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Case Report

Cystic Metastasis of Papillary Thyroid Microcarcinoma in Acromegalic

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ABSTRACT

Microcarcinoma is defined as a tumor less than or equal to 1 cm and represents an indolent pathology with very low mortality, when it comes to classic papillary carcinoma. The appearance of metastases in neck ganglion chains is relatively frequent, they are generally micro metastasis, but sometimes they can be larger. In the general population, the secondary lymph node in these cases does not change mortality, but if it is associated with certain diseases such as acromegaly, the prognosis may be somewhat bleaker. We present the case of a patient whose diagnosis of papillary carcinoma comes through a cystic lymph node metastasis almost six times larger than the size of the neoplasm that originated it.

Keywords: Microcarcinoma; Indolent pathology; Ganglion chains; Papillary Carcinoma

Introduction

Acromegaly is a rare disease caused by sustained hypersecretion of growth hormone (GH), usually caused by a pituitary tumor. It produces concomitant elevation of insulin-like growth factor type 1 (IGF-1). A population prevalence of up to 1000 per million individuals is suggested[1]. It is associated with premature mortality from cardiovascular disease and the development of benign and malignant tumors. IGF-1 is proposed to play an important role in thyroid growth and the genesis of goiter. The thyroid size measured with ultrasound is larger than in the normal population, depending on the evolution of the disease.

Differentiated thyroid cancer (CDT) is the most prevalent thyroid cancer and is among the most commonly diagnosed cancers in the United States[2]. The prevalence of this type of tumor is slightly elevated in patients with acromegaly. Prolonged stimulation of the thyroid follicle by GH/IGF-1 induces both enlargement and hyperactivity and nodule formation, therefore, multinodular goiter is a common finding. The chance of nodules increases with disease progression and IGF-1 values. In a systematic review, 4% of patients with acromegaly also had thyroid cancer, which is higher rates than for the general population[3].

Thyroid function is usually normal, but some patients with goiter have subclinical hyperthyroidism and a small amount of it has central hypothyroidism caused by the pituitary tumor[4].

Case Report

A 35-year-old man, heavy smoker, cognitive impairment and schizophrenia, with acromegaly of 10 years of evolution, who underwent 3 surgeries by sphenoidal transept and then treatment with octreotide 20 mg every 30 days for 6 months. He had been in remission for the past 4 years with IGF1: 81.9 ng/mL, which was normal for his age and sex. In the last MRI, asymmetrical remaining pituitary sun was observed at the expense of a depressed left lateral area with heterogeneous enhancement. He presented hypopituitarism and was substituted with prednisone 5mg/day, levothyroxine sodium 125 mcg/day and testosterone enanthate 250 mg every 21 days, intramuscularly. From the repercussions of his disease, he developed mild obstructive sleep apnea syndrome; in the cardiovascular area, he had an echocardiogram with mild biventricular and biauricular dilation, normal LVEF. Video colonoscopy was performed and showed hyperplastic polyps, without other lesions; Fibro gastroscopy showed no lesions. The examination highlights acromegalic facies, great magnification of supraciliary arches, diastema, wide, light hands and feet. Weight: 88 Kg Size: 189 cm. At the level of the neck, she presented palpable thyroid, without clearly delimiting nodules; Left mobile lower carotid adenopathy, approximately 4 cm. Increased dorsal kyphosis, dextro-convex scoliosis. Thyroid ultrasound showed thyroid volume of 14 cc, bilateral thyroid nodules, the largest on the left of 10 x 10 x 7 mm, poorly defined with microcalcifications and peripheral vascularization. At the left lower carotid jugular level, there is evidence of cystic image with echoes inside in relation to an already known brachial cyst, measuring 31 x 28 x 25 mm (L, T, AP) **(Figure 1)**. It is noteworthy that when reviewing the previous history, it was found that the left cystic nodular lesion had at least 5 years of evolution, the follow-up was done with ultrasound and FNA on four occasions, it had maintained its size in that period of time and the reports were of brachial cyst, cystic tumor with macrophages, detritus and cholesterol crystals. The ultrasound-guided puncture of the left thyroid nodule was reiterated again, which reported colloid substance, small and medium-sized thyroid cells scattered and in plaques, with frequent micro and macrofollicular arrangement, it is classified as follicular lesion (Bethesda III). The puncture of the left tumor reported macrophages and plaques of epithelial cells, reminiscent of medium thyroid cells, with a moderate degree of anisocariosis, prominent nucleoli, some nuclear pseudo-inclusion and intense cytoplasmic vacuolization. Thyroglobulin by needle lavage was greater than 500 ng/ml. Cytologically: although the presence of a neoplastic nodule at the thyroid level could not be evidenced, the ultrasound, cytological and biochemical characteristics led to the suggestion of metastatic adenopathy of CDT. Because he is a young male patient, with a presumptive diagnosis of CDT lymph node metastasis, associated with acromegaly, which increases the risk of thyroid pathology, with a greater potential for nodule growth, it was decided to perform thyroidectomy. Surgery was performed without complications and the pathology reported: papillary carcinoma (PC), with conventional and follicular pattern of 7 mm major axis in the left lobe; it is intraparenchymal, does not involve the organ capsule **(Figures 2 and 3)**. It associates adenomatoid nodular hyperplasia with Hürthlerian change. From recurrent dissection: 7 lymph nodes were obtained, of which 2 had PC micro metastasies. They measure 0.2 mm, one is capsular and the other subcapsular. From the low jugular-carotid ganglion: cystic metastasis of the PC, 41 mm major axis. The preserved lymph node parenchyma is referred to a small peripheral cap. He underwent 100 mCi of I131 with Thyrogen® for his secondary hypothyroidism, without complications and the dose of levothyroxine was subsequently increased to 150 mcg/day.

