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Adrenalectomy for Sporadic Isolated Adrenal Pheochromocytoma: Case Report and Discussion

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Abstract

Background: Adrenalectomy is the treatment for Pheochromocytoma, a rare neuroendocrine tumor. Many surgical techniques and approaches exist, and the choice mostly relies on clinical indications, logistic resources, and surgeon's experience. This case report highlights the challenges of diagnosing and managing pheochromocytoma in resource-limited settings and it equally advocates for open adrenalectomy as a viable option in such contexts. **Case Presentation:** A 56 years old woman presented on routine consultation, for a reluctant paroxysmal hypertension, associated with a painless right flank mass. History was remarkable for type 2 diabetes mellitus, followed-up for over 6 years and abdominal surgery 20 years earlier. On clinical assessment, the patient presented with the classic symptoms of Menard's Triad and elevated serum metanephrine and normetanephrine. Imaging revealed a large homogenous right adrenal mass. Preoperative medical care consisted in initiation of catecholamine blockade. Due to resource limitations, the patient underwent an open transperitoneal adrenalectomy, resulting in resolution of symptoms and normalization of biochemical markers. **Conclusion:** Adrenalectomy is the treatment for Pheochromocytoma; Transperitoneal laparotomy remains an option in resource-limited settings with substantial positive outcomes.

Keywords

Pheochromocytoma, Adrenalectomy, Transperitoneal Laparotomy

1. Introduction

Adrenalectomy is the treatment for Pheochromocytoma, a rare tumor of the catecholamine-producing cells of the adrenal medulla. It is a neuroendocrine condition, considered benign anatomically and malignant physiologically. Unlike familial forms, nonhereditary cases account for nearly two third of Pheochromocytomas, and are most often diagnosed in the fourth and fifth decades of life. The diagnosis relies on catecholamine response symptoms, biochemical testing and imaging. Treatment is surgical, and requires a tailored multidisciplinary approach. Minimal invasive adrenalectomy has become the gold standard in developed countries, owing its reputation to low rates of perioperative morbidity and mortality. Nevertheless, open adrenalectomy, a complex surgical procedure, which can either be Transperitoneal or extraperitoneal, is mainly indicated for large tumors and is still broadly applied in sub-Saharan settings. So far, the prognosis following surgical resection is exceedingly favourable and requires a long-term follow-up. The scarcity of this condition, alongside with its diagnosis and management challenges led us to report a case of non-metastatic adrenal Pheochromocytoma at the "Laquintinie hospital of Douala".

2. Case Presentation

A 56 years old woman was addressed from the endocrinology unit, for a reluctant paroxysmal hypertension, associated with a painless right flank mass. History dates back 6 months ago, by recurrent episodes of sudden perspiration, associated with headache and palpitations. These symptoms prompted consultation in our healthcare facility, where the initial treatment consisted in anti-hypertensive drugs along with anti-anxiety medications. The persistency of symptoms associated with the discovery of a painless right flank mass prompted transfer to routine consultation of urology unit for re-assessment.

She was a known Type 2 diabetes patient, followed by an endocrinologist in the same institution, treated with metformin and compliant to treatment. There was no history of tobacco consumption, alcohol intake nor of similar symptoms in her family. She successfully underwent a caesarean section 20 years ago, and became menopausal in her late forties.

On systemic review, the patient had constitutional symptoms (nausea, weight loss, and tiredness), heavy sudden sweating and intermittent headache. There was no bone pain, abdominal pain, nor respiratory symptom.

On physical exam, we had an ill looking anxious patient with a BMI of 23.4 kg/m^2, presenting with hyperhidrosis. The systolic blood pressure varied between 180 and 208 mmHg, and the diastolic between 100 and 115 mmHg; the heart rate varied between 100 and 120 bpm. On abdominal examination, there was a lower umbilical midline scar on inspection. On palpation there was a painless right flank mass, soft in consistency, regular in shape, and mobile. The Murphy kidney punch was negative and the rest of physical exam was unremarkable.

For Diagnostic workup purposes, we requested for her plasma-free metanephrine and normetanephrine levels, which were respectively elevated at 24.8 and 39.9 µmol/l. we excluded Cushing Syndrome through a negative 24-hour urinary free cortisol evaluation. We also ruled out Primary Aldosteronism with a normal serum potassium level of 4.1 mEq/ml.

CT scan showed a right homogenous adrenal mass measuring 63 × 71 × 90 mm, with a density of 44 HU on unenhanced films (see Figure 1). Furthermore, CT contrast washout strategies using iodine contrast media was estimated at 30%, in favour of a benign mass. Both kidneys were homogenous and symmetric in size. There were no suspicious lesions on thoracic and pelvic films.

