Radiology Case Reports 16 (2021) 3168–3171

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/radcr

Case Report

ACTH-independent Cushing's syndrome due to bilateral adrenocortical adenoma: A case report ☆

Majd Sharaf, MD candidate[a,*], *Rama Al-Saqqa, MD candidate*[a], *Mouhammad Kourabi, Associate Professor*[b]

[a] *Faculty of Medicine, Damascus University, Damascus, Syria*
[b] *Department of General Surgery, Al-Mouwasat University Hospital, Damascus, Syria*

ARTICLE INFO

Article history:
Received 11 July 2021
Revised 27 July 2021
Accepted 31 July 2021
Available online 25 August 2021

Keywords:
Cushing's syndrome
Adrenal adenoma
Adrenocortical adenoma
Adrenalectomy

ABSTRACT

The chronic excess of glucocorticoids results in Cushing's syndrome. Cushing's syndrome presents with a variety of signs and symptoms including: central obesity, proximal muscle weakness, fatigue striae, poor wound healing, amenorrhea, and others.

ACTHindependent Cushing's syndrome is usually due to unilateral adenoma. A rare cause of it is bilateral adrenal adenomas.

In this paper we report a case of a 43-year-old woman with Cushing's syndrome due to bilateral adrenal adenoma.

Introduction

Cushing's syndrome (CS) is caused by chronic excess glucocorticoids [1]. It is associated with increased morbidity and mortality due to hypertension, diabetes, coagulopathy, cardiovascular disease, infections, and fractures .[2]. The excess of glucocorticoid can be endogenous or exogenous. Endogenous CS can be divided into adrenocorticotropic hormone (ACTH)-independent and ACTH -dependent forms [3]. ACTH-independent CS accounts for 15-20% of endogenous CS cases, mostly caused by unilateral adrenocortical adenomas [4]. Bilateral adrenocortical adenoma (BAA) is a rare cause of ACTH-independent CS [3].

In this paper, we report a case of a 43-year-old woman suffering from Cushing's syndrome due to bilateral adrenocortical adenoma (BAA).

Case presentation

A 43-year-old female patient presented to endocrinology clinic at Al-Mouwasat University Hospital complaining of fatigue, lower back pain, increased weight, muscle weakness, and amenorrhea. She is a smoker but consumes no alcohol.

The patient's history included left hip joint replacement 1 year ago (fracture after trauma) and hypertension since

☆ Declaration of interests: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

* Corresponding author.
E-mail addresses: majed4409@gmail.com (M. Sharaf), rama1997med@gmail.com (R. Al-Saqqa), mhdkourabi@hotmail.fr (M. Kourabi).

https://doi.org/10.1016/j.radcr.2021.07.093

3 years which was not well-controlled by medication. There is no family history of hypertension but a history of diabetes mellitus was found. She also mentioned a history of irregular steroid use.

Her vital signs at admission were as follows: blood pressure 150/90 mm Hg, heart rate = 77 beats per minute, body temperature = 36.5°C, respiratory rate = 20 breathes per minute, oxygen saturation = 98% on room air.

On physical examination, we found ecchymosis, thinning of the skin, purple striae, buffalo hump, lower limbs edema, and proximal muscle weakness with no evidence of acne or hirsutism.

Biochemical and radiological assessment were done. Laboratory work-up found a high level of fasting blood glucose (135 mg/dL; normal range: 70-99 mg/dL), slightly elevation of HbA1c level (6.5%; normal range: 5.7%-6.4%), normal level of cholesterol and triglycerides (total cholesterol = 176 mg/dL; normal range: <200 mg/dL, triglycerides = 145 mg/dL; normal range: <150 mg/dL), and low level of 25(OH) vitD (15.6 ng/mL; normal range: 30-50 ng/mL). A high level of midnight serum cortisol was observed (37.8 mcg/dL; normal range: <7.5 mcg/dL) and low level of ACTH (2 pg/mL; normal range: 10-60 pg/mL) that was followed by cortisol suppression test which was abnormal (37.1 mcg/dL). Plasma metanephrine and plasma normetanephrine were normal (61 pg/mL; normal range: 0-140 pg/mL and 151 pg/mL; normal range: 70-1700 pg/mL, respectively).

Magnetic resonance imaging (MRI) of pituitary gland revealed evidence of a partial empty sella turcica, however, Multi-slice Computed Tomography (MSCT) of the abdomen showed bilateral, heterogeneous, well-demarcated adrenal masses with moderate contrast enhancement with no evidence of hemorrhage or calcification (Fig. 1).

Laparoscopic bilateral adrenalectomy was performed and sent to pathology lab for examination. The level of serum cortisol has been significantly reduced after surgery and the pathological evaluation confirmed the diagnosis of bilateral adrenocortical adenomas (Figs. 2 Figs. 3).

She was administered with oral prednisolone 10 mg BID (5 mg at morning + 5 mg at night), 0.2 mg of fludrocortisone, 1000 mg of metformin and supplemental calcium with vitamin D3. Clinical and laboratory follow-up showed improvement of her fatigue, blood pressure 110/80, muscle strength, and fasting blood glucose (80 mg/dL).

