

11. Ozdemir D, Dagdelen S, Erbas T. Endocrine involvement in systemic amyloidosis. *Endocr Pract.* 2010;16:1056–63.
12. Ozdemir BH, Akman B, Ozdemir FN. Amyloid goiter in Familial Mediterranean Fever (FMF): a clinicopathologic study of 10 cases. *Ren Fail.* 2001;23:659–67.
13. Ozdemir BH, Uyar P, Ozdemir FN. Diagnosing amyloid goitre with thyroid aspiration biopsy. *Cytopathology.* 2006;17:262–6.
14. Siddiqui MA, Gertz M, Dean D. Amyloid goiter as a manifestation of primary systemic amyloidosis. *Thyroid.* 2007;17:77–80.

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## Long-standing differentiated thyroid carcinoma<sup>☆</sup>

### Carcinoma papilar de larga evolución

Papillary thyroid carcinoma has been defined as a malignant epithelial tumor that shows evidence of follicular differentiation and is characterized by papilla formation and/or a set of characteristic nuclear changes.<sup>1</sup> Papillary carcinoma is the most common thyroid neoplasm and accounts for 50–90% of differentiated follicular cell thyroid carcinomas.<sup>2</sup> Most of them are diagnosed between 30 and 50 years of age, and they predominantly occur in females. Approximately one third of patients have clinically evident adenopathies at presentation. Only 1–7% of patients have distant metastases at the time of diagnosis. Approximately 15% of patients experience recurrent disease, and an even lower proportion (5%) have a fatal prognosis.<sup>3</sup>

We report the case of a 51-year-old male patient with a history of respiratory tract infection who was diagnosed with pulmonary tuberculosis at 28 years (for which the patient adequately completed treatment) and with left pneumothorax 15 years earlier, and who was an active smoker of 60 cigarettes daily.

He was admitted to the infectious diseases department of the hospital for joint and muscle pain during the previous year. In the physical examination, an adenopathy approximately 3 cm in diameter was palpated in the right side of the neck. Chest X-rays revealed multiple lung nodules. Given the patient's history, miliary tuberculosis was suspected. A complete work-up consisting of chemistry, bacilloscopy, and bronchial aspirate was negative for infection. A chest X-ray upon admission showed bilateral pulmonary nodules, mainly at the lung bases, and a condensation image each at the upper right and left lobes. A chest CT revealed a spiked nodule at the posterior segment of the upper right lobe, as well as a second nodule at the posterior segment of the left lobe. Multiple bilateral pulmonary nodules were seen in the middle and lower fields. There were also nodules

in the right side of the neck, in the area adjacent to the sternocleidomastoid muscle.

PET/CT showed radiotracer uptake by the two nodules described in the CT report, located at the posterior segment of both upper lobes. None of the other nodules showed uptake.

Based on the results of the different tests, an active tuberculous infection was considered unlikely. A neoplastic condition was therefore suspected, and puncture of the upper left nodule, transbronchial biopsy of the right middle lobe, and puncture of the dominant cervical adenopathy were requested.

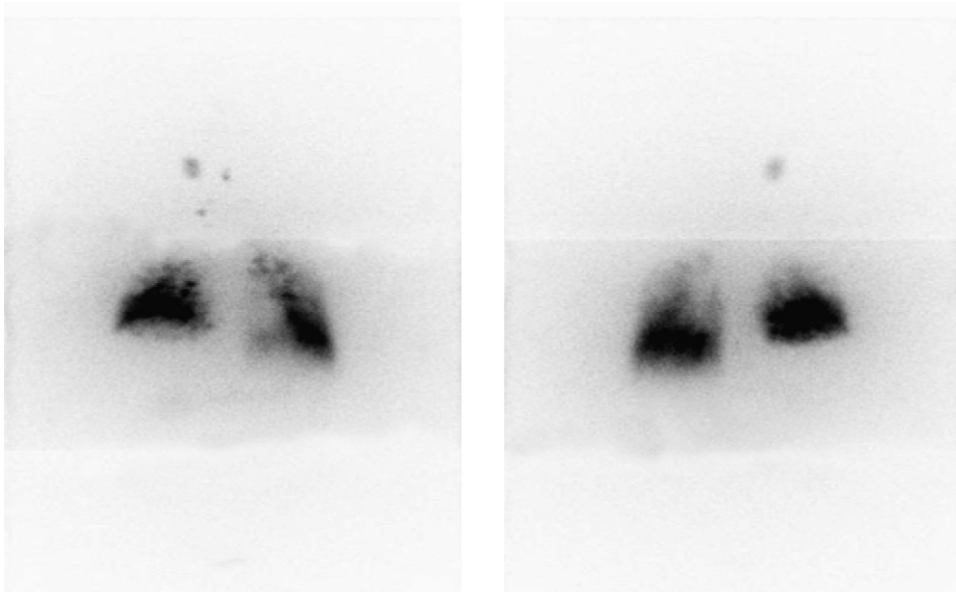
Pathological examination of the pulmonary nodule revealed the presence of cells of large cell lung cancer. However, the results of transbronchial biopsy and adenopathy puncture were consistent with metastases from an as yet undiagnosed papillary thyroid carcinoma.

