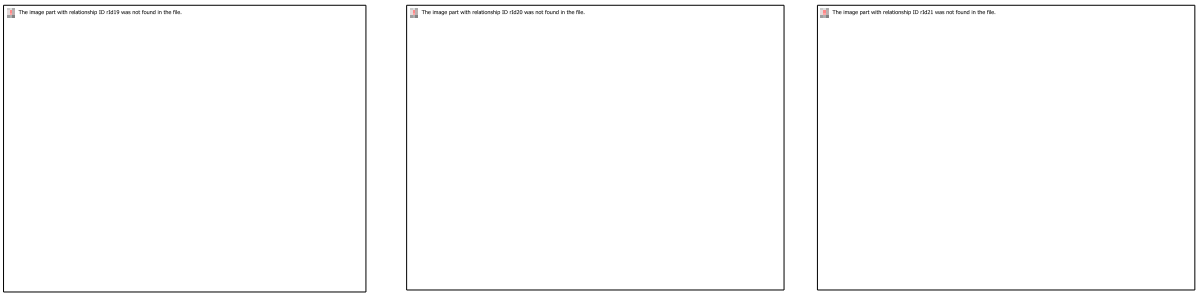

Figure 2:- Anatomopathological images of the surgical sampleshowing foci of anaplastic carcinoma developed within a papillary thyroid carcinomatous proliferation.

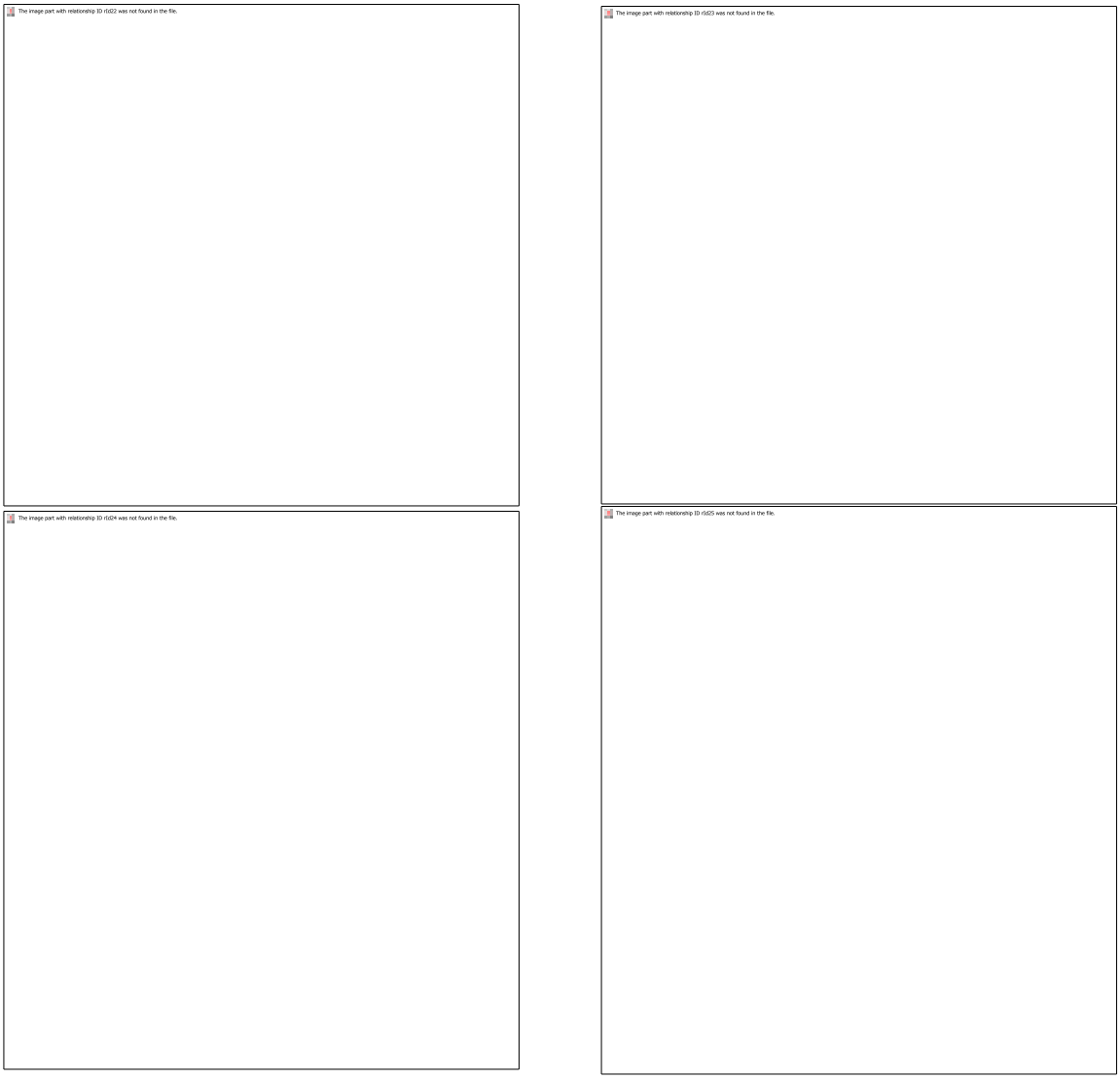

Figure 3:- Control CT scan performed at 03 months after surgery, showing control of cervical citis but significant progression of pulmonary metastases.

Conclusion:-

Anaplastic thyroid carcinoma is a severe tumor with a very poor prognosis. The transformation of a differentiated thyroid carcinoma to an anaplastic form may develop on the primary lesion or on distant metastases even after

several years of initial treatment. The rigorous management and long-term monitoring is very important for these patients.

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