The Tiupalkov[2] study reported a follow-up of 25 patients who underwent surgery for craniopharyngioma, and found a correlation between the height appropriate for bone age and the body mass index of patients. Hyperinsulinism was seen in one third of the patients, almost all of whom had suprasellar tumor expansion and hyperphagia . These findings agree with those reported by Di Batista et al[8], who found normal growth in eight out of 32 patients despite GH deficiency. Obesity, hyperphagia, and hyperinsulinism were also found in most of them.

Patients with panhypopituitarism after surgery for teratoma[9] and congenital panhypopituitarism[10] associated with normal growth and hyperinsulinism have been reported.

Clinical presentation of this case and a review of the literature on the subject suggest a significant effect of hyperinsulinism on IGF-IR, a promoter of longitudinal growth. This suggests the need for reflection and the conduct of large observational studies, minimizing bias, at a time when the role of insulin and its analogues on cell proliferation is being questioned.

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Follicular thyroid cancer presenting as radiculopathy. Ten years of follow-up

Radiculopatía como forma de presentación de un carcinoma folicular de tiroides. Evolución a 10 años

Differentiated thyroid carcinoma (DTC) is the most common endocrine cancer. An increased incidence of this tumor, both real and resulting from improved diagnostic techniques, has been reported in recent decades[1,2]. Distant metastatic disease occurs in 5%-15% of patients[3] and usually consists of asymptomatic pulmonary lesions. DTC diagnosis based on symptoms of metastases is exceptional[4,5]. However, an atypical presentation is seen in some cases, such as the one reported below.

In 1999 a 54-year-old woman attended the orthopedic surgery clinic reporting radicular pain over the previous year along with loss of strength in the left lower limb and constitutional symptoms. Lumbosacral magnetic resonance imaging (MRI) showed an expansive mass in the left hemisacrum, the biopsy of which was consistent with the metastasis of a follicular differentiated thyroid carcinoma. Examination revealed a mass on the right side of the neck. Tumor mass was completely resected by total thyroidectomy and resection of a grossly involved tracheal fragment. A histopathological study revealed a 4 x 3 x 2.5 cm follicular

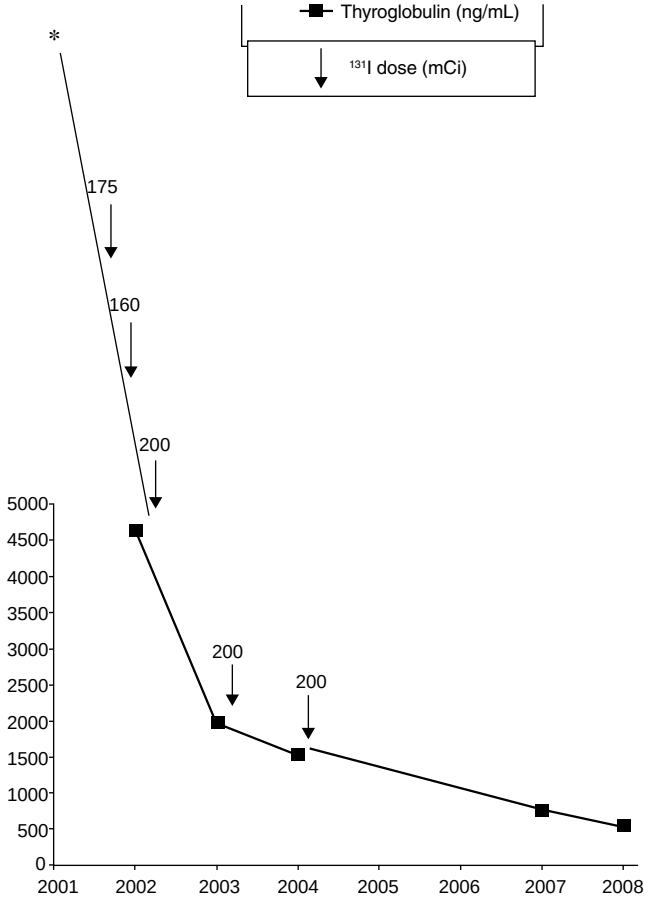

Figure 1 Change over time in thyroglobulin levels.

thyroid carcinoma in the right thyroid lobe with involved margins that infiltrated the capsule and invaded the trachea (stage T4aN x M1). The patient refused surgery of the sacral tumor.

