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## Papillary thyroid microcarcinoma diagnosed based on cyst-like mediastinal metastasis<sup>☆</sup>

### Microcarcinoma papilar de tiroides diagnosticado por una metástasis quística en el mediastino

#### Introduction

Papillary thyroid microcarcinoma (PMC) is defined as a papillary carcinoma 1 cm or less in size. PMC is a variant of papillary carcinoma, the most common thyroid cancer, which has a very good prognosis and in which distant metastases and death (0.4–1% per year) are exceptional.<sup>1</sup>

We report a patient who was diagnosed with metastasis of a papillary microcarcinoma as the result of an evaluation of a mediastinal mass. This was an asthmatic patient aged 38 years with no history of neck irradiation or family history of thyroid cancer. The surgery department referred the patient to the endocrinological department after surgery for a cystic tumor, 7 cm in diameter, in the posterosuperior mediastinum (Figs. 1 and 2) after the histological study reported the finding in an intraoperative biopsy of a cystic wall of fibrous tissue with thyroid follicles without atypia and associated lymphocyte infiltrate consistent with pharyngeal pouch abnormalities. The final pathological study showed a cystic formation with a wall consisting of fibrous stroma with thyroid follicles, many of them with involutive phenomena, while others showed slight anisonucleosis and some “frosted glass” nuclei. Lymphoid tissue sectors coexisted with histiocyte clusters and calcification foci. The final diagnosis was metastasis from a papillary carcinoma in the cyst-like lymph node. The patient was clinically euthyroid, with a normal thyroid gland on palpation and no adenopathies on physical examination. Ultrasound examination of the thyroid and neck showed a hypoechoic image 5.7 mm × 3.1 mm in size in the left lobe with no pathological nodes. The functional thyroid study was within normal parameters, with negative antithyroid antibodies. Additional surgery performed in this case consisted of total thyroidectomy with bilateral level VI lymph node excision and the examination of both jugular

chains. A delayed biopsy revealed a thyroid papillary microcarcinoma in the right lobe, 2 mm in diameter limited by the gland and a small 5-mm follicular adenoma in the left lobe, with bilateral recurrent lymph nodes negative for metastasis. In a hypothyroid state with a TSH level of 85 mIU/L and stimulated thyroglobulin level of 2.55 ng/mL with negative antithyroid antibodies as measured by an ultra-

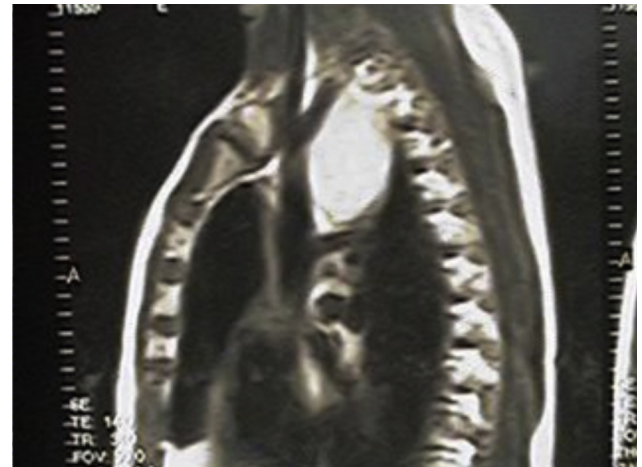


Figure 1 Preoperative MRI of the chest showing an image in the posterosuperior mediastinum.

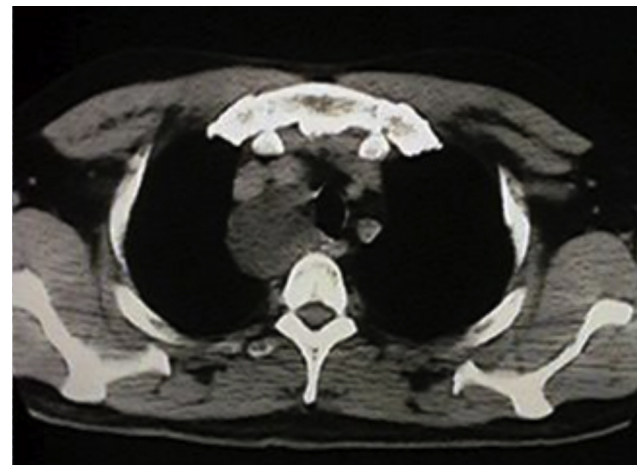


Figure 2 Preoperative MRI of the chest showing an image in the posterosuperior mediastinum.