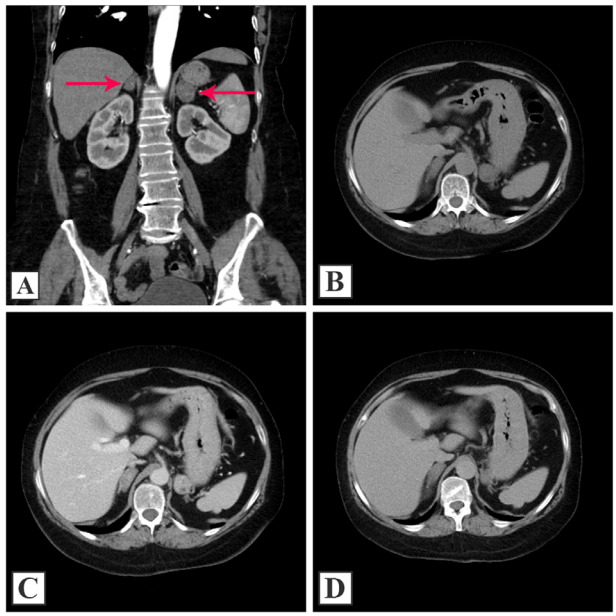

Fig. 1 – Coronal view (A) shows right and left adrenal masses "red arrows", transverse views during different phases (B, C, D) reveal bilateral, heterogeneous, well demarcated adrenal masses with moderate contrast enhancement suggesting lipid-poor adenoma, measuring 3.7 cm for the right mass and 3.3 cm for left one.

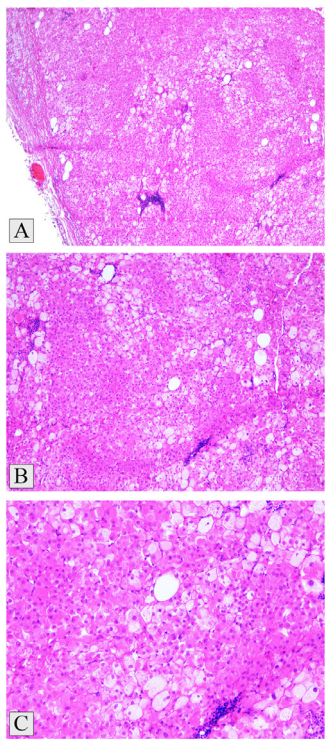

Fig. 2 – H&E stain of the right adrenal gland show adrenocortical adenoma with adjacent cortical atrophy. A (x 40), B (x 100), and C (x 200).

Discussion

Adrenocortical adenoma is the most common benign tumor of the adrenal gland, it accounts for approximately 52% of adrenal tumor cases [5]. The prevalence of adenoma varied according to age, it is 0.14% in patients with age of 20-29 years and 7% in those with older than 70 years [6].

Adenomas are mostly unilateral [4] and the frequency of bilaterality is only 20% of cases in one series [7].

Adrenocortical adenoma may secret glucocorticoids, aldosterone or sex hormones causing different clinical manifestations diseases [8]. Glucocorticoid-producing adenoma

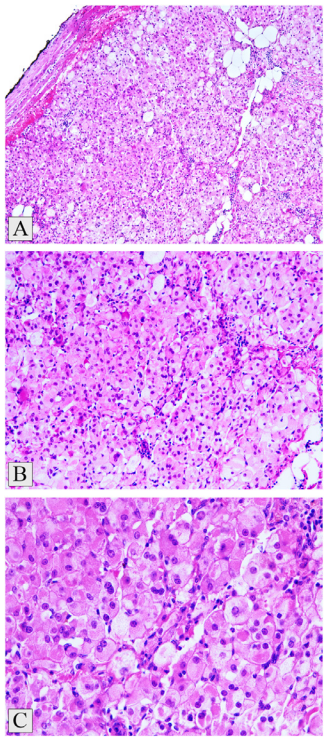

Fig. 3 – H&E stain of the left adrenal gland show adrenocortical adenoma with vacuolated (clear) cells A (× 40), B (× 100), and C (× 200).

present with the symptoms and signs of Cushing syndrome (CS) [9].

CS patients present with obesity or weight gain (95% of cases), facial plethora (90%), moon face (90%), thinning of skin (85%), menstrual irregularity (80%), hypertension (75%), hirsutism (75%), easy bruising (65%), weakness (60%), glucose intolerance/diabetes (60%), decreased bone mineral density/fracture (50%) [9] purple striae (44-50%) [1], back pain, peripheral edema [11], and others. Our patient presented with typical symptoms.

Initial recommended laboratory tests include (late night salivary cortisol, midnight serum cortisol, urine cortisol, 1 mg overnight or 2 mg 48-hour dexamethasone suppression test), a second abnormal result is recommended to establish the diagnosis of CS. Other diagnostic laboratory tests include awake midnight serum cortisol test which has 90%-92% sensitivity with specificity of 96% for values greater than 8.3–12 pg/dL [10]. In our patient, cortisol suppression test and midnight serum cortisol were high confirming the diagnosis of CS.