Thyroid ultrasound examination revealed a partly calcified tumor, 29 × 13 × 14 mm in diameter, occupying the lower half of the right thyroid nodule, and multiple metastatic adenopathies.

To sum up, this patient had lesions consistent with nodal and pulmonary metastases from an undiagnosed papillary carcinoma, and two pulmonary images which suggested synchronous primary lung neoplasms.

Elective surgery of both dominant pulmonary nodules and the thyroid tumor in a second stage was performed. Biopsy of both lung specimens confirmed synchronous, intermediately differentiated primary carcinomas sparing the surgical resection margins. There were no adenopathies. The tumor was thyroglobulin-negative (T2 N0 M0, stage II). A subsequent total thyroidectomy found a right posterior thyroid nodule that had invaded the recurrent and the right perichondrium. The superior mediastinal lymph nodes involved and lymph nodes of the right recurrent and right internal jugular chains were excised. Bilateral central lymph node dissection and functional dissection of the right lateral cervical lymph nodes were performed. A pathological examination revealed a multifocal, mixed papillary and follicular non-encapsulated thyroid carcinoma with infiltrating margins that had invaded the thyroid capsule, soft tissue, and perithyroid lymphatic and blood vessels, and metastasized to multiple mediastinal and right jugular lymph nodes (T4a N1b M1, stage IV C).

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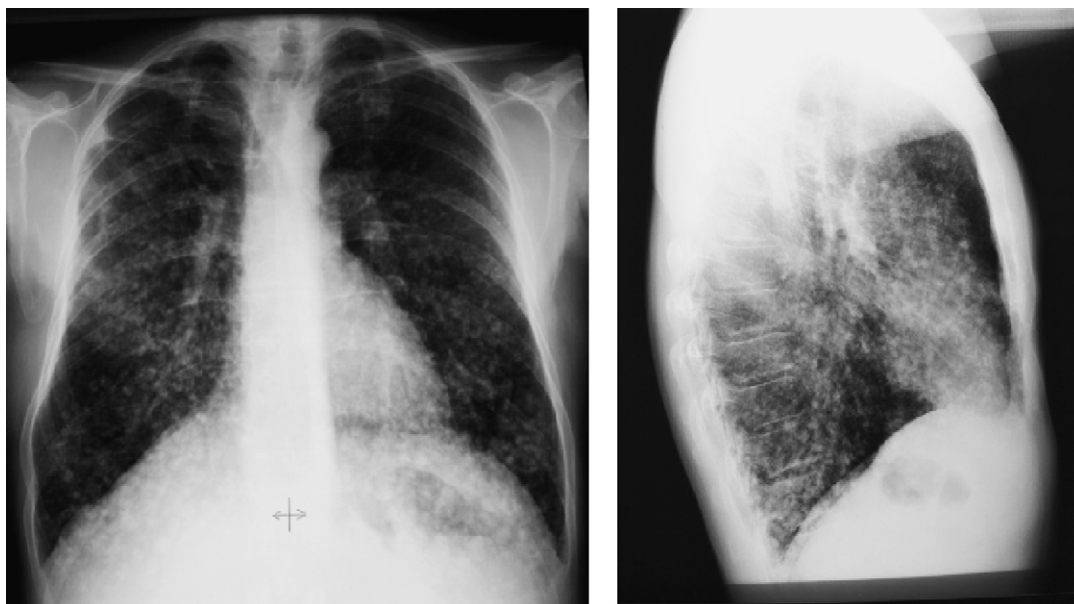
**Figure 1**  $^{123}\text{I}$  scan after rTSH.

