World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(CASE REPORT)

Management of primary bilateral macronodular adrenal hyperplasia causing primary hyperaldosteronism and Cushing's syndrome: Case report and review of the literature

IMANE BOUBAGURA *, SANA RAFI, GHIZLANE EL MGHARI and NAWAL EL ANSARI

Department of Endocrinology, Diabetes, Metabolic diseases and Nutrition, Mohammed VI university hospital, Marrakech, Morocco.

World Journal of Advanced Research and Reviews, 2023, 17(01), 236–239

Publication history: Received on 01 December 2022; revised on 07 January 2023; accepted on 10 January 2023

Article DOI: https://doi.org/10.30574/wjarr.2023.17.1.0022

Abstract

Primary bilateral macronodular adrenal hyperplasia (PBMAH) is a very heterogeneous entity. The incidental identification of an increasing number of cases has shifted its clinical expression. Both in terms of cortisol excess and adrenal hyperplasia with mild forms of asymptomatic and oligosymptomatic cases with less impressive imaging phenotypes.

Activation of the cAMP/PKA pathway, either due to alteration of various downstream signaling pathways or by aberrantly expressed G protein-coupled receptors, is linked to both cortisol secretion and adrenal growth. Germline mutations in ARMC5 are a frequent genetic defect.

We report the case of a 35 -year-old female patient with primary hyperaldosteronism associated with Cushing's syndrome in the setting of macronodular adrenal hyperplasia treated by left adrenalectomy in the first instance and whose evolution was marked by a clinical and biological improvement of hypercorticism and hyperaldosteronism questioning the indication of controlteral adrenalectomy.

The appropriate management of PBMAH remains controversial. Bilateral adrenalectomy results in lifelong steroid dependence. And is best reserved for patients with severe Cushing's syndrome. Unilateral adrenalectomy may be considered in selected patients. In cases where regulation of cortisol secretion is mediated by aberrant receptors, there is some potential for medical therapy.

Keywords: Primary bilateral macronodular adrenal hyperplasia (PBMAH); Cushing's syndrome; Autonomous cortisol secretion; Surgical management

1. Introduction

Bilateral macronodular adrenal hyperplasia (PBMAH) is a very rare cause of endogenous ACTH-independent cushing syndrome (<2%).

PBMAH presents on imaging with a characteristic appearance of multiple bilateral macronodules (>10 mm) with hyperplasia of the adrenal cortex.

Pathophysiologically, the expression of aberrant membrane receptors in the adrenal cortex has an important role. In most cases, PBMAH is a sporadic disorder, although familial cases have been described.

* Corresponding author: IMANE BOUBAGURA

Recent studies have shown an association between germline/somatic mutations in the tumor suppressor gene ARMC5 in approximately 50% of cases.

The increased frequency of early diagnosed familial PMAH has resulted in subclinical hypercortisolism becoming a frequent manifestation of this disease.

The treatment of choice to control hypercortisolism in patients with PBMAH is bilateral adrenalectomy, which inevitably leads to lifelong glucocorticoid dependence and, consequently, a risk of adrenal crisis. To avoid induction of adrenal insufficiency, resection of a single adrenal gland has been proposed. Indeed, several recent studies have reported clinical and biochemical improvement after unilateral adrenalectomy, however, the number of documented patients and the associated follow-up time is still limited.

Due to the heterogeneity of the presentation and severity of this disease, therapeutic management represents a challenge to clinicians.

2. Case report

We report a case of a combination of primary hyperaldosteronism (basal Aldosterone 1035 pmoL/L, Renin 9.6 mIU/L, RAR 108, and clinical and biological independent ACTH cushing syndrome: urinary free cortisol UFC = 333 ug/24h (4.5 times normal), negative dexamethasone minute braking test (cortisol=17.7), unbroken cortisol cycle, ACTH braked at 1.3 pg/mL in the setting of a primary bilateral macronodular adrenal hyperplasia in a 35 year old female patient, hypertensive for 5 years with moderate hypokalemia.

In the absence of adrenal vein catheterization, a left adrenalectomy was performed in the first instance (size criterion) by laparoscopy. The counterlateral adrenalectomy could not be performed because of the Covid 19 pandemic.

The patient was reconvened 10 months later for control: we noted regression of the signs of hypercorticism, normalization of the blood pressure figures under monotherapy,and normalization of the biological balance: Aldosterone: 391pmol/l, RAR: 31,47, normalized UFC = 51,8 µg/24h but still a negative dexamethasone minute braking test.

The indication of contralateral adrenalectomy was questioned.

3. Discussion and review of the literature

(PBMAH) is a highly heterogeneous entity.

Its identification is becoming increasingly incidental,which has shifted its clinical expression from severe forms that are currently rarely encountered, both in terms of cortisol excess as well as adrenal hypertrophy, to rather benign asymptomatic forms with less impressive imaging phenotypes.

The appropriate management of PBMAH remains controversial. Bilateral adrenalectomy results in lifelong steroid dependence and is best reserved only for patients with severe CS. Unilateral adrenalectomy could be considered in selected patients. And finally,in cases where the regulation of cortisol secretion is mediated by aberrant receptors, there is some potential for medical therapy (1).

Unilateral superrenalectomy is recently considered as a therapeutic approach with less complications compared to bilateral, but low recommendation due to the small number of studies(1,9).

Initial remission is reported in 90% of cases, with clinical improvement and stabilization of complications related to hypercorticism (diabetes, hypertension, obesity, dyslipidemia...), with normalization of the UFC however some patients may still have negative breaking to dexamethasone(1).