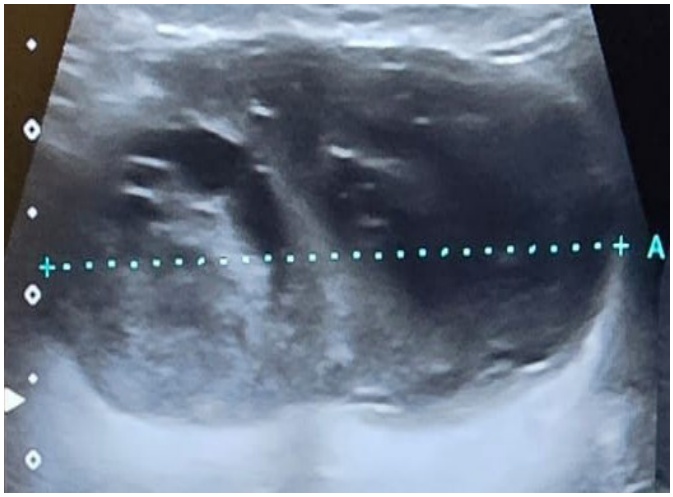

Figure 1: Thyroid ultrasound showed the presence of a rounded lesion with irregular and poorly defined contours, rounded morphology, heterogeneous echogenicity, with internal hyperechogenic areas that could correspond to microcalcifications. The cystic component of the lesion is observed in the dark sector.

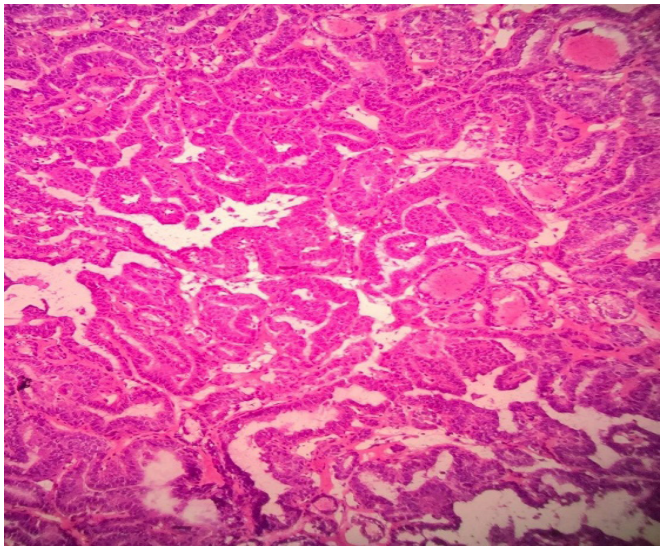

Figure 2: Pathology (H and E). Micrograph showing an epithelial proliferation with a predominant papillary pattern, fibrovascular projections covered by neoplastic cells. Areas with complex follicular formations and patterns are also identified. The cells that line the papillae have enlarged, oval nuclei with irregular margins.

Discussion

Thyroid gland enlargement is described in patients with acromegaly and can be diffuse or multinodular. There was a report that showed that of 37 acromegalic patients, 92% had an increased thyroid by ultrasound; The mean thyroid size was more than five times normal[5]. Another found that 87% had palpable diffuse or multinodular goiter[6].

Long-term excess GH-IGF1 causes overgrowth of tissues, such as connective, cartilage, bone, skin and organ meats. Other systemic complications include cardiovascular disease, sleep apnea, metabolic disorders and colon neoplasia[4].

In addition to these patients' increased risk of colon polyps and cancer, acromegaly may be associated with other tumors. In men, a greater number of malignant tumors, such as adenocarcinomas of the colon, stomach, esophagus and melanoma, were observed in a cohort of 1041 men with acromegaly and increased frequency of thyroid cancers has also been reported[7].