Sustained positive uptake was seen during follow-up, and successive radioiodine therapies were therefore administered up to a cumulative dose of 950 mCi with no significant side effects. A progressive decrease in thyroglobulin levels (Fig. 1) and stabilization of the metastatic lesion were achieved, suggesting sustained tumor control despite no new radioiodine doses having been administered during the previous 6 years (Table 1). No pathological adenopathies were seen in serial cervical ultrasound examination, and thyroid bed showed a 1.4 x 0.6 cm image consistent with thyroid residues that remained unchanged throughout follow-up. The final sacral MRI revealed a 6.8 x 7.6 x 5 cm lesion, unchanged as compared to prior studies. The patient experienced a marked improvement in clinical signs, returned to her usual activities, and at the time of writing was only occasionally in need of non-steroidal anti-inflammatory drugs for pain relief.

Distant metastases are rarely found at the time of DTC diagnosis, and have been reported in 3%-4% of patients in some series[6]. Bone is the second most common site of metastases after the lung, and the axial skeleton (ribs, vertebrae, pelvis) is predominantly affected. The occurrence of metastases, which have been reported to range from 15% to 26%[8-10] depending on their histological type and location, decreases 10-year survival[7] by more than 50%. A better survival rate has been found with lung-confined metastases.

The follicular variant of DTC most frequently induces distant metastases, which occur in more than 30% of patients in some series[11], and shows the greatest predilection for bone. In the Schlumberger et al series, predictors of complete response to treatment of bone metastases included young age, radioiodine uptake, and a limited extent of the disease[3]. DTC with bone metastases is sometimes diagnosed after very large lesions have been found, which only exceptionally show a complete response despite radioiodine uptake[9]. Radioiodine therapy is the treatment of choice and increases survival, and although the cure rate is lower as compared to other locations, it achieves long stability periods[9]. Some authors therefore suggest successive treatments with radioiodine while uptake exists, even if cumulative doses are high, because these are associated with a relatively low risk of a second tumor.

These results support aggressive treatment with radioiodine or surgery to try and remove as much tumor mass as possible[9], given the lack of other effective and safe therapeutic options. Palliative treatments available include embolization, to provide rapid, transient pain relief[12], and bisphosphonates, to decrease pathological fracture rate and bone pain[7]. The tyrosine kinase inhibitors, sorafenib and sunitinib, are currently being tested in patients with metastatic differentiated thyroid carcinoma refractory to radioiodine and with disease progression. Partial response and stabilization have been achieved with these agents in patients with wide metastatic involvement, particularly in pulmonary lesions. However, some series have reported minimal responses in lymph node, pleural, and bone metastases[13].

In our patient, successive radioiodine treatments achieved disease stabilization for 10 years. It was decided to space out radioiodine scans and therapeutic doses in an attempt to maintain a balance between disease activity and treatment risk.

Patients with DTC with metastatic bone involvement who show radioiodine uptake may live for a long time with a good quality of life. The main problem occurs when the recommended radioiodine doses, conventionally fixed to range from 600 to 800 mCi, are exceeded, because of the risk of inducing second tumors. However, doses should be individualized because there is no maximum dose. The convenience of continuing metabolic therapy should be weighed in these cases by assessment of the risks and benefits, because no other effective and safe antiproliferative treatment is currently available. On the other hand, and as shown by our case report, radioiodine therapy shows a sustained efficacy, suggesting that once the safety doses are reached a watchful waiting approach is recommended, including continued close monitoring of tumor progression by thyroglobulin measurements and imaging tests. Embolization, external radiotherapy, or bisphosphonates could be used as palliative treatment for pain relief.

Table 1 Change over time in thyroglobulin levels in relation to 131I scans

Date	TG* (ng/mL)	TG** (ng/mL)	^{131}I dose (mCi)	Scan after therapy
February 2001	21,900			
April 2001			175	Residues in thyroid bed. High pelvic uptake
September 2001		38,828	160	Persistent focus in sacroiliac joint
April 2002	1,166			
October 2002		4,615	200	Persistent uptake in left sacroiliac joint and thyroid bed
January 2003	425			
May 2003		1,943	200	Persisting uptake in sacroiliac joint and thyroid bed
May 2004		1,524	200	Persistent sacroiliac uptake and small residue of thyroid tissue
February 2005	252			
February 2006	200			
March 2007		763.7		
March 2008	132			
August 2008		545.4		
July 2009	110			
September 2010	93.5			

TG*: thyroglobulin under suppressive therapy with levothyroxine. TG**: thyroglobulin in induced hypothyroidism (endogenous TSH higher than 50 mIU/mL).

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