Despite the clinical improvement and the normalization of blood pressure and blood sugar levels, comorbidities persist in cases of unilateral surgery(2).

The choice of the adrenal gland to be removed is not simple, the size is the main criterion used in most of the reported cases, however, in other studies adrenal vein catheterization or nor-iodocholesterol scintigraphy is used to determine the lateralization(3).

A recent study has shown a statistically significant correlation between the size of the adrenal gland and its behavior on functional tests, which may allow to operate on the largest adrenal gland as in our patient(4,7).

According to published data, the recurrence rate and the need to perform controlateral adrenalectomy are quite low at 10-15% in comparison with bilateral adrenalectomy.

However, 3 deaths were recorded in patients with PBMAH who underwent unilateral adrenalectomy as opposed to none in patients who underwent bilateral surrenalectomy. These cases of death were noted in patients with inadequate biochemical control, or in patients lost to follow-up, thus emphasizing the need for close hormonal follow-up after unilateral adrenalectomy(5,6,10).

"Adrenal spearing surgery' has recently been described as a new surgical approach by performing total adrenalectomy of the largest adrenal gland and partial adrenalectomy of the contralateral gland, to overcome lifelong hormone replacement and the risk of acute adrenal insufficiency while minimizing the risk of relapse of hypercortisolism; but current evidence regarding the use of this approach is limited(8).

4. Conclusion

Bilateral adrenalectomy is the standard option for the treatment of patients with Cushing's syndrome in relation to PBMAH, however this modality leads to permanent adrenal insufficiency and has the disadvantage of requiring lifelong hormone replacement. In addition, these patients have been found to have a significantly impaired quality of life and a high risk of acute adrenal insufficiency, with mortality ranging from 6% to 8%.

To avoid this, unilateral adrenalectomy has been proposed as a treatment option for patients with mild Cushing's syndrome.

Unilateral adrenalectomy for bilateral adrenal disease might not seem a safe option for fear of leaving the patient with an abnormal adrenal gland, which may be responsible for persistent or recurrent Cushing's syndrome.

However, recent studies have shown very encouraging results; with the achievement of an initial remission in almost all patients with normalization of UFC and improvement of clinical and metabolic parameters, with a much lower risk of adrenal insufficiency compared to bilateral with a low rate of recurrence.

These studies have important limitations, namely, the small number of patients, the absence of a control group, and the lack of multicenter studies.

Further prospective studies are needed to better assess the long-term benefits of unilateral adrenalectomy.

Given the heterogeneous presentation of this entity, there are probably patients for whom unilateral adrenalectomy is more appropriate, while in others the same approach may lead to early recurrence of hypercortisolism. Therefore, the gold standard of treatment for PBAH is not yet well defined and must be chosen according to each specific presentation.

Compliance with ethical standards

Acknowledgments

Thanking the patient for consent to describe her clinical case for the purpose of continuing education.

Disclosure of conflict of interest

The authors declare that they have no conflict of interests.

Statement of ethical approval

The present research work does not contain any studies performed on animals/humans subjects by any of the authors.

Statement of informed consent

Informed consent was obtained from the patient included in the study.

References

[1] Fabio Yoshiaki Tanno, 1 Victor Srougi, 1 Madson Q. Almeida, A New Insight into the Surgical Treatment of Primary Macronodular Adrenal Hyperplasia, 2020

[2] debillon E, Velayoudom-Cephise FL, Salenave S, et al. Unilateral Adrenalectomy as a first-line treatment of Cushing's syndrome in patients with primary bilateral macronodular adrenal hyperplasia. J Clin Endocrinol Metab. 2015, 100(12):4417-4424.

[3] Andrea Oßwald, Marcus Quinkler, Long-term outcome of primary bilateral macronodular adrenocortical hyperplasia after unilateral adrenalectomy , The Journal of Clinical Endocrinology & Metabolism Endocrine Society , 2018

[4] Kirschner MA, Powell RD, Lipsett MB. Cushing's syndrome: nodular cortical hyperplasia of adrenal glands with clinical and pathological features suggesting adrenocortical tumor. J Clin Endocrinol Metab. 1964, 24:947-955.

[5] Lacroix A, Baldacchino V, Bourdeau I, Hamet P, Tremblay J. Cushing's syndrome variants secondary to aberrant hormone receptors. Trends Endocrinol Metab. 2004, 15(8):375-382.

[6] AssiéG, LibéR, EspiardS, etal. ARMC5 mutations in macronodular adrenal hyperplasia with Cushing's syndrome. N Engl J Med. 2013, 369(22):2105-2114.

[7] Lacroix A. ACTH-independent macronodular adrenal hyperplasia. Best Pract Res Clin Endocrinol Metab. 2009, 23(2):245-259.

[8] LacroixA, N'DiayeN, MircescuH, TremblayJ, HametP. The diversity of abnormal hormone receptors in adrenal Cushing's syndrome allows novel pharmacological therapies. Braz J Med Biol Res. 2000, 33(10):1201-1209.

[9] Nagai M, Narita I, Omori K, Komura S, Arakawa M. Adrenocorticotropic hormone-independent bilateral adrenocortical macronodular hyperplasia treated with mitotane. Intern Med. 1999, 38(12):969-973.

[10] Obata Y, Yamada Y, Baden MY, et al. Long-term efficacy of trilostane for Cushing's syndrome due to adrenocorticotropin-independent bilateral macronodular adrenocortical hyperplasia. Intern Med. 2011, 50(21):2621-2625.