The annual incidence of CDT in the general population tripled from 4.9 per 100,000 in 1975 to 14.3 per 100,000 in 2015. Approximately 25% of new thyroid cancers diagnosed between 1988 and 1989 were <1 cm, compared with 39% of new thyroid cancer diagnoses between 2008 and 2009[2,8].

PC is typically indolent and is associated with long-term survival of 96% at 5 years, 93% at 10 years and more than 90% at 20 years. Overall, PC mortality rates are 1% to 6.5%, with an overall recurrence rate of 15% to 35%; Tumor recurrence usually occurs in the tumor bed, cervical lymph nodes or more rarely at distant sites[2,9,10].

However, the evolution with acromegaly can be more torpid and these patients have cancers as the third cause of death. These include those of the colon, prostate, but thyroid may be the most common malignancy associated with the disease[11]. IGF-I may promote tumor progression and perhaps facilitate neoplastic initiation[12].

Several studies have shown a positive correlation between thyroid volume and serum IGF-I concentration[13].

Another study showed no correlation between goiter and IGF1 levels. It was described that patients with secondary hypothyroidism had a thyroid volume twice as small. Goiter was diagnosed in 87% of patients, including diffuse (17.1%) and nodular (69.9%) goiter, with no significant differences between patients with active or controlled disease or among those with secondary hypothyroidism[14].

Although goiter occurs with high frequency in patients with acromegaly, it is not yet clear whether normalization of IGF-1 levels could decrease it. However, it has been reported that the increase in thyroid volume associated with acromegaly, but not nodular goiter, could be reversed in cured acromegaly[15].

Active surveillance in low-risk papillary thyroid microcarcinomas should be the first-line management modality, because only a small percentage of low-risk patients progress (10-15%)[16]; this was not the case in our patient, so it was not considered.

Regarding the microcarcinoma that occurred in this case, it has been documented that multifocality and extracapsular invasion of papillary thyroid microcarcinoma (PTCM) are associated with the presence of metastatic adenopathy. But it was not the case that there was only one focus despite the large metastatic size. Metastatic PCM, with more aggressive treatments, has an excellent long-term prognosis[17].

The presence of metastatic adenopathy in papillary carcinoma is a factor associated with recurrences[18].

PC lymph node metastases may appear as solid or cystic masses. When they are solid, they are usually not a diagnostic problem, but solitary cystic lymph node metastases could be misinterpreted as a benign cervical cystic mass. In one study[19] conducted for most cystic metastases, they were ipsilateral to the primary tumor (87.8%) and were located in the middle or inferior jugular chain (73.2%). In 14.9% of cases, cystic metastases in the lymph nodes were the initial manifestation of the disease. Only 6.2% of all lymph node metastases were purely cystic (all of these occurred in patients younger than 35 years). This study concludes that in most patients, cystic lymph node metastases are characterized by ultrasound by having a thickened external wall, internal echoes, internal nodularity and septa (as happened in this case). However, in younger patients, the lymph nodes may present a purely cystic appearance, simulate gill cysts and thus require biopsy for definitive diagnosis and treatment planning. This patient spent several years with punctures in what was said to be a brachial cyst and it was the thyroglobulin needle washing that alerted mainly that it corresponded to a metastasis[19].

Cervical metastases due to carcinoma can produce subcortical liquefaction resulting in a discrete fluid-filled cervical mass. Diagnostic procedures such as FNA, ultrasound, CT or MRI may fail to diagnose the nature of these lateral cervical lesions. Excision of the cystic mass is often needed to confirm the diagnosis[20].

Reports suggest that the most common presentation of thyroid cancers is a palpable thyroid nodule, but secondary lymph nodes in the neck appear in 20 to 70% of cases. Metastasis in cervical nodes as the first and only manifestation of PC is uncommon. Cervical adenopathy as the only presentation of metastatic thyroid carcinoma has been reported in up to 13.4% by some series[21]. Ultrasound features that suggest the presence of metastatic lymph nodes include enlargement (this patient had years with the same size of adenopathy), irregular borders, round shape, poorly defined contours, absence of echogenic hilum, microcalcifications, cystic areas and hypervascularity8,9. Cystic changes in the cervical lymph nodes are suggestive of metastatic PC[22,23].

In our center, a study of microcarcinoma in 10 years was published, we found that 83.3% did not have lymph node metastases and 14.3% presented the diagnosis[24].

Conclusion

The incidence of tumors is higher in patients with acromegaly, both benign and malignant, being the third cause of death, after cardiovascular and respiratory. The prevalence and mortality of the different tumors are independent of the general population.

PC is the most common histological type in general and also associated with GH hypersecretion.

The follow-up of these patients is essential, since the risk of developing cancer is directly proportional to the duration of the underlying disease.

The particular thing about the case is that the diagnosis is reached by metastasis of 4 cm, whose primitive was a papillary microcarcinoma and in a patient who is in remission of his acromegaly, periodic ultrasound controls of the thyroid in the follow-up of patients with acromegaly.

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