10.5005/jp-journals-10002-1159

CASE REPORT

A Cautionary Case: Adrenal Insufficiency after Unilateral Adrenalectomy for Adrenocortical Carcinoma

[1]Heather Player, [2]Robert Babkowski, [3]Xiang Dong

ABSTRACT

Subclinical Cushing's syndrome among patients with incidentally discovered adrenal masses has been well documented in the literature. This population does not exhibit the classic signs of Cushing's syndrome, but nonetheless present with postoperative adrenal insufficiency after unilateral adrenalectomy of nonfunctioning incidentalomas. Further, the results of extensive preoperative testing do not correlate with postoperative hypoadrenalism with adequate sensitivity. The patient is an 84-year-old male, who presented with vague complaints of abdominal pain and fatigue, with computed tomography (CT) scan demonstrating an enlarging left adrenal gland up to 5.5 cm. The patient had no evidence of hypothalamic-pituitary-adrenal axis dysfunction based on history, physical examination and preoperative testing. Thus, the lesion was presumed nonfunctional and was excised laparoscopically. Pathology demonstrated an unfortunate diagnosis of adrenocortical carcinoma (ACC). On postoperative day 1, the patient exhibited hypotension and hypoglycemia, with a cortisol level of 0.3 μg/dl. The patient responded to hydrocortisone, supporting the presumed diagnosis of hypoadrenalism. ACC is a rare and aggressive tumor, with only 300 documented cases per year in the United States. Thus, there is a paucity of data related to pre- and postoperative management. Since a third of the patients present with nonfunctioning tumors, postsurgical care are based on literature from nonfunctional incidentalomas until further research establishes guidelines. Our experience with acute hypoadrenalism after unilateral adrenalectomy in the setting of ACC suggests the need for routine postoperative testing of cortisol levels.

Keywords: Adrenocortical carcinoma, Adrenal insufficiency, Adrenalectomy, Steroid replacement, Hypoadrenalism.

How to cite this article: Player H, Babkowski R, Dong X. A Cautionary Case: Adrenal Insufficiency after Unilateral Adrenalectomy for Adrenocortical Carcinoma. World J Endoc Surg 2015;7(1):17-20.

Source of support: Nil

Conflict of interest: None

INTRODUCTION

Subclinical Cushing's syndrome among patients with incidentally discovered adrenal masses has been well documented in the literature.[1,2] The increased prevalence of abdominal imaging has uncovered otherwise asymptomatic adrenal masses, a number of which (3-30%) have subclinical findings.[2-4] The appropriate management—surgical *vs* medical—continues to be debated.[5] However, what has been established is that even in the setting of mild cortisol excess, though insufficient to instigate the typical findings of Cushing's syndrome, does predispose patients to metabolic and cardiovascular sequelae, including insulin resistance, type 2 diabetes, obesity and dyslipidemia.[1,3,5,6] This suggests that the hypothalamic-pituitary-adrenal axis is impacted despite lack of overt clinical findings.

After unilateral adrenalectomy for a nonfunctional tumor, the remaining adrenal gland usually has sufficient reserve to maintain homeostasis. However, care must be taken to recognize subclinical adrenal insufficiency. Such ongoing suppression of the contralateral adrenal gland due to a subclinical hypercortisolism is sufficient to produce deleterious postoperative effects on the patient undergoing unilateral adrenalectomy. This dictum has led to thorough preoperative testing and reflexive postoperative cortisol supplementation among patients undergoing unilateral adrenalectomy for incidentalomas.

Preoperative testing lacks sensitivity in predicting which patients will require postoperative cortisol repletion among patients with incidentalomas. This highlights the importance of vigilant postoperative cortisol level monitoring and repletion in the patient who has undergone unilateral adrenalectomy for incidentaloma.

There is, however, a lack of studies for patients undergoing unilateral adrenalectomy for apparently nonfunctioning adrenocortical carcinoma, likely owing to the rarity of the disease. Although suggestions can be drawn from the data on incidentalomas, it must be acknowledged that this vacancy presents a potentially serious risk for postoperative complications of hypoadrenalism.

