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SCIENTIFIC LETTER

Thyroid angiosarcoma

Angiosarcoma tiroideo

Thyroid angiosarcoma is a very rare malignancy, corresponding to less than 1% of sarcomas.[1] Its highest prevalence has been described in alpine regions (Switzerland, Austria and northern Italy), where it can represent up to 16% of all malignant thyroid tumours. Away from these regions, its prevalence is significantly lower. It tends to affect women in advanced ages more frequently, with a history of multinodular goitre for years.[2,3]

We present the case of a 71-year-old male patient referred for a cervical tumour progressing for months, associated with dysphagia to solids and odynophagia. His personal history included: right hemithyroidectomy for multinodular goitre in 1990 with benign pathology, arterial hypertension, dyslipidaemia, atrial fibrillation, obstructive sleep apnoea syndrome and prostatectomy for prostate adenocarcinoma. He had no known family history of thyroid disease.

On physical examination, he presented a poorly defined left lateral cervical mass, of a stony consistency and large size. Thyroid function tests were normal. Cervical ultrasound showed a greatly enlarged left thyroid lobe (LTL) with endothoracic growth, with marked diffuse nodular alteration, presenting multiple nodules, most of them isoechoic with various hypoechoic zones without being able to delimit the largest one. No pathological adenopathies were observed in the right cervical region. In the left cervical region of the neck, a submandibular ganglion of about 30×10.5 mm stood out, with a suspicious appearance of malignancy. Multiple superficial nodes were also observed in the posterolateral part, adjacent to the sternocleidomastoid muscle, very hypoechoic, suspicious for malignancy, the largest about 18×11 mm. FNA of the left nodule was performed, being compatible with poorly differentiated thyroid carcinoma. CT of the larynx and neck revealed a tumour mass in LTL of 6.7 (CC) $\times$ 7.8 (AP) $\times$ 4.5 (T) cm with local oedema and caudal extension passing through the thoracic outlet, as well as left cervical adenopathies (Fig. 1).

Intraoperative examination revealed an enlarged left lobe with a stony consistency and infiltration of omohyoid, prethyroid and pharyngeal constrictor muscles. Left hemithyroidectomy was performed with modified radical left laterocervical dissection of compartments II, III, IV, and V. The *pathology study* reported thyroid angiosarcoma (pT3N1) with a tumour size of $6 \times 4 \times 3.5$ cm less than 1 mm from the surgical edge. He presented lymph node metastasis in 6 lymph nodes out of 30 extracted, one of them with extracapsular invasion. The immunohistochemical study was positive for CD31 and ERG and factor VIII (FVIII), and negative for thyroid transcription factor-1 (TTF-1).

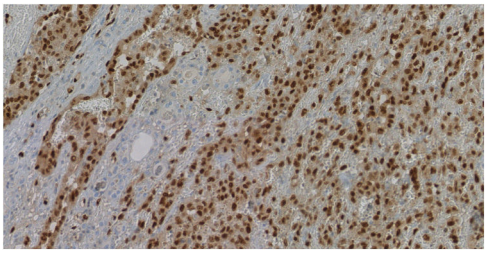

Figure 1 Immunohistochemical staining: ERG. Tumour invasion of thyroid parenchyma and vessels.

In the postoperative period, the patient presented very productive cervical blood drainage, and underwent urgent surgery on two occasions, where the remaining tumour of 3×4 cm was removed from the thyroid bed, without finding a clear source of bleeding. Given the persistence of bleeding, with significant anaemia, radiotherapy was administered urgently on the surgical site (8 Gy in a single session), for its haemostatic effect. Despite this, the patient's condition worsened and he died eight weeks after the intervention.

Thyroid angiosarcoma is characterised by its aggressive behaviour and poor prognosis. At diagnosis, patients often already present lymphatic spread followed by pulmonary, bone, cerebral and even intestinal spread.[4] Cytological diagnosis is complex, so it is frequently confused with other malignant diseases, such as epithelioid sarcoma or anaplastic carcinoma.[5] As in other published cases, the diagnosis is reached after complete analysis of the surgical specimen. Due to the morphological and immunophenotypic similarities between angiosarcomas and anaplastic carcinomas, they were initially considered to be the same variant, making it essential to study their immunohistochemistry. It is currently known that thyroid angiosarcomas are characterised by vessel formation and display phenotypic characteristics of endothelial differentiation, including being positive for CD31, CD34, ERG and the FVIII-related antigen, with CD31 being the most sensitive and specific marker for this type of tumour.[6] On the other hand, anaplastic carcinomas are composed of mesenchymal cells that have lost the morphological and functional characteristics of normal thyroid follicular cells and are positive for PAX-8.[3,7]

Regarding treatment, due to the small number of cases described, a reference treatment has not been established. Radical surgery together with complementary radiation seems to improve the prognosis and survival.[8] Generally, prolonged treatment and high doses of radiation (more than

50 Gy) are required.[9] Chemotherapy has been used in adjuvant or neo-adjuvant protocols, as well as in combination with radiotherapy, but the overall result is not good.[3]

Taking into account that tumour growth depends on the formation of new vessels, other studies have investigated new lines of treatment, such as drugs that target the vascular endothelial growth factor (VEGF) pathway and its receptor (VEGFR), as well as tyrosine kinase inhibitors with activity against VEGFR, without encouraging results according to the data available to date.[9,10]

Conclusions

Publications in recent years have shown that, despite its low frequency, there are more and more cases of thyroid angiosarcoma being described in non-alpine regions. For this reason, this condition must be taken into account in the differential diagnosis of malignant thyroid disease. The presence of bleeding could make us suspicious. However, no effective treatment is currently available.

Conflicts of interest

None of the authors have any conflict of interest to declare.

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Role of plasmapheresis in the management of severe amiodarone-induced hyperthyroidism refractory to conventional medical treatment

Papel de la plasmaféresis en el manejo del hipertiroidismo severo inducido por amiodarona y refractario a tratamiento médico convencional

Amiodarone is a class III antiarrhythmic drug widely used in our setting for the treatment of cardiac arrhythmias. It is a benzofuran derivative with high iodine content, which can have a bearing on thyroid function at different levels (hypophysis, thyroid and peripheral receptors). In many cases, it can modify the circulating concentrations of thyroid hormones and be accompanied by both hypo- and hyperthyroidism, although the majority of patients remain euthyroid.[1,2]

The first-line treatment of amiodarone-induced hyperthyroidism is fundamentally medical with synthetic antithyroid drugs In the case of Type 1 thyrotoxicosis (iodine induced), or with glucocorticoids in type II (owing to glandular destruction). Other less conventional drugs include potassium perchlorate and cholestyramine.[3,4] Plasmapheresis has occasionally been used in cases of intolerance to antithyroid drugs, refractory hyperthyroidism, and to achieve euthyroidism prior to thyroidectomy, though clinical experience is scant.[5]

We present the case of a patient with structural cardiopathy with severe amiodarone-induced hyperthyroidism refractory to medical treatment which required a high number of plasmapheresis cycles prior to definitive treatment with thyroidectomy.

53-year-old male with Arterial hypertension, dyslipidaemia, obesity, sleep apnoea syndrome, and persistent anticoagulated atrial fibrillation, owing to which he had received treatment with amiodarone (200 mg/day) over 3