

ria included unilateral disease located before surgery by at least two imaging techniques, one of them scintigraphy with sestamibi. All patients were discharged on the first postoperative day. There was no morbidity, and disease persistence was reported in one patient.

Literature reports of MIP in patients with PTS are exceptional; the MIP series published do not specify this situation, or directly exclude patients with PTS from this approach⁵ or warn that it may prevent it.⁶ MIP in patients with persistent or recurrent PHP is more common.⁷

The use of IOPM has been recommended for patients who undergo MIP based on a single localization procedure.⁸⁻¹⁰ If no agreement exists in preoperative localization with sestamibi and ultrasound and the surgeon decides to perform MIP, the use of IOPM is indicated because the prevalence of multiglandular disease in this group is 17%.⁸⁻¹⁰

Although two patients, in addition to those previously reported, are insufficient for any conclusions to be drawn, MIP may be a valid option in patients with PTS, even with a single localization technique such as scintigraphy. The limited dissection involved and the targeted character of the procedure are theoretical advantages for the patient (a decreased risk of complications, a shorter hospital stay, a smaller scar) and decrease costs, although specific studies are needed to provide adequate evidence of this.

References

1. Gracie D, Hussain SS. Use of minimally invasive parathyroidectomy techniques in sporadic primary hyperparathyroidism: systematic review. *J Laryngol Otol*. 2012;126:221-7.
2. Norman J, Denham D. Minimally invasive radioguided parathyroidectomy in the reoperative neck. *Surgery*. 1998;124:1088-92.
3. Spiros D, Nikolaos R, Ioannis C. Minimally invasive parathyroidectomy in patients with previous endocrine surgery. *JLS*. 2011;15:499-503.
4. Dimas S, Michas S, Christakis I, Augoustis C, Alevizaki M. Minimally invasive parathyroidectomy in patients with previous neck surgery. *Hormones (Athens)*. 2012;11:160-5.
5. Kandil E, Malazai AJ, Alrasheedi S, Tufano RP. Minimally invasive/focused parathyroidectomy in patients with negative sestamibi scan results. *Arch Otolaryngol Head Neck Surg*. 2012;138:223-5.
6. Mihai R, Barczynski M, Iacobone M, Sitges-Serra A. Surgical strategy for sporadic primary hyperparathyroidism: an evidence-based approach to surgical strategy, patient selection, surgical access, and reoperations. *Langenbecks Arch Surg*. 2009;394:785-98.
7. Karakas E, Müller HH, Schlosshauer T, Rothmund M, Bartsch DK. Reoperations for primary hyperparathyroidism – improvement of outcome over two decades. *Langenbecks Arch Surg*. 2013;398:99-106.
8. Barczynski M, Konturek A, Cichon S, Hubalewska-Dydejczyk A, Golkowski F, Huszno B. Intraoperative parathyroid hormone assay improves outcomes of minimally invasive parathyroidectomy mainly in patients with a presumed solitary parathyroid adenoma and missing concordance of preoperative imaging. *Clin Endocrinol (Oxf)*. 2007;66:878-85.
9. Bergenfelz AO, Hellman P, Harrison B, Sitges-Serra A, Dralle H, European Society of Endocrine Surgeons. Positional statement of the European Society of Endocrine Surgeons (ESES) on modern techniques in pHPT surgery. *Langenbecks Arch Surg*. 2009;394:761-4.
10. Harrison BJ, Triponez F. Intraoperative adjuncts in surgery for primary hyperparathyroidism. *Langenbecks Arch Surg*. 2009;394:799-809.

Roberto de la Plaza Llamas*, José Manuel Ramia Ángel, Andreé Wolfgang Kühnhardt Barrantes, Jhonny David Gonzales Aguilar, José del Carmen Valenzuela Torres

Servicio de Cirugía General y del Aparato Digestivo, Hospital Universitario de Guadalajara, Guadalajara, Spain

* Corresponding author.

E-mail address: rdplazal@sescam.jccm.es (R. de la Plaza Llamas).

