according to the literature causes hypothyroidism in iodine excess conditions, rather than hyperthyroidism as occurred in the reported case.

The temporal proximity of the cessation of iodinated salt use and thyroid function changes does not show a definite cause-effect relationship between the two. Despite the marked influence of iodine on thyroid gland physiology, it cannot be ruled out that the condition reported was independent of changes in iodine provision. The measurement of urinary iodine levels before and after iodinated salt use could have helped support one or the other option. An attractive possibility is the one suggested by recent classifications of autoimmune thyroiditis, which include both Graves' and Hashimoto's diseases under the same heading, as the two extremes of the same condition.[8] This patient may have had a type 3 autoimmune thyroiditis which had evolved (spontaneously or as a result of a change in iodine consumption) to type 2 autoimmune thyroiditis.

References

1. Conclusiones de la reunión del Grupo de Trabajo sobre Trastornos Causados por Deficiencia de Yodo de la Sociedad Española de Endocrinología y Nutrición. Málaga, 27 February 1998.
2. Escobar del Rey F, Morreale de Escobar G. Yodación universal de la sal: un derecho humano de la infancia. Endocrinología. 1998;45:3–14.
3. Wolff J, Chaikoff IL. Plasma inorganic iodide as a homeostatic regulator of thyroid function. J Biol Chem. 1948;174:555–64.
4. Bürgi H. Iodine excess. Best Pract Res Clin Endocrinol Metab. 2010;24:107–15.
5. Surks M.I. Iodide and thyroid function. UpToDate [updated 13 February 2009]. Available in: www.uptodate.com
6. Martins MC, Lima N, Knobel M, Medeiros-Neto G. Natural course of iodine-induced thyrotoxicosis (Jodbasedow) in endemic goiter area: a 5 year follow-up. J Endocrinol Invest. 1989;12:239–44.
7. Braverman LE. Iodine and the thyroid: 33 years of study. Thyroid. 1994;4:351–6.
8. Kronenberg HM. Williams Tratado de Endocrinologia, Vol. 1, 10.ª ed. Editorial Elsevier; 2004. p. 476, [Table 12–3].

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The value of selective parathyroid venous sampling for localizing occult parathyroid adenomas☆

Utilidad del cateterismo de paratiroides en la localización de un adenoma de paratiroides recidivante oculto

Surgery is the only curative treatment for primary hyperparathyroidism (PHP).[1] In the hands of an expert surgeon, peroperative bilateral cervical examination achieves curing rates of 86–100% without the need for preoperative localization tests. Localization tests are, however, essential in the event of minimally invasive surgery or repeat surgery for disease relapse/recurrence.[1] Thanks to technological advances and the high resolution of current imaging tests, most pathological parathyroid glands may easily be identified using noninvasive procedures. However, these sometimes provide non-significant or conflicting results. When this occurs, invasive procedures such as parathyroid catheterization are required.