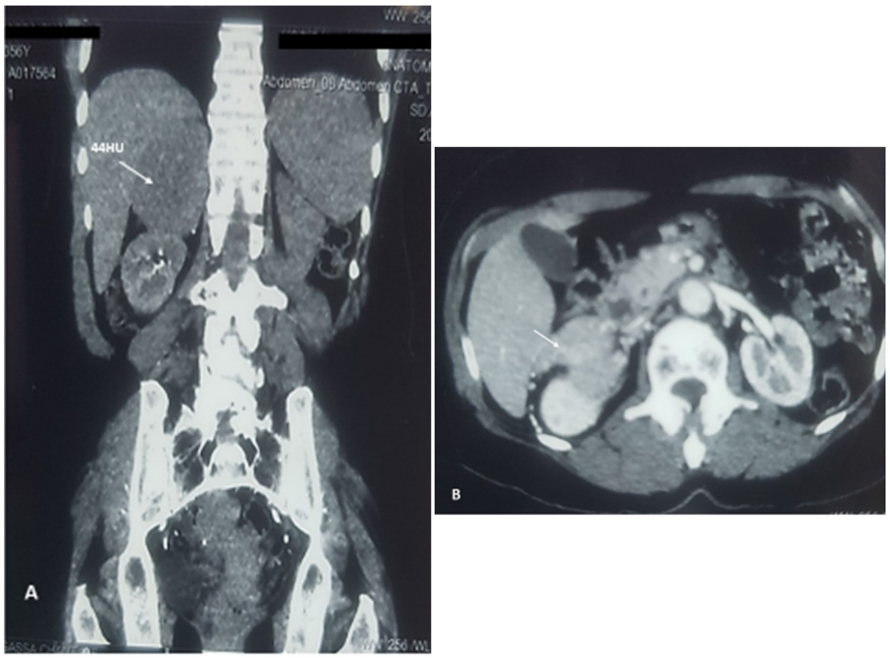

Figure 1. (A) Plain thoraco-abdomino-pelvic unenhanced CT scan, showing the right adrenal mass; (B) T-12 axial CT washout study performed to characterize the adrenal mass, demonstrating enhancement 60 seconds following an intravenous contrast bolus.

Genetic testing for *RET*, *VHL*, *SDHB*, and *SDHD* gene mutations was sought, to rollout a familial form of Pheochromocytoma, known to be more aggressive, with high rates of relapse following surgery. We later on postponed it because of logistic and financial issues.

Based on the above picture and with respect to epidemiology, we considered the diagnosis of a sporadic isolated right adrenal Pheochromocytoma associated to a controlled diabetes mellitus. The indication of adrenalectomy was therefore established.

3. Preoperative Assessment

As we sought to manage our patient, a preoperative medical care consisted in initiation of catecholamine blockade using Methydopa tablets, 02 weeks prior to

surgery with an oral dosage of 500 mg twice daily. Preoperative assessment was unremarkable, and the patient was classified ASA 1 (American Society of Anaesthesiology), Altemeier 1, and booked for a right open Transperitoneal adrenalectomy under general anaesthesia.

4. Surgical Technique

After obtaining informed consent from the patient, we proceeded to an open adrenalectomy under general anaesthesia with endotracheal intubation in the supine position. A midline xypho-pubic Transperitoneal incision was made, followed by Incision at the line of Toldt (Kocher's manoeuver, shown in Figure 2) with medial mobilization of the ascending colon. The hepato-colic ligament was divided and the hepatic flexure mobilized medially. Operative findings were a right solid well-circumcised adrenal mass with no morphological sign of local tissues invasion, nor para-caval or para-aortic lymphadenopathies (see Figure 3).

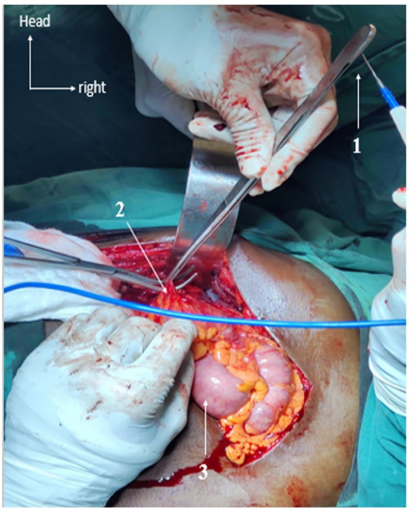

Figure 2. Kocher's manoeuver (1) Hemostasis; (2) Toldt ligament; (3) Ascending colon (Source: Douala Laquintinie Hospital).

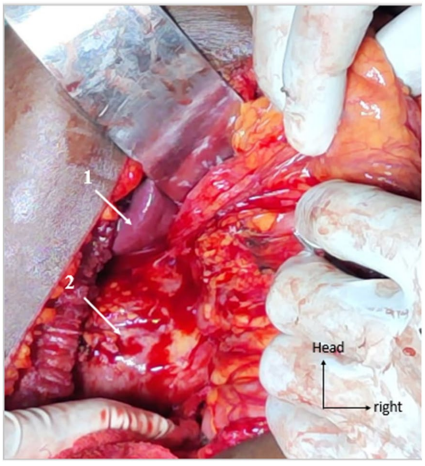

Figure 3. Findings: (1) Adrenal mass; (2) liver (Source: Douala Laquintinie Hospital).

We identified the right adrenal vein, as well as the great retroperitoneal vessels, and a few accessory renal arterial branches. We achieved haemostasis by traction on vascular loops and the use of Gil Vernet retractors (Figure 4). As we noticed an increase in arterial blood pressure during the intervention, we alerted the anaesthesiology team prior to mobilization of the adrenal mass. We ensured to manipulate the tumor as less as possible and progressively freed it by clamping all its vascular afferents and efferents. The adrenal vein was progressively exposed with the aid of a Gil Vernet retractor. During this process, we coagulated nervous and lymphatic tracts, ligated small veins, and clamped the right adrenal vein. Subsequently, we freed the superior pole of the gland by sectioning the hepatoparietal peritoneum. The renal artery was then retracted, and the small branches of the inferior adrenal pedicle were ligated. With the tumor thus devascularized (Figure 5), we completed the peritoneal incision at its periphery and bluntly dissected its posterior surface. With vascular control and tumor release thus accomplished, the gland was delicately extracted, as the vascular clamps were maintained and the vessels ligated together. Tumor size was about 10 cm with no macroscopic sign of ipsilateral renal infiltration (Figure 6). After verification of haemostasis of the adrenal bed (Figure 7), we proceeded on a parietal drainage of the retroperitoneum, followed by closure of the peritoneum and the abdominal wall. The duration of intervention was about 180 minutes, and blood loss was about 500 ml, requiring 01 pint of blood intraoperatively.

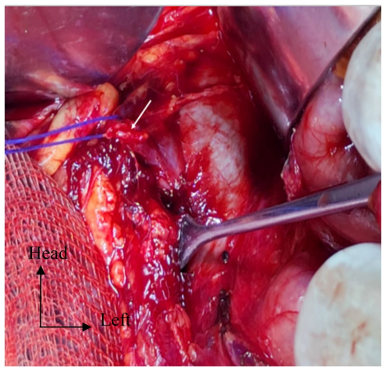

Figure 4. Haemostasis using Gil Vernet retractor (arrow).

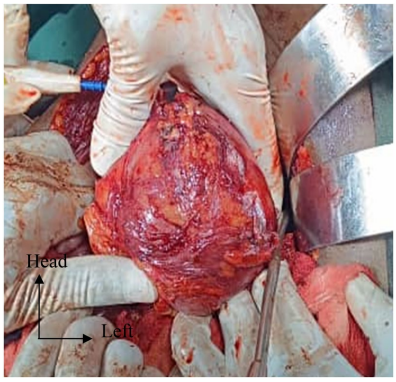

Figure 5. Devasculization of the adrenal mass (Source: Douala Laquintinie Hospital).

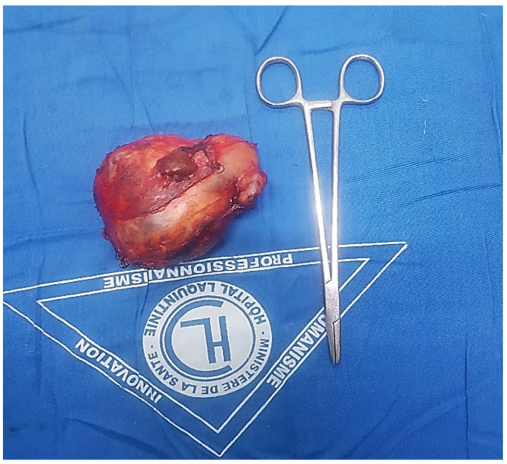

Figure 6. Right adrenal mass (Source: Douala Laquintinie Hospital).

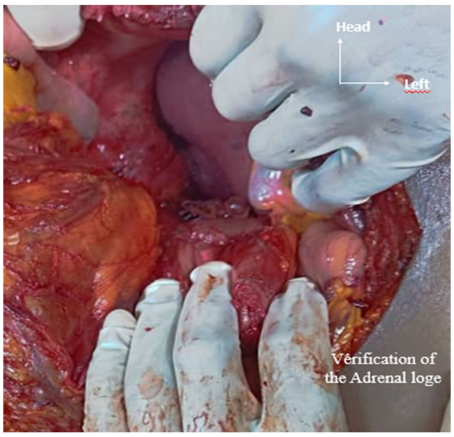

Figure 7. Adrenal loge after extraction (Source: Douala Laquintinie Hospital).

Immediate postoperative management consisted of close monitoring of blood pressure and blood glucose level at the intensive care unit, multimodal pain-killers, antacids, and broad spectrum prophylactic antibiotics. We discontinued antihypertensive treatment on day 1, first wound dressing was done on day 4 (see **Figure 8**) and patient was discharged on day 7 postoperative on oral relay drugs. Two weeks after surgery, patient was doing exceedingly well, the systolic blood pressure varied between 130 and 140 mmHg, the Heart rate between 69 and 80 bpm and repeated metabolic testing showed normal serum levels of metanephrines and normetanephrine. The fasting blood glucose varied between 1 and 1.5 g/dl, and oral metformin was discontinued. We reassessed the patient 01 month