Cushing's syndrome associated with an adrenocortical oncocytoma[☆]



Síndrome de Cushing asociado a oncocitoma adrenocortical

Case report

Oncocytic neoplasms or oncocytomas usually arise in organs such as the kidney, thyroid, parathyroid, salivary, or pituitary glands. Adrenal cortex oncocytomas are extremely rare and are usually discovered as incidental findings. The case

of a female patient with Cushing's syndrome caused by a benign adrenal oncocytoma is reported.

The patient was a 61-year-old woman referred to the endocrinology outpatient clinic for obesity in February 2014. When questioned, she reported a tendency to overweight since she was 30 years old, but this had exacerbated in the last year, in which her weight had increased by 10 kg for no apparent reason. The patient had also had HBP for the previous 8 years, and was being treated with five antihypertensive drugs (ARB, beta-blocker, alpha-blocker, thiazide, and calcium channel blocker).

Her personal history included menopause at 50 years of age; she had no other remarkable personal or family history.

Physical examination findings included: 96.4 kg of weight with BMI of 38.6 kg/m², BP of 130/90 mmHg, facial plethora with slight "full moon" appearance, facial hirsutism, atrophic skin, increased posterior cervical and supraclavicular fat, increased abdominal circumference with fat redistribution, and muscle atrophy in her lower limbs.

[☆] Please cite this article as: Calderón Vicente DM, Ronquillo Rubio A, Yunta Abarca P, Quílez Toboso R, Aranda Regules J. Síndrome de Cushing asociado a oncocitoma adrenocortical. *Endocrinol Nutr*. 2015;62:416-418.

The results of the laboratory tests initially requested included: hemoglobin 16.7 g/dL and hematocrit 51.8% in a complete blood count, which was otherwise normal. The chemistry results were normal except for a glucose level of 107 mg/dL. Oral glucose (75 g) tolerance test: 106–280 mg/dL; plasma cortisol 15.9 mcg/dL after 1 mg of dexamethasone, and urinary free cortisol 233.9 mcg/24 h (No. = 0–100).

Cushing's syndrome was suspected, and the following measurements were performed, some of them repeated on two consecutive days: plasma cortisol at 8 h: 14.1 and 13.9 mcg/dL, plasma cortisol at 23 h: 12.3 and 10.9 mcg/dL, ACTH: <5 and <5 pg/mL. Weak suppression with dexamethasone (0.5 mg/6 h 2 days): plasma cortisol 13.7 mcg/dL, urinary free cortisol 160 mcg/24 h.

Catecholamine and metanephrine levels in 24 h urine were normal, as were all other androgen levels measured (testosterone 0.27 ng/mL, androstenedione 2.04 ng/mL, DHEAS 1.3 mcg/mL). Gonadotropin and estradiol levels were FSH 42.80 mIU/mL, LH 7.21 mIU/mL, and estradiol 13 pg/mL.

Abdominal CT with contrast revealed an oval lesion, well defined and homogeneous, dependent on the left adrenal gland, approximately 33 mm × 30 mm in size. Hounsfield units (HU) were 23 HU without contrast; after intravenous contrast injection, 102 HU at 65 s and 40 HU at 10 min. This showed the lesion to be benign because washout was greater than 50%, despite showing low lipid content behavior and being denser than normal.

The patient underwent a left laparoscopic adrenalectomy. Intravenous hydrocortisone 100 mg was administered before surgery, which was uneventful. The postoperative course was favorable, with hospital discharge 6 days after surgery. Three months after surgery. BP values were normal

without antihypertensive treatment, the patient had lost 4 kg of weight, and her facial plethora had clearly improved. At 11 months, the patient continues on replacement therapy with hydrocortisone 30 mg/day, because in the most recent laboratory tests, her cortisol level after ACTH had increased from 3.4 to 7.6 mcg/dL.