CASE REPORT

This is the case of an 84-year-old man with an unexplained enlargement of the left adrenal gland. His medical history is significant for esophageal leiomyoma and recurrent syncopal events with rapid atrial fibrillation, status postpacemaker placement. Patient first

[1]Resident, [2]Chair, [3]Assistant Clinical Professor

[1,3]Department of Surgery, Stamford Hospital, Stamford, USA

[2]Department of Pathology, Stamford Hospital, Stamford, USA

Corresponding Author: Xiang Dong, Assistant Clinical Professor, Department of Surgery, Stamford Hospital, Stamford USA, Phone: 12032765959, e-mail: xdong@stamhealth.org

presented to the surgical service 4 years prior, when he was found to have positron emission tomography (PET)-positive retroperitoneal lymphadenopathy. Patient at that time underwent a laparoscopic retroperitoneal nodal biopsy, which demonstrated neither active lymphoma nor evidence of other malignancy.

Patient returned to the surgical service for evaluation for vague symptoms of weight loss and mild abdominal discomfort. Physical examination revealed no Cushingoid features. Computed tomography (CT) of the abdomen was repeated, and demonstrated a 3-year interval increase in size of the left adrenal gland mass from 1.4 to 5.5 by 2.8 cm (Figs 1A and B). Right adrenal gland decreased in size from 3.6 to 1.6 cm. Retrocrural adenopathy at the level of the superior mesenteric artery additionally demonstrated improvement from 9.0 × 3.4 to 6.8 × 2.0 cm. Biochemical workup demonstrated no evidence of a functioning adrenal mass: 24-hour urine cortisol level was 7.4 mcg (3.5-45 mcg/24 hours). Positron emission tomography scan was performed the following week, showing the left adrenal gland having a sigh SUV uptake of 6.8 (Fig. 2).

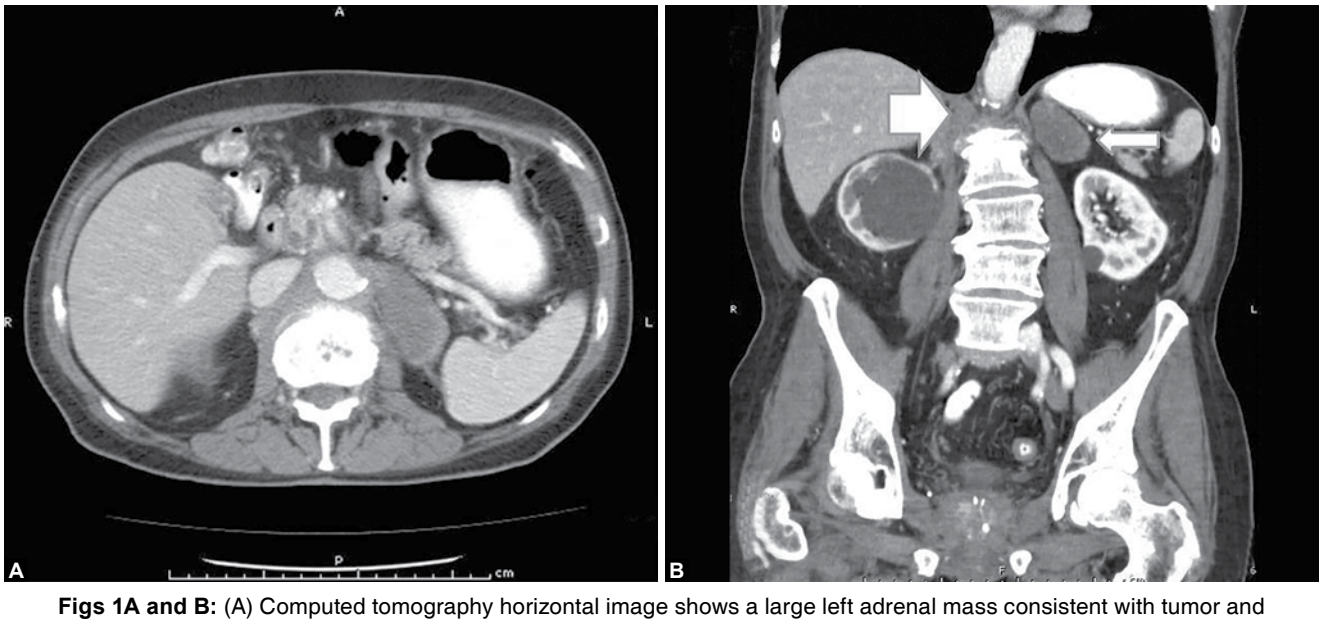
Based on the increase in size as well as PET positivity, surgery was planned for the risk of malignancy. Patient underwent a laparoscopic left adrenalectomy with concurrent celiac node excisional biopsy. Intraoperatively, the patient was found to have a large adrenal mass, with no invasion of adjacent glands.