We report the case of a 65-year-old female patient with a history of multinodular goiter and PHP due to parathyroid adenoma who had undergone total thyroidectomy and right superior parathyroidectomy. The adenoma could not be localized with standard imaging tests (cervical ultrasound, technetium-sestamibi scan, and cervical magnetic resonance imaging) performed before surgery, so a bilateral exploratory cervicotomy was performed. A 1.5 cm parathyroid adenoma was found adhering to the posterosuperior aspect of the right thyroid lobe and resected. All the other parathyroid glands identified (left upper, left lower, and right lower glands) were normal. The patient is currently on thyroxine therapy (100 mcg/day). One year after surgery, asymptomatic hypercalcemia and high parathormone (PTH) levels were again found 1 year after surgery (Table 1). Laboratory tests also showed severe hypovitaminosis D, and treatment was therefore started with calcidiol despite hypercalcemia (4 drops/day). All other laboratory test results were normal. Based on a suspicion of PHP relapse as the first diagnostic possibility, perhaps due to a prior partial adenoma resection or the presence of a double adenoma, localization studies were requested. Two parathyroid technetium-sestamibi scans showed no pathological deposits. A cervical ultrasound showed no suspicious images either. Finally, magnetic resonance imaging (MRI) of the neck showed no relevant findings. During this time, and despite strong hydration, plasma and urinary calcium and PTH levels continued to increase. For this reason, and based on a diagnosis of PHP relapse with negative localization tests, treatment was started with low-dose cinacalcet (30 mg/day) and surgical assessment was requested. Plasma calcium levels normalized one month after the start of the calciomimetic drug. Surgery was therefore rejected because of the difficulties and risks of ''blind'' repeat surgery in a previously operated area. Plasma calcium levels increased again four months later, and the cinacalcet dose was increased to 30 mg/12 h, which normalized calcium levels. Four months later, calcemia increased again, and the cinacalcet dose was increased to 60 mg/12 h. At this point, and because of poor drug tolerability (nausea and epigastric pain) and poor calcemia control, surgery

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Table 1 Changes in plasma calcium, PTH, and 25OHvitD levels and urinary calcium levels before and after surgery.

				Cinacalcet (30mg/24h)			Cinacalcet (30mg/12h)		Cinacalcet (60mg/12h)	Surgery	
	09/07	**02/08**	**09/08**	**11/08**	**12/08**	**02/08**	**03/08**	**04/08**	**07/08**	**09/08**	**12/09**
Calcium (8.7-10.6 mg/dl)	11.4	10.9	12.5	11.9	10.2	10.4	11.5	10.9	11.4	10.9	8.8
PTH (12-72 pg/ml)	133	164	332	322	252	302	249	285	299	269	100
25OHvitD (ng/ml)		<5	9	5	<4		12	11	8	23	25
Urinary calcium (mg/day)		223	466	304				425			

was decided upon as the only possible definitive treatment. In order to minimize risks and facilitate surgical success, parathyroid catheterization was performed before surgery. For this, the thyroid-parathyroid veins were catheterized and PTH samples were taken (Fig. 1). The right lower thyroid vein could not be catheterized due to technical difficulties and anatomical variants. Despite this, catheterization showed a clear right lateralization. During surgery, a 1.3 cm adenoma was again found in the right superior parathyroid gland and resected. Fifteen minutes after resection, PTH levels decreased by 80% (initial PTH, 239 pg/mL; final PTH, 51 pg/mL). Calcemia also normalized after surgery (8.8 mg/dL), and cinacalcet was therefore discontinued. One year later, calcium and PTH levels continue to be normal.

The need for the localization of pathological parathyroid glands before initial surgery for PHP is controversial. This is because while their identification allows for minimally invasive surgery (with less costs and complications), conventional surgery with peroperative bilateral cervical examination still has success rates >95% with morbidity rates of only 1–2%.[2]

However, PHP persists or recurs in 5–10%[3] of cases, requiring repeat surgery. This is technically more complex due to postoperative fibrosis and anatomical distortion and involves higher costs[4] and risks of complications[2] such as recurrent nerve paralysis, permanent hypoparathyroidism, local bleeding, pseudoaneurysm, thrombosis, or infection. Moreover, one-third of patients undergoing repeat surgery have hyperplasia in several parathyroid glands or ectopic adenomas.[3]

For these reasons, there is general agreement that adequate localization is mandatory in patients with familial PHP or undergoing repeat surgery. Localization is not possible in most cases using noninvasive procedures, having a predictive value of 40–80%.[3] A technetium-sestamibi scan is the procedure with the greatest sensitivity (91%) and specificity (98%), mainly when combined with single-photon emission computed tomography (SPECT).[3] Ultrasonography is another commonly used technique, mainly as a supplementary procedure in patients with a negative scan or as a confirmatory test. It has an intermediate sensitivity for adenoma detection (77–80%).[3] Finally, computed tomography (CT) or MRI is used in selected cases; these are of particular value in ectopic mediastinal adenomas.[3] There is currently no agreement as to how many or which tests should be performed.[5] Although results vary depending on the center, it appears that the combination of MRI and a scan would be the one with the highest sensitivity (94%).[5]

