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Case Report

Simultaneous Bilateral Pheochromocytoma: A Case Report of Multiple Endocrine Neoplasia Type 2A

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Abstract

Pheochromocytomas are rare neuroendocrine tumors, representing 1% of all secondary Hypertension (HTN). The majority are unilateral and sporadic. However, 20% are associated with familial syndromes such as Multiple Endocrine Neoplasia type 2A (MEN2A).

MEN2A is a rare genetic syndrome associated with RET (REarranged during Transfection) gene mutation, characterized by medullary thyroid carcinoma, pheochromcytoma and parathyroid hyperplasia or adenoma.

We are reporting the case of a 46-year-old female with severe Hypertension (HTN) due to synchronous bilateral pheochromocytomas associated with MEN2A.

The patient underwent a successful total laparoscopic left adrenalectomy first, followed by right cortical-sparing adrenalectomy with significant improvement of HTN.

Current literature shows that cortical-sparing adrenalectomy should be the preferred approach for patients, diagnosed with bilateral pheochromocytomas, especially those associated with hereditary syndromes.

Keywords: Multiple Endocrine Neoplasia type 2A; Pheochromocytoma; Bilateral; Laparoscopic; Cortical-sparing adrenalectomy

Introduction

Pheochromocytoma is a rare neuroendocrine tumor that arises from chromaffin cells of the adrenal medulla or extra-adrenal sympathetic paraganglia [1], occurring in less than 0.2 percent of patients with Hypertension (HTN) [2].

Classically, patients present paroxysmal episodes including headaches, profuse sweating, palpitations and HTN, and therefore tumor resection remains the gold standard of treatment [3].

Most pheochromocytomas are sporadic and unilateral [4]. However, the incidence of bilateral pheochromocytoma is increased in familial cases such as Multiple Endocrine Neoplasia Type 2 (MEN2) [5].

We report an observation of the management of bilateral multicentric pheochromocytoma associated with MEN2A, in the urology department of Academic Hospital, Sfax Tunisia.

Case Presentation

A 46-year-old woman, with a 2-month history of diabetes mellitus, presented with asthenia and occasional headaches. The initial laboratory testing revealed elevated calcium (2.75 mmo/l), parathyroid hormone level (280 ng/l) and calcitonin (278 pg/ml).

Neck ultrasound showed right thyroid nodule measuring 18mm in greatest dimension and a 2.8 cm mass at the posterior inferior aspect of the right thyroid gland suggestive of parathyroid adenoma.

The patient underwent a total thyroidectomy and sub-total parathyroidectomy.

The histopathological examination revealed a right parathyroid adenoma and Medullary Thyroid Carcinoma (MTC). Subsequently, the diagnosis was MEN2A (Sipple syndrome).

Two weeks later, the patient presented paradoxical palpitations and hypertensive crisis.

Plasma metanephrines level was significantly elevated (805 ng/ml) (N<73). However, serum normetanephrines level was normal (140 ng/ml) (N<170).

The Computed Tomography (CT) scan of the abdomen revealed 3 masses in both adrenal glands: a right adrenal mass (21 mm × 14 mm) and two nodules of the left adrenal gland (41 mm × 23 mm and 15 mm × 14 mm respectively) (Figure 1).

Metaiodobenzylguanidine (MIBG) scintiscan identified increased bilaterally radio tracer uptake in the adrenal glands (Figure 2).

The patient was prepared for surgery and was given an alpha blocker (Prazosin) to normalize blood pressure.

A transperitoneal laparoscopic total left adrenalectomy was successfully performed first, because of the multicentric nature and the larger size of pheochromcytoma on the left side (Figure 3).

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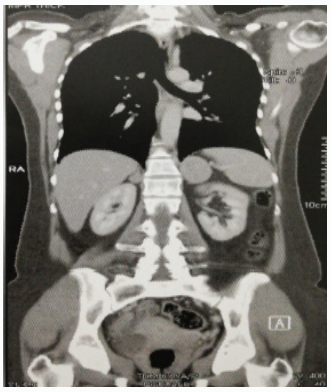

Figure 1: Preoperative CT scan showing bilateral adrenal pheochromocytoma.