A whole body scan with  $^{123}\text{I}$  after stimulation with recombinant TSH disclosed bilateral thyroid remnants, a metastatic adenopathy in the right side of the neck, and generalized, predominantly basal, metastatic lung disease (Fig. 1). Thyroglobulin levels of 4830 ng/mL with negative antithyroglobulin antibodies were found.

Because of his multiple conditions, which involved surgery for two synchronous lung tumors and with severe centrilobular emphysema and extensive metastatic lung involvement from his thyroid tumor, the patient was evaluated by the department of physics and radioprotection, which contraindicated the use of  $^{131}\text{I}$  because of the risk of

acute pneumonitis, with subsequent respiratory failure that would be life-threatening.

After discussion with the oncological department six months after surgery, palliative chemotherapy with the antiangiogenic drug sorafenib, a tyrosine kinase inhibitor, was decided upon. The patient did not tolerate regular cycles due to the occurrence of hand-foot syndrome. Subsequent controls with chest X-rays (Fig. 3) and CT scans every six months (Fig. 4) showed no nodule changes or decreases in thyroglobulin levels. The last value found on suppressant therapy was 1,921 ng/mL with negative antithyroglobulin antibodies.



**Figure 2** Posteroanterior chest X-rays taken in 1988.



Figure 3 Current chest X-rays.

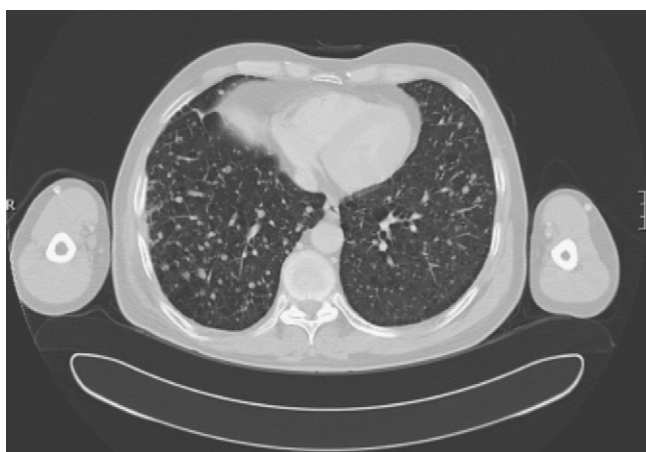


Figure 4 CT scan of the chest.

Only 1–7% of patients with papillary thyroid carcinoma have distant metastases at diagnosis.<sup>3</sup> Clinical symptoms of lung involvement are not common. The involvement pattern may range from macronodular to diffuse infiltrates. The latter pattern, when undetected in the chest X-ray, is usually diagnosed using a <sup>123</sup>I whole body scan, and may be confirmed with a spiral CT. Almost all patients have high serum thyroglobulin levels despite the fact that lung metastases are not visible in X-rays. In our patient, lung micrometastases were visualized from the start, but were not initially interpreted as such. Clinical records corresponding to the patient's previous stay at the hospital for tuberculosis were requested. Chest X-rays were then reviewed (Figs. 2 and 3) and were seen to be similar to the current X-ray films, taken 23 years later. Thus, the patient already had at that time the metastatic micronodular lung infiltrate, which in the setting of clinical respiratory signs was interpreted as an infectious process, while these new findings suggested, although it could not be categorically stated, that it was a metastatic lung disease of a thyroid origin. The very slow development in this case of a tumor that had remained silent for years should be noted. It should be stressed that the patient had not consulted a specialist during this time.