However, all of these procedures have limitations in the event of small adenomas, multiple hyperplasia, or coexistent thyroid disease,[2] and their sensitivity markedly decreases in patients undergoing prior surgery.[3] In such cases, invasive procedures such as parathyroid catheterization are helpful. For this, bilateral femoral catheterization is used to take PTH samples from the superior/inferior internal jugular, superior/inferior thyroid, subclavian and brachiocephalic, thymic-mediastinal, superior cava, azygos, and left superior intercostal veins and from the right atrium.[2] The thymic-mediastinal vein is the vein most difficult to catheterize, but this is essential for localizing mediastinal PHP and thus for deciding on the surgical approach.[2] A positive gradient is defined as a twofold greater PTH concentration at the central (right or left) as compared to the peripheral level.[2] Peripheral levels are calculated using the mean of measurements in both subclavian veins. Although this is an invasive, expensive, and cumbersome procedure, it has a high chance of success.

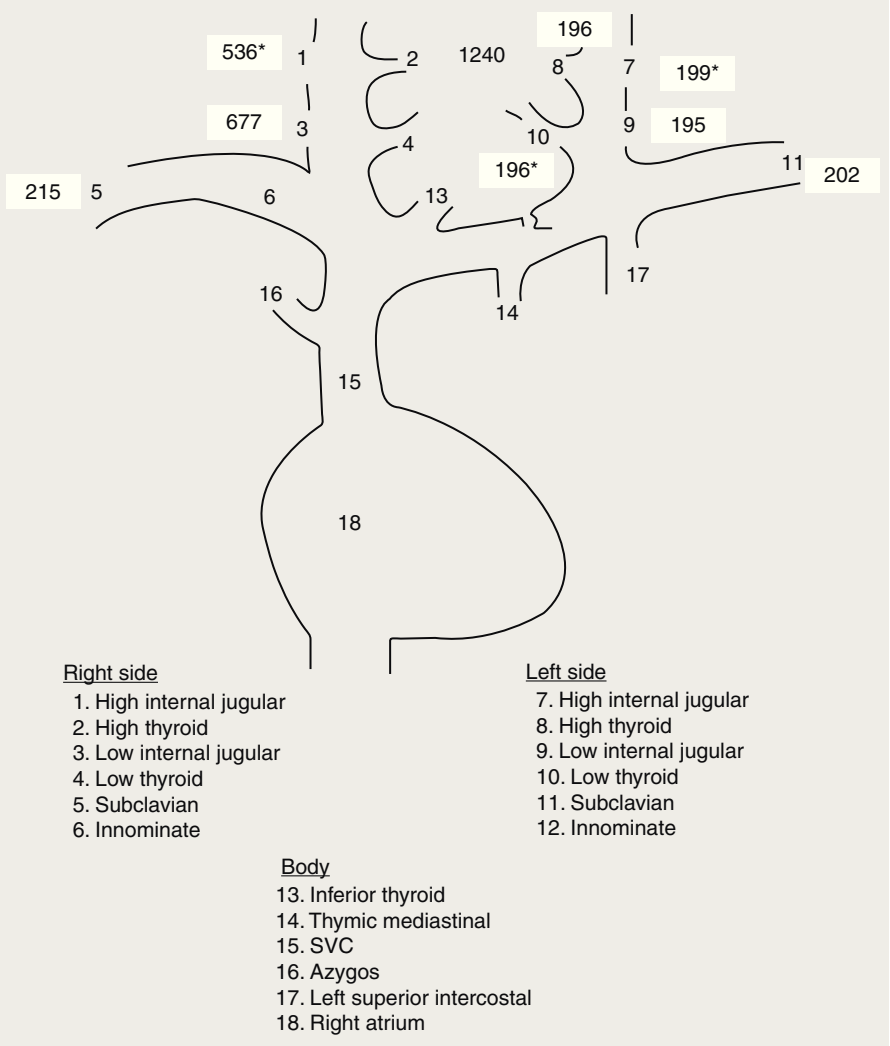

Figure 1 Representation of parathyroid vein catheterization. Peripheral concentration (the mean of both subclavian veins) is 208 pg/mL; a twofold greater PTH gradient is achieved in the upper part of the right thyroid lobe.

The largest series was published by the *National Institutes of Health*[6] and reported parathyroid catheterization in 98 patients with persistent/recurrent PHP and two or more negative, discordant, or equivocal localization tests. Parathyroid catheterization showed a true positive rate of 76% and a false positive rate of 4%, and was the most sensitive and specific procedure. These results were supported by Jones et al.,[7] who reported sensitivity and specificity rates of 76% and 88%, respectively. Ogilvie et al.[1] found in 27 patients with complicated PHP a positive predictive value of 81%, similar to prior studies[6,7] and higher than reported for all other noninvasive procedures. Parathyroid catheterization is therefore indicated in the following conditions[1,2]: (1) discordant/inconclusive imaging tests; (2) more than one scintigraphic uptake area, suggesting the presence of pluriglandular disease or ectopic adenomas; (3) patients with familial PHP; and/or (4) patients with prior neck surgery, as