A 24 gm left adrenal gland was delivered to pathology, measuring 7.1 by 4.5 by 2.3 cm. Serial sectioning revealed red-tan, diffusely friable tissue (Figs 3A and B). The tumor was positive for NSE with a high proliferation (Ki-67 at 80%), along with extensive necrosis and extracapsular invasion. Mitotic rate was greater than 5 per 50 high power field (HPF). These pathologic findings were consistent with adrenal cortical carcinoma according to modified Weiss criteria.[7] No lymphatic or vascular invasion was defined, and all surgical margins were negative for malignancy. A pathologic stage of T2, Nx, Mx (stage II) was ascertained.

Postoperative day 1, the patient became acutely lethargic, and demonstrated a blood pressure drop from baseline of 145/75 to 70/40. The hypotension was unresponsive to fluid boluses. A random serum cortisol was drawn, and resulted in a level of 0.3 µg/dl. Hydrocortisone 100 mg every 8 hours was initiated for acute adrenal insufficiency. Additionally, a troponin elevation (6.29 ng/ml, which continued until a peak of 18.82 ng/ml) was identified. There were no obvious EKG changes, and bedside echo showed a hyperdynamic left ventricle with no wall-motion abnormalities. Cardiology consult suggested a non-ST elevation myocardial infarction on the basis of demand ischemia from prolonged hypotension. The patient's hypoadrenal state responded to hydrocortisone with resolution of his symptoms. Troponin elevations resolved, and the patient was discharged to home in good condition on postoperative day 7 with no further incident.

DISCUSSION

Adrenocortical carcinoma (ACC) is a rare and aggressive tumor. Surgical resection remains the single potentially curative option from this diagnosis.[8,9] The mean survival rate is 3 to 9 months, which is increased to 13 to 28 months with complete resection.[10-12] The low incidence, 300 documented cases per year in the United States, lends



Figs 1A and B: (A) Computed tomography horizontal image shows a large left adrenal mass consistent with tumor and (B) coronal image of the abdomen shows the tumor (small arrow) as well as adenopathy (large arrow) in the abdomen

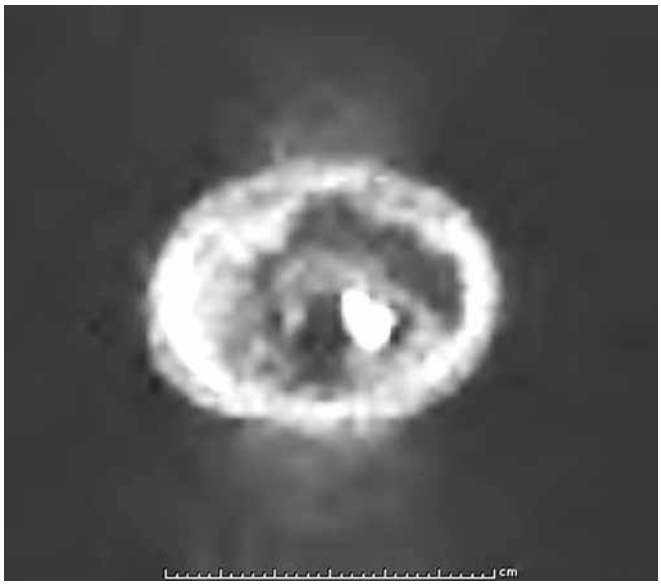


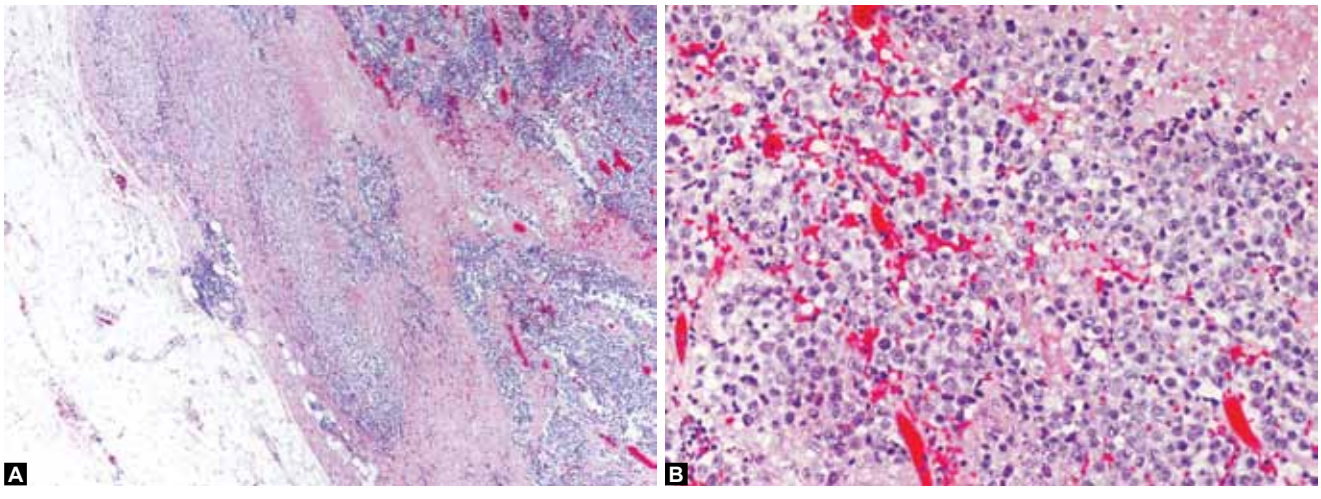
Fig. 2: Positron emission tomography scan shows high SUV within the left adrenal gland location