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sensitive method, the patient was administered an ablation dose of 150 mCi of radioactive iodine, and a whole body scan 1 week later showed radioisotope uptake in the thyroid bed only. Long-term follow-up showed negative total body scans with 2 mCi of  $^{131}\text{I}$ , negative neck ultrasound examinations, and thyroglobulin levels on TSH inhibitory treatment and in a hypothyroid state following the discontinuation of levothyroxine treatment lower than 2 ng/mL. The patient was therefore considered to be free of disease and subsequently underwent annual clinical, ultrasound, and laboratory monitoring. Tumor recurrence was not found after 11 years of follow-up.

Most papillary microcarcinomas remain occult (incidental microcarcinoma) in clinical examination and are found in autopsy studies in up to 36% of patients dying from non-endocrine causes.<sup>1</sup> They are also commonly found incidentally in specimens from thyroidectomy performed for a benign disease. Very occasionally, papillary microcarcinoma becomes evident as palpable nodules or metastasis in the cervical lymph nodes. The incidence of papillary thyroid microcarcinoma increased by 100% between 1988 and 2005,<sup>2</sup> and the detection of tumors less than 1 cm in diameter increased by 49% between 1988 and 2002.<sup>3</sup> In our own experience, the incidence of thyroid carcinoma has doubled in the past 20 years.<sup>4</sup> It has been postulated that such an increase in detection is due to the widespread use of high-resolution thyroid ultrasound, which allows for the visualization of non-palpable nodules, as well as other imaging diagnostic methods used for various neck examinations, such as echo Doppler of the neck vessels, computerized axial tomography, magnetic resonance imaging, thyroid scintigraphy, and positron emission tomography.

The clinical significance of microcarcinoma is controversial because most series report very low mortality rates, which only exceptionally exceed 2%.<sup>5</sup> The incidence of cervical lymph node metastases ranges from 17% to 43%.<sup>1</sup> It has been reported that patients with tumors greater than 5 mm in size also have metastasis in the lymph nodes of the central compartment with greater frequency.<sup>6</sup> This subdivision between 5 mm and 10 mm and less than 5 mm appears to be related to the prevalence of lymph node metastases (59% versus 13% respectively) and extrathyroid extension of the tumor (10% versus 3% respectively),<sup>1</sup> i.e. the smaller the tumor, the lower the risk of metastasis. Lymph node metastases have been reported to be associated with multicentricity, extrathyroid infiltration, and disease recurrence.<sup>6</sup> However, the presence of these lesions does not result in higher mortality. Extension outside the thyroid capsule, mainly microscopic, is seen in approximately 15–21% of cases, while vascular invasion may occur in approximately 3.5%.<sup>7</sup> The development of distant metastases also correlates with tumor diameter, advanced age, and the presence of lymph node metastases at diagnosis.<sup>8</sup> The reported prevalence of distant metastases ranges from 1.0% to 2.8%.<sup>1,7</sup>

The prognosis of papillary thyroid microcarcinoma is usually excellent. However, a significant number of patients may already have at diagnosis multifocal disease or locoregional nodal metastases, which are associated with an increased risk of recurrence from 14% in low risk patients to 86% in high risk patients. The American Thyroid Association currently recommends clinical staging, not only to

predict the risk of recurrence or mortality, but to define the use of adjuvant postoperative treatments, including radioiodine ablation, as well as follow-up frequency and modality.<sup>9</sup> While the clinical course of thyroid microcarcinoma is considered to be very good, and the different scientific societies think that radioiodine ablation is not required in very low risk patients, the reported case demonstrates that microcarcinoma may show in some cases aggressive behavior leading to distant clinical manifestations. In such cases, molecular analysis can be of value by showing the mutations associated with greater aggressiveness. In recent years, many markers have been assessed in order to optimize diagnostic accuracy and predict the aggressive behavior of tumors even in presurgical cytology samples. More recent prospective studies support the value of certain genetic (*BRAF*, *Ras*, *RET/PTC*) and protein (galectin-3) markers as diagnostic tools for these patients. Although they are not widely used in the clinical setting, the combination of some of these markers will allow in the near future for accurate diagnosis, and also in thyroid microcarcinoma.<sup>10</sup>

Clinically occult papillary thyroid carcinoma with extensive gross and microscopic metastases in cervical adenopathies is well documented in the literature, but the occurrence of a mediastinal cystic metastasis without clinically detectable metastases in the cervical lymph nodes, as in the reported case, is a rare event.