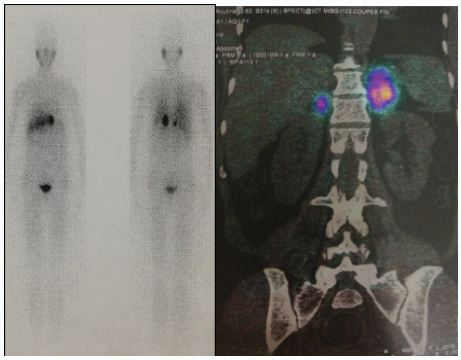

Figure 2: MIBG scintiscan shows a diffuse hyperfixation of both arenal glands.

Figure 3: Surgical specimen of the left pheochromocytoma.

One month later, the patient underwent a right laparoscopic cortical-spring adrenalectomy.

Histologic examination revealed a well-circumscribed tumor at the right gland measuring 2.5 cm × 1.5 cm × 1 cm. The left nodules were respectively 4 cm × 2.5 cm × 4 cm and 2.5 cm × 1.5 cm in size. The tumor cells showed a zeeballen architecture which is characteristic of pheochromocytomas.

The postoperative course was unremarkable.

Following surgery, the patient's blood pressure and plasma metanephrines levels recovered to normal ranges at the seventh postoperative day and remained stable until November 2020.

MEN2A was confirmed by genetic analysis identifying RET gene mutation in 634 codon.

Discussion

Multiple Endocrine Neoplasia type 2A (MEN2A) is a rare autosomal dominant cancer syndrome [6] occurring with an incidence rate of 1.3 per 100,000 in the general population [7].

MEN2A is associated with Medullary Thyroid Carcinoma (MTC) in almost 100% cases, parathyroid adenomas and pheochromocytomas, due to a germline RET (REarranged during Transfection) mutation [8]. It is usually diagnosed in the 2nd - 3rd decade, significantly younger than in the sporadic cases [9].

According to the literature, pheochromocytoma has a variable penetrance in MEN2A patients, depending on the mutation of RET [10].

The highest frequency is found in patients with mutation of codon 634 [11]. It is frequently bilateral, multicentric and not always synchronous [12].

Our patient had bilateral adrenal pheochromocytoma and it was multifocal on the left side.

Diagnosis requires clinical evaluation, cathecolamines measurement, as well as an adrenal CT [13].

In MEN2A-related pheochromocytoma, an increased adrenaline secretion is observed making the HTN more paroxysmal than maintained, contrary to sporadic pheochromocytomas that often produce large amounts of noradrenalin [5]. In addition, the risk of malignancy in MEN2A-related pheochromocytoma is very low [14].

Definitive treatment for pheochromocytomas in patients with MEN2A is bilateral adrenalectomy.

For years, traditional surgical treatment for bilateral pheochromocytomas, whether synchronous or metachronous, has been total bilateral adrenalectomy [15]. Nowadays, cortical-sparing adrenalectomy has been the preferred approach for patients at risk for, or diagnosed with bilateral pheochromocytoma especially those presenting a predisposing genetic mutation [16].

Recent studies have described cortical-sparing surgery as a potential advantage in preventing the adrenal insufficiency resulting from total bilateral adernalectomy [17,18].

Undergoing cortical-sparing adrenalectomy allows patient to conserve a normal cortical function and ovoid morbidity associated with lifelong steroid dependence [16]. The concept of preserving a sufficient part of the adrenal cortex permit to maintain corticoid function and reduce the possibility of adrenal insufficiency [19].

In a series by Hartmut et al. [16] reporting on 625 patients with bilateral pheochromocytoma, primary adrenal insufficiency occurred in all patients treated with total adrenalectomy but only in 23.5% of patients treated with attempted cortical-sparing adrenalectomy.

In our case, left laparoscopic total andrenalectomy was performed first because of the multicentric nature and the largest size of pheochromcytoma on the left side, followed by laparoscopicc right cortical sparing adrenalectomy. Our patient did not require postoperative steroid replacement.

Conclusion

This reported case presents a urological challenge to manage MEN2A-related pheochromocytoma.

Cortical- sparing adrenalectomy has become the preferred approach for hereditary and bilateral pheochromocytoma. This advanced surgery, in expert hands, makes possible to avoid lifelong steroid replacement.

Patients with pheochromocytoma, even when presenting with apparently sporadic, should be referred for genetic evaluation, in order to choose the most appropriate surgical approach.

A long-term follow-up is also required in patients with genetic tumor syndromes.

Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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