itself to a distinct paucity of data related to the pre- and postoperative management of ACC, and thus a lack of clear guidelines. As surgery remains the only potentially curative option for ACC, this deficiency allows for potentially hazardous outcomes, as demonstrated in this case.

Adrenocortical carcinoma may be distinguished from benign lesions based on radiographic findings as well as functional status, which provide additional insight. The likelihood of malignancy is doubled for adrenal masses larger than 4 cm, and increases to over nine-fold when the mass exceeds 8 cm, leading to the recommendation that masses greater than 4 cm be surgically excised, in the past.[13] General consensus indicates surgery for adrenal mass with continued growth during observation is warranted. In addition to size criteria, CT features may be suggestive of neoplasm, including irregular borders, attenuation greater than 10 Hounsfield units, lymphadenopathy, metastatic disease, and calcifications.[9] Recommendations continue for resection of all functional adrenal masses. It must be noted that FNA is not recommended; it carries a high false-negative rate as well as risk for complications particularly if the tumor is a pheochromocytoma.[14]

Adrenocortical carcinoma is frequently discovered once advanced in size, with more than half demonstrating local-regional spread. This pattern seems to persist despite increased frequency of high-quality imaging and greater frequency in scanning.[15] As with this patient, nonfunctional tumors are more likely to be discovered incidentally, as their symptoms are vague: abdominal pain, nausea, weight loss and fatigue, whereas functional tumors present with hyperadrenalism.

Suggestions for pre- and postoperative management may be borrowed from experience with patients with incidentalomas, as the physiology of suppression to the contralateral adrenal gland is identical. The question remains as to the prevalence of subclinical Cushing's syndrome among patients with ACC. Frank hyperaldosteronism is rare in ACC, yet 40 to 50% present with hypercortisolism.[16,17] If similar rates are found, then several authors have suggested that patients undergoing unilateral adrenalectomy with concomitant subclinical hypocortisolism should undergo replacement postoperatively owing to a described difficulty in prediction.[18,19] Evaluation of the HPA axis may suggest which patients are more likely to suffer from postoperative hypocortisolism. The workup panel includes abnormality in midnight serum cortisol as a single parameter; midnight serum cortisol with 1 mg dexamethasone stimulation test or the finding of two abnormalities when examining midnight serum cortisol, urine-free cortisol, adrenocorticotropin hormone and the 1 mg dexamethasone stimulation test.[20]



Figs 3A and B: (A) Hematoxylin and eosin staining image shows the tumor with capsular invasion and necrosis (H&E: 40×) and (B) pathology image shows marked cellular pleomorphism and atypia (H&E: 400×)

CONCLUSION

Based on our experience with this case as well as the frequency of hormonally active ACC, we recommend vigilance for adrenal insufficiency in patients undergoing unilateral adrenalectomy for ACC. Routine cortisol replacement needs to be considered in this patient population.