occurred in our case. In addition, in order to perform routine catheterization and decrease its invasiveness/complications, rapid PTH measurements may be performed during catheterization[8] or both internal jugular veins may be catheterized with rapid PTH measurement during surgery[9] with good and promising results. In the latter case, lateralization is considered to exist in the event of differences >5% in PTH levels.

In conclusion, parathyroid catheterization (before or during surgery) performed at specialized centers is a valuable, sensitive, and specific technique for patients with complicated PHP and one which increases the chance of surgical success.

References

1. Ogilvie CM, Brown PL, Matson M, Dacie J, Reznek R, Britton K, et al. Selective parathyroid venous sampling in patients with complicated hyperparathyroidism. Eur J Endocrinol. 2006;155:813–21.
2. Lau J, Drake W, Matson M. The current role of venous sampling in the localization of endocrine disease. Cardiovasc Intervent Radiol. 2007;30:555–70.
3. Marazuela M, Dominguez-Gadea L, Bravo-Linfante JM, Larrañaga E. Tratamiento quirúrgico y técnicas de localización en el hiperparatiroidismo primario. Endocrinol Nutr. 2009;56 Suppl. 1:20–8.

4. Doherty GM, Weber B, Norton JA. Cost of unsuccessful surgery for primary hyperparathyroidism. Surgery. 1994;116:954–7.
5. Fayet P, Hoeffel C, Fulla Y, Legmann P, Hazebroucq V, Luton J, et al. Technetium-99m sestamibi scintigraphy, magnetic resonance imaging and venous blood sampling in persistent and recurrent hyperparathyroidism. Br J Radiol. 1997;70:459–64.
6. Jaskowiak N, Norton JA, Alexander HR, Doppman JL, Shawker T, Skarulis M, et al. A prospective trial evaluating a standard approach to reoperation for missed parathyroid adenoma. Ann Surg. 1996;224:308–22.
7. Jones JJ, Brunaud L, Dowd CF, Duhn QY, Morita E, Clark OH. Accuracy of selective venous sampling for intact parathyroid hormone in difficult patients with recurrent or persistent hyperparathyroidism. Surgery. 2002;132:944–51.
8. Ito F, Sippel R, Lederman J, Chen H. The utility of intraoperative bilateral internal yugular venous sampling with rapid parathyroid hormone testing. Ann Surg. 2007;245:959–63.
9. Udelsman R, Aruny J, Doniovan P, Sokoll L, Santos F, Donabedian R, et al. Rapid parathyroid hormone analysis during venous localization. Ann Surg. 2003;237:714–21.