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## Multifocal osteonecrosis in long-term corticoid treatment secondary to panhypopituitarism: A case report<sup>☆</sup>

### Osteonecrosis multifocal en el tratamiento corticoideo prolongado secundario a panhipopituitarismo: a propósito de un caso

Osteonecrosis is an ischemic process in the juxta-articular bone. Two forms of osteonecrosis are distinguished, one in which infarction occurs in bone marrow, causing no clinical signs, and another involving the cortical medulla, with a more florid clinical picture.

Multifocal osteonecrosis is defined as a disease affecting three or more separate anatomical regions. Its preferential locations include the femoral head, distal femur, proximal humeri, and calcanei.

As regards its pathogenesis, it has been related to long-term corticosteroid treatment, alcohol abuse, hemoglobinopathies, malignant tumors, human immunodeficiency virus, connective tissue disease, Gaucher's disease, or radiotherapy, with glucocorticoids being one of the causes in 5–25% of cases. No prior trigger is known in 40% of cases, and the condition is then considered idiopathic.<sup>1</sup>

We report the case of a 32-year-old female patient who reported mechanical pain in both knees and was referred to the radiodiagnosis department for bilateral magnetic resonance imaging (MRI). Her history included, in addition to smoking five cigarettes daily, an infrachiasmatic suprasellar tumor detected by cranial MRI one year and a half before during work-up for infertility and increased prolactin levels. A pituitary adenoma inducing panhypopituitarism was diagnosed and surgery was performed. Hormone replacement therapy consisting of different drugs, including hydrocortisone at doses of 20 mg in the morning and 10 mg in the evening, was subsequently administered. Fourteen months later, and without having received higher hydrocortisone doses for any intercurrent condition, bilateral pain in the hips and shoulders (Fig. 1) led to MRI being performed, which revealed avascular necrosis in these locations. Surgery was performed on both heads, consisting of decompression and filling with a bone graft, and hydrocortisone dosage was decreased to 10 mg in the morning and 5 mg in the evening. At the time

of evaluation, MRI was performed on both knees, revealing several lesions with signal intensity similar to that in the bone marrow, with geographical contours and peripheral hyperintensity in STIR sequence, in the femoral metaphyso-diaphyseal region, some of which reached the condylar cortical surface, as well as the tibial epiphysis, consistent with bone infarcts (Fig. 2). Overall, the findings described were consistent with multifocal osteonecrosis secondary to corticosteroid treatment.

Osteonecrosis is bone death with the collapse of its structure causing joint pain, bone destruction, or function loss.<sup>2</sup> Several terms have been used as synonyms, but there are nuances that differentiate them. The term avascular necrosis should be used when bone involvement occurs in the epiphyseal region or subchondral bone. We will speak of bone infarcts when the involved areas are the metaphysis or diaphysis, although such infarcts may extend up to the epiphysis or subchondral bone.<sup>3</sup> Avascular necrosis is usually post-traumatic, occurring after a femoral neck fracture or hip fracture-dislocation. In the absence of prior trauma, osteonecrosis is usually bilateral and occurs in younger subjects. It may be due to multiple causes, already mentioned.

There are two theories regarding the pathogenesis of bone infarcts secondary to the use of corticosteroids. According to the mechanical theory, osteonecrosis induced by steroids causes microfractures and bone collapse. The second theory attributes such infarcts to fat accumulation in bone marrow, fat embolism due to fatty liver, vasculitis, or blood hyperviscosity resulting from the use of such substances.<sup>4</sup>

In the pathological study of bone specimen including the bone infarct, four areas are distinguished: a central area of dead cells surrounded by an area of ischemic damage, an area of active hyperemia, and a normal tissue area.

The clinical course of osteonecrosis is unpredictable. The clinical signs depend on the affected site. In osteonecrosis of the hip, one of the main locations, the patient has pain in the gluteal region or hip which worsens on walking, going up and down stairs, and sitting, with difficulty in rotating. Early diagnosis is required in order to start treatment as soon as possible. While plain X-rays are the most accessible imaging procedure, they only detect the condition in advanced cases. MRI is the most sensitive test, and may detect osteonecrosis in its early stages.<sup>5</sup> Imaging procedures should help to determine disease severity and guide treatment. The extent of epiphyseal involvement (established by several classifications as less than 15%, 15–30%, or greater than 30% of epiphyseal volume<sup>6</sup>) is the best predictor of bone collapse.<sup>7</sup>

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