Gross pathological examination of the adrenalectomy specimen showed a round, well-circumscribed, encapsulated tumor that measured 3 cm in its longer axis and was mahogany brown in color upon sectioning. Microscopic examination showed a tumor population with a solid growth pattern; more than 50% of tumor cells had eosinophilic and granular cytoplasm. These oncocytic cells had nuclei with mild pleomorphism; no mitotic figures were found. Immunohistochemistry tests were positive for vimentin, alpha-inhibin, and melan-A, weakly positive for calretinin, and focally positive for synaptophysin, with no staining for chromogranin, S-100, EMA, and CD10. The cell proliferation index was less than 1% (Fig. 1).

Oncocytoma is a tumor which is characterized by consisting only or predominantly of oncocytes, large cells with abundant eosinophilic and granular cytoplasm as a consequence of mitochondrial accumulation. Adrenocortical oncocytoma is extremely uncommon; since it was first reported in 1986, approximately 148 cases have been published in the literature,¹ and most tumors were benign and non-functioning. Because of these characteristics, oncocytomas are usually diagnosed incidentally.² These tumors have been reported at all ages, with no clear preference (mean age 47 years, range 3–77 years), and are more common in females (2.5:1) and in the left adrenal gland (3.5:1). However, approximately 20% of adrenal oncocytomas may show some degree of malignancy, and hormone hyperproduction is found in 17% of cases.^{3,4}

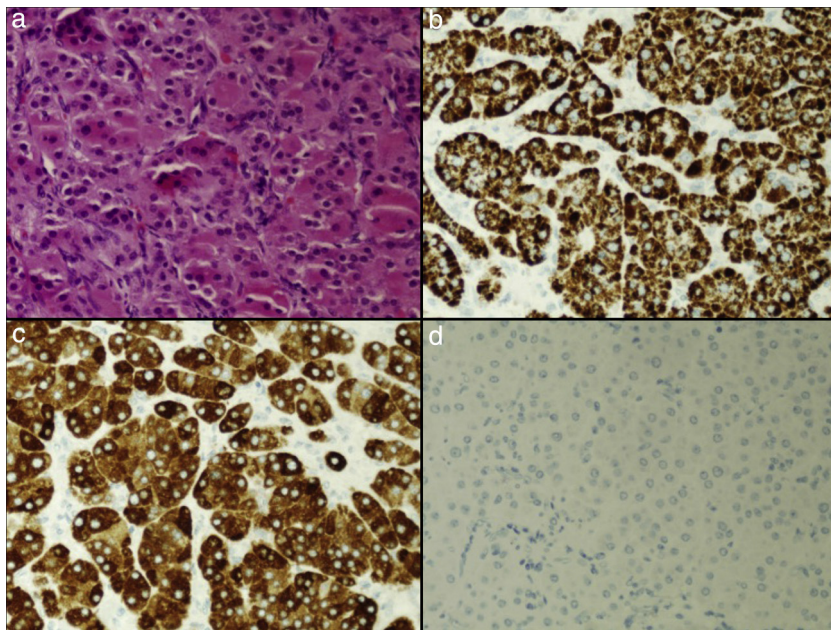


Figure 1 (a) Proliferation of tumor cells with large eosinophilic and granular cytoplasm, with a diffuse growth pattern, showing nuclear pleomorphism. (b–d) Tumor cell cytoplasm shows strong, diffuse staining with melan-A and alpha-inhibin, but no staining for chromogranin.