Treatment with <sup>131</sup>I for 6–12 months was advised for micrometastases, in the knowledge that that complete remission could be achieved with doses higher than 200 mCi.<sup>4</sup>

Lung macrometastases are also treated with <sup>131</sup>I if they are shown to take up the radioactive agent. In this case, it was possible to decrease thyroglobulin levels and size. However, it should be noted that complete remission is rarely achieved.<sup>5</sup>

Complications of treatment with high doses of <sup>131</sup>I include pneumonitis and pulmonary fibrosis. If these are suspected, lung function should be assessed and may limit treatment continuation.<sup>6</sup>

If lung metastases do not take up <sup>131</sup>I, chemotherapy (cisplatin, doxorubicin) may be given, with its attendant risk of toxicity and low response.<sup>7</sup> Partial remission is achieved in 15% of patients.

Treatment with antiangiogenic agents such as tyrosine kinase inhibitors (axitinib, motesanib, and sorafenib) is under investigation, but they have many side effects, including arterial hypertension, diarrhea, fatigue, skin erythema and rash, and weight loss.<sup>8–12</sup>

## References

1. Rosai J. Papillary carcinoma. *Monogr Pathol.* 1993;35:138–65.
2. Hay ID. Papillary thyroid carcinoma. *Endocrinol Metab Clin North Am.* 1990;19:545–76.
3. Larsen PB, Kronenberg HM, Melmed S, Polonsky KS. *Williams Textbook of Endocrinology.* 2006;13:516–30.
4. Ilgan S, Karacalioglu AO, Pabuscus Y, Atac GK, Arslan N, Ozturk E, et al. Iodine-131 treatment and high-resolution CT: results in patients with lung metastases from differentiated thyroid carcinoma. *Eur J Nucl Med Mol Imaging.* 2004;3: 825–30.
5. Ronga G, Filesi M, Montesano T, Di Nicola AD, Pace C, Travascio L, et al. Lung metastases from differentiated thyroid carcinoma. A 40 years' experience. *Q J Nucl Med Mol Imaging.* 2004;48:12–9.
6. Cooper DS, Doherty GM, Haugen BR, Kloos RT, Lee SL, Mandel SJ, et al. Management guidelines for patients with thyroid nodules and differentiated thyroid association guidelines taskforce. *Thyroid.* 2009;1192–223.
7. Sarlis NJ. Metastatic thyroid cancer unresponsive to conventional therapies: novel management approaches through translational clinical research *Curr Drugs Targets Immune. Endocr Metabol Disord.* 2001;1:103–15.
8. Kloos RT, Ringel MD, Knopp MV, Hall NC, King M, Stevens R, et al. Phase II trial of sorafenib in metastatic thyroid cancer. *J Clin Oncol.* 2009;27:1675–84.
9. Zhang J, Yang PL, Gray NS. Targeting cancer with small molecule kinase inhibitors. *Nat Rev Cancer.* 2009;9:28.
10. Schlumberger M, Sherman SI. Clinical trials for progressive differentiated thyroid cancer: patient selection, study design, and recent advances. *Thyroid.* 2009;19:1393–9.
11. Gupta-Abramson V, Troxel AB, Nellore A, Puttaswamy K, Redlinger M, Ransone K, et al. Phase II trial of sorafenib in advanced thyroid cancer. *J Clin Oncol.* 2008;26: 4714–9.
12. Cabanillas ME, Waguespack SG, Bronstein Y, Williams MD, Feng L, Hernández M, et al. Treatment with tyrosine kinase inhibitors for patients with differentiated thyroid cancer: the M.D. Anderson experience. *J Clin Endocrinol Metab.* 2010;95: 2588–93.

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## Large adrenal cavernous hemangioma as an unexpected finding after work-up of an abdominal mass<sup>☆</sup>

### Hemangioma cavernoso adrenal de gran tamaño como hallazgo inesperado tras estudio de masa abdominal

A cavernous hemangioma (CH) is a benign tumor commonly occurring in skin and liver, but extremely rare in the adrenal glands.<sup>1</sup> Although the first case of an adrenal cavernous hemangioma (ACH) was reported in 1955,<sup>2</sup> only 60 cases of ACH have been reported to date in the medical literature. ACHs are in most cases unilateral, non-functioning lesions occurring at between 50 and 70 years of age. Females are mainly affected, with a 2:1 sex ratio.<sup>3</sup> Differential diagnosis of ACH with adrenal carcinoma represents a challenge for clinicians because the tumors are usually very large and, although they show some typical features in radiographic studies, the vast majority are only discovered after surgery and histological study.