Measurement of plasma ACTH levels is the next step to define the cause of CS [1]. Our patient's results imply ACTH-independant CS.

Imaging of adrenal glands is needed to define adrenal lesions causing CS [1]. On computerized tomography scan, adrenocortical adenoma is usually well defined, homogeneous and attenuation values varied depending on the amount of lipid present [12]. In our case, CT scan suggesting bilateral heterogeneous lipid-poor adenoma.

The radiological findings of patient with bilateral adrenal mass vary based on the underlying pathology. In the case of a low level of ACTH, the differential diagnosis of ACTH-independent CS includes: BAAs, primary pigmented nodular adrenocortical disease, ACTH-independent macronodular adrenal hyperplasia (AIMAH) [3].

The definitive diagnosis of adrenocortical adenoma puts according to pathology evaluation. Tumors associated with CS present as sharply circumscribed mass that usually measure 3 to 4 cm in average diameter. Adenomas are most often composed of small nests, cords, or alveolar arrangements of vacuolated (clear) cells that most closely resemble those of the normal fasciculate [13]. Our case has typical findings.

Treatment is laparoscopic unilateral or bilateral adrenalectomy. Bilateral adrenalectomy leads to rapid resolution of hypercortisolemia and related morbidity but patients need lifelong glucocorticoid and mineralocorticoid replacement [1].

Conclusion

Although Cushing's syndrome due to bilateral adrenal adenoma is rare, it should be considered in mid-aged females with typical symptoms and radiological assessment finds bilateral well-encapsulated adenomas of 2.0-3.5 cm in diameter, with the presence of single or multiple nodules.

Patient consent

Patient consent has been obtained.

Acknowledgments

We would like to thank Dr.Yazan al-abdullah, Dr. Rahaf Dreaby, Dr. Amer Ebrahim and Mouaz al-obary for their contributions.

REFERENCES

[1] Sharma ST, Nieman LK, Feelders RA. Cushing's syndrome: epidemiology and developments in disease management. Clin Epidemiol 2015;7:281–93 Published 2015 Apr 17. doi:10.2147/CLEP.S44336.
[2] Nieman LK. Recent updates on the diagnosis and management of Cushing's syndrome. Endocrinol Metab (Seoul) 2018;33(2):139–46. doi:10.3803/EnM.2018.33.2.139.
[3] Gu YL, Gu WJ, Dou JT, et al. Bilateral adrenocortical adenomas causing adrenocorticotropic hormone-independent Cushing's syndrome: a case report and review of the literature. World J Clin Cases 2019;7(8):961–71. doi:10.12998/wjcc.v7.i8.961.
[4] Kiernan CM, Solórzano CC. Surgical approach to patients with hypercortisolism. Gland Surg 2020;9(1):59–68. doi:10.21037/gs.2019.12.13.
[5] Franco M, Nora A. A comprehensive approach to adrenal incidentalomas. Arq Bras Endocrinol Metab [Internet]

2004;48(5):583–91 [cited 2021 Apr 30]. doi:10.1590/S0004-27302004000500003.
[6] Kloos RT, Gross MD, Francis IR, Korobkin M, Shapiro B. Incidentally discovered adrenal masses. Endocr Rev 1995;16:460–84. doi:10.1210/edrv-16-4-460.
[7] Johnson P, Horton K, Fishman E. Adrenal imaging with multidetector CT: evidence-based protocol optimization and interpretative practice. Radiographics 2009;29:1319–31. doi:10.1148/rg.295095026.
[8] Barzon L, Sonino N, Fallo F, Palu G, Boscaro M. Prevalence and natural history of adrenal incidentalomas. Eur J Endocrinol 2003;149(4):273–85 PMID: 14514341. doi:10.1530/eje.0.1490273.
[9] Mahmood E, Adenoma Anastasopoulou CAdrenal. StatPearls [Internet], Treasure Island (FL): StatPearls Publishing; 2020. 2021 Jan–. PMID: 30969728.
[10] Lila AR, Sarathi V, Jagtap VS, Bandgar T, Menon P, Shah NS. Cushing's syndrome: Stepwise approach to diagnosis. Indian J Endocrinol Metab 2011;15(Suppl4):S317–21. doi:10.4103/2230-8210.86974.
[11] Nieman Lynnette K, Biller Beverly MK, Findling James W, Newell-Price John, Savage Martin O, Stewart Paul M, Montori Victor M. The diagnosis of Cushing's syndrome: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab 2008;93(5):1526–40. doi:10.1210/jc.2008-0125.
[12] Wang F, Liu J, Zhang R, et al. CT and MRI of adrenal gland pathologies. Quant Imaging Med Surg 2018;8(8):853–75. doi:10.21037/qims.2018.09.13.
[13] Wieneke JA, Lack EE, et al. The adrenal gland. In: Silverberg's Principles and Practice of Surgical Pathology and Cytopathology. Philadelphia, PA: Churchill Livingstone (Elsevier); 2006. p. 2169.