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Amyloid goiter secondary to rheumatoid arthritis. A case report☆

Bocio amiloide secundario a artritis reumatoide. A propósito de un caso

Amyloidosis includes different diseases characterized by the extracellular accumulation of insoluble, toxic protein in different tissues and organs. The most common forms of systemic amyloidosis are primary amyloidosis (PA) of light chains and secondary amyloidosis (SA) caused by chronic inflammatory diseases.[1–4]

In autopsy studies, amyloid material is found in the thyroid gland of 80% of patients with SA and 50% of patients with PA.[5,6]

Amyloid goiter (AG) is an uncommon condition that is characterized by thyroid tissue infiltration by amyloid material, which causes thyroid gland enlargement.[6,7] In SA, the deposition of amyloid A (AA) protein is associated with atrophy of thyroid follicles.[7,8] The clinical picture of these patients is characterized by rapid, painless thyroid gland enlargement which may be associated with dysphagia, dyspnea, or hoarseness. Thyroid function is not impaired in most cases.[5–7]

A female patient with amyloid goiter associated with amyloidosis secondary to rheumatoid arthritis is reported below.

A 46-year-old female patient diagnosed with rheumatoid arthritis at 21 years of age attended the emergency room of our hospital complaining of gradual, painless thyroid gland enlargement for the previous 8 months. She reported dysphagia, odynophagia, cough, and fever during the three months prior to admission. Her regular treatment consisted of prednisone (15 mg/day) and methotrexate (7.5 mg/day). The patient had no history of kidney failure or altered thyroid function. Physical examination findings included: BP, 100/60 mmHg; HR, 102 bpm; RR, 22 breathings/min; and oral temperature, 37 °C. Other findings included pale skin, multiple cervical adenopathies, thyroid gland enlargement (grade 1b) with multiple nodules on palpation and an increased consistency, and joint deformity without active synovitis. Thyroid ultrasound examination in the emergency room showed multinodular goiter.

Laboratory test results included: WBC, 16,000/mm^3; hemoglobin, 8.3 g/dL; albumin, 1.9 g/dL; creatinine, 1.7 mg/dL; glucose, 90 mg/dL; TSH, 1.24 μIU/dL (normal range, 0.4–4.0); free T4, 1.61 ng/dL (normal range, 0.8–1.9); creatinine clearance, 56 mL/min; and 24-h proteinuria, 1.9 g/day. The erythrocyte sedimentation rate was 70 mm/h, and urine examination revealed WBCs. Intravenous ceftriaxone was therefore added to treatment.

Because of compressive symptoms, a computed tomography (CT) scan was performed before surgery, showing multinodular goiter with no tracheal compression (Fig. 1).

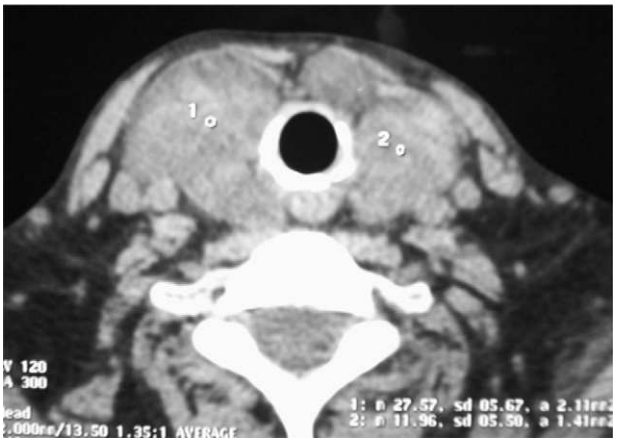

Figure 1 Computed tomography of the neck showing an enlarged thyroid gland with multiple nodules.

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