We report the case of a 65-year-old male patient who was referred to our endocrinology outpatient clinic after an abdominal mass, probably dependent on the left adrenal gland, was found in an ultrasound examination. The patient first attended the gastroenterology outpatient clinic complaining of continuous, persistent pain in his left flank for the previous three months. Abdominal examination at the outpatient clinic revealed a palpable mass. An abdominal ultrasound examination showed a heterogeneous nodule with lobulated margins, approximately 7.5 × 6 cm in diameter, in the upper pole of the left kidney, probably related to and originating in the left adrenal gland.

The patient's history included type 2 diabetes mellitus (T2DM), high blood pressure (HBP), and dyslipidemia, which were well controlled with medical treatment. The patient smoked two packs of cigarettes daily and had previously experienced a right carotid transient ischemic attack. Clinical examination at the endocrinology outpatient clinic found a weight of 78.7 kg, a height of 172 cm, and a BMI of 26.6 kg/m<sup>2</sup>. Blood pressure levels were 137/85 mmHg. Examination by organs and systems was unremarkable, except for a doubtful palpable mass in the left flank.

Laboratory tests reported normal complete blood count and coagulation values. The results of blood chemistry, including kidney, liver, bone, and lipid parameters, were also

normal. HbA1c level was 5.4%. TSH and FT4 levels were normal. Basal cortisol was 12.53 µg/dL (normal range, 6–28), and ACTH 17 pg/mL (normal, 7.2–63.3). Urinary free cortisol (UFC) level was 88 µg/24 h. Normal levels were found of total and free testosterone, dehydroepiandrosterone sulphate (DHEA-S), prolactin, and 17-OH progesterone. Tumor markers: alpha-fetoprotein, β-HCG, carcinoembryonic antigen (CEA), CA 19.9, CA 125, cyfra 21.1, and prostate-specific antigen (PSA) levels were normal. Catecholamines and metanephrines in 24-h urine after a five-day diet were normal in two consecutive tests. Basal cortisol levels after a 1-mg overnight dexamethasone (DXM) suppression test were 4.89 mcg/dL. After a subsequent 3-mg overnight dexamethasone (DXM) suppression test, the basal cortisol level was 1.6 mcg/dL.

Based on these findings, resonance magnetic imaging (MRI) was performed with gadolinium, showing a bilobulated lesion 8 × 6 cm in diameter with a heterogeneous signal in T1 and T2 sequences related to small hemorrhagic foci inside the lesion. After contrast administration, heterogeneous enhancement was seen, which was consistent with a left adrenal lesion/tumor, probably an adrenal carcinoma, although a pheochromocytoma could not be ruled out (Fig. 1). Because of this, and although the two consecutive catecholamine tests had been negative, a metaiodobenzylguanidine (MIBG) scintigraphy was performed, which was also negative.

After this comprehensive diagnostic work-up and based on the results of the supplemental tests, a preliminary diagnosis of a left adrenal carcinoma was made, and surgical removal of the mass for histological study was decided upon. After approval by the anesthesiologist, a left adrenalectomy was performed through a subcostal approach. Gross examination revealed an adrenalectomy specimen 164.5 g in weight and 8.5 × 6 × 4 cm in diameter with a highly vascularized surface and two well-circumscribed, brownish red 4.3 cm and 4.2 cm nodules (Fig. 2). Microscopic examination showed a tumor well circumscribed by a fibrous capsule with two nodules consisting of a proliferation of dilated blood vessels with endothelium without atypia or mitosis, red blood cells with endothelial proliferation, and infarction areas with hemorrhage and fibrin. Final histological diagnosis was a large left adrenal cavernous hemangioma.

While a CH is a common benign tumor in certain sites, such as the liver, a CH originating in the adrenal glands is extremely rare. The importance of our case lies in the complexity of the preoperative diagnosis of this tumor. Differential diagnosis with an adrenal carcinoma and sometimes with a pheochromocytoma is difficult.<sup>4</sup> In addition, massive spontaneous retroperitoneal hemorrhage has been reported as a complication of adrenal CH causing high morbidity and mortality rates.<sup>5</sup>

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