REFERENCES

1. Tsinberg M, Liu C, Duh Q. Subclinical cushing's syndrome. J Surg Oncol 2012;106(5):572-574.
2. Terzolo M, Reimondo G, Bovio S, Angeli A. Subclinical cushing's syndrome. Pituitary 2004;7(4):217-223.
3. Mantero F, Terzolo M, Arnaldi G, Osella G, Masini AM, Ali A, Giovagnetti M, Opocher G, Angeli A. A survey on adrenal incidentaloma in Italy. J Clin Endocrinol Metabol 2000;85(2):637-644.
4. Muth A, Hammarstedt L, Hellström M, Sigurjónsdóttir HÁ, Almqvist E, Wängberg B. Cohort study of patients with adrenal lesoins discovered incidentally. Br J Surg 2011 May; 98(10):1383-1391.
5. Di Dalmazi G, Vicennati V, Rinaldi E, Morselli-Labate AM, Giampalma E, Mosconi C, Pagotto U, Pasquali R. Progressively increased patterns of subclinical cortisol hypersecretion in adrenal incidentalomas differently predict major metabolic and cardiovascular outcomes: a large cross-sectional study. Eur J Endocrinol 2012;166(4):669-677.
6. Ivović M, Marina LV, Vujović S, Tančić-Gajić M, Stojanović M, Radonjić NV, Gajić M, Soldatović I, Micić D. Nondiabetic patients with either subclinical Cushing's or nonfunctional adrenal incidentalomas have lower insulin sensitivity than healthy controls: clinical implications. Metabolism 2013 Jun; 62(6):786-792.
7. Aubert S, Wacrenier A, Leroy X, Devos P, Carnaille B, Proye C, Wemeau JL, Lecomte-Houcke M, Leteurtre E. Weiss system revisited: a clinicopathologic and immunohistochemical study of 49 adrenocortical tumors. Am J Surg Pathol 2002; 26(12):1612-1619.
8. Cobb WS, Kercher KW, Sing RF, Henifort BT. Laparoscopic adrenalectomy for malignancy. Am J Surg 2005 Apr;189(4): 405-411.
9. Paton BL, Novitsky YW, Zerey M, Harrell AG, Norton HJ. Outcomes of adrenal cortical carcinoma in the United States. Surgery 2006;140(6):914-920.
10. Kebebew E, Reiff E, Duh QY, Clark OH, McMillan A. Extent of disease at presentation and outcome of adrenocortical carcinoma: have we made progress? World J Surg 2006;30(5): 872-878.
11. Ng L, Libertino JM. Adrenocortical carcinoma: diagnosis, evaluation and treatment. J Urol 2003 Jan;169(1):5-11.
12. Bourdeau I, MacKenzie-Feder J, Lacroix A. Recent advances in adrenocortical carcinoma in adults. Current Opin Endocrinol Diabetes Obes 2013 Jun;20(3):192-197.
13. Sturgeon C, Shen WT, Clark OH. Risk assessment in 457 adrenal cortical carcinomas: how much does tumor size predict the likelihood of malignancy? J Am College of Surgeons 2006;202(3):423-430.
14. McCorkell SJ, Niles NL. Fine-needle aspiration of catecholamine-producing adrenal masses: a possibly fatal mistake. Amer J Roentgenol 1985;145(1):113-114.
15. Kutikov A, Mallin K, Canter D, Wong YN, Uzzo RG. Effects of increased cross-sectional imaging on the diagnosis and prognosis of adrenocortical carcinoma: analysis of the national cancer database. J Urol 2011 Sep;186(3):805-810.
16. Seccia TM, Fassina A, Nussdorfer GG, Pessina AC, Rossi GP. Aldosterone-producing adrenocortical carcinoma: an unusual cause of Conn's syndrome with an ominous clinical course. Endocr Relat Cancer 2005;12(1):149-159.
17. Ayala-Ramirez M, Jasim S, Feng L, Ejaz S, Deniz F, Busaidy N, Waguespack SG, Naing A, Sircar K, Wood C, et al. Adrenocortical carcinoma: clinical outcomes and prognosis of 330 patients at a tertiary care center. Eur J Endocrinol 2013 Oct;169(6):891-899.
18. Terzolo M, Bovio S, Reimondo G, Pia A, Osella G, Borretta G, Angeli A. Subclinical Cushing's syndrome in adrenal incidentalomas. Endocrinology and Metabolism Clinics of North America 2005;34(2):423-439.
19. Tsagarakis S, Vassiliadi D, Thalassinos N. Endogenous subclinical hypercortisolism: diagnostic uncertainties and clinical implications. J Endocrinol Investig 2006;29(5):471-482.
20. Eller-Vainicher C, Morelli V, Salcuni AS, Torlontano M, Coletti F, Iorio L, Cuttitta A, Ambrosio A, Vicentini L, Carnevale V, et al. Post-surgical hypocortisolism after removal of an adrenal incidentaloma: is it predictable by an accurate endocrinological work-up before surgery? Eur J Endocrinol 2010; 162:91-99.