Cushing's syndrome associated with adrenal oncocytoma has been reported in very few cases.^{5–8} The reported patient was diagnosed with Cushing's syndrome of adrenal origin, and therefore underwent surgery, which is the usually recommended therapeutic alternative⁹ and achieved resolution of her hypercorticism. The surgical specimen was examined based on the description by Bisceglia et al.¹⁰ for oncocytic adrenal tumors, according to which, adrenal tumors with more than 90% oncocytic cells are considered pure oncocytic tumors (A), those with 50–90% oncocytic cells are considered as mixed oncocytic tumors (B), and those with less than 50% oncocytic cells are classified as conventional adrenocortical tumors with oncocytic differentiation (C). Our case belonged to category B. The immunohistochemical profile of the tumor reported is superimposable on that of oncocytic adrenocortical tumors. These tumors are typically positive for vimentin, melan-A, alpha-inhibin, synaptophysin, and calretinin, and negative for CK20, chromogranin, S-100, EMA, and CD10.¹ There are several classifications for determining the behavior of oncocytic adrenal tumors, of which the most widely accepted is the Lin–Weiss–Bisceglia classification.² This system proposes major and minor criteria, so that the presence of at least one of the three major criteria (mitotic index greater than 5 per 50 high-power fields, atypical mitoses, and venous invasion) suggests malignancy, at least one of the four minor criteria (size greater than 10 cm and/or weight greater than 200 g, microscopic necrosis, capsular invasion, and sinusoid invasion) involves an uncertain malignant potential, and the absence of major and minor criteria suggests a benign potential. No major or minor criteria were found in our patient, and a potentially benign tumor was therefore diagnosed.

Adrenal oncocytoma should be considered in differential diagnosis of Cushing's syndrome of adrenal origin, or even adrenal incidentaloma, because most oncocytomas are non-functioning.

References

1. Mearini L, del Sordo R, Costantini E, Nunzi E, Porena M. Adrenal oncocytic neoplasm: a systematic review. *Urol Int*. 2013;91:125–33.
2. Bisceglia M, Ludovico O, di Mattia A, Ben-Dor D, Sandbank J, Pasquinelli G, et al. Adrenocortical oncocytic tumors: report of 10 cases and review of the literature. *Int J Surg Pathol*. 2004;12:231–43.
3. Tahar GT, Nejib KN, Sadok SS, Rachid LM. Adrenocortical oncocytoma: a case report and review of literature. *J Pediatr Surg*. 2008;43:E1–3.
4. Xiao G, Pertsemlidis D, Unger P. Functioning adrenocortical oncocytoma. A case report and review of the literature. *Ann Diagn Pathol*. 2005;9:295–7.
5. Kabayegit OY, Soysal D, Oruk G, Ustaoglu B, Kosan U, Solmaz S, et al. Adrenocortical oncocytic neoplasm presenting with Cushing's syndrome: a case report. *J Med Case Rep*. 2008;2:228.
6. Lee SS, Baek KH, Lee YS, Lee JM, Kang MI, Cha BY, et al. Subclinical Cushing's syndrome associated with an adrenocortical oncocytoma. *J Endocrinol Invest*. 2008;31:675–9.
7. Sahin SB, Yucel AF, Bedir R, Ogullar S, Ayaz T, Algun E. Testosterone- and cortisol-secreting adrenocortical oncocytoma: an unusual cause of hirsutism. *Case Rep Endocrinol*. 2014;2014:206890.
8. Singhai A, Banzal S. Oncocytic adrenal tumour presenting as Cushing syndrome: rare presentation of a rare tumour. *Egypt J Intern Med*. 2014;26:184–5.
9. Muñoz de Nova JL, García-Sanz Í, del Campo Val L, Delgado Valdeuza J, Martín-Pérez E. Oncocytoma: una lesión infrecuente en la glándula suprarrenal. *Endocrinol Nutr*. 2015;62:144–5.
10. Bisceglia M, Ben-Dor D, Pasquinelli G. Oncocytic adrenocortical tumors. *Pathol Case Rev*. 2005;10:228–42.

Dulce M. Calderón Vicente^{a,*}, Araceli Ronquillo Rubio^b, Pedro Yunta Abarca^c, Rosa Quílez Toboso^a, Jaime Aranda Regules^a

^a Sección de Endocrinología y Nutrición, Hospital Virgen de la Luz, Cuenca, Spain

^b Servicio de Anatomía Patológica, Hospital Virgen de la Luz, Cuenca, Spain

^c Servicio de Cirugía General, Hospital Virgen de la Luz, Cuenca, Spain

* Corresponding author.

E-mail address: dmcv2000@yahoo.es

(D.M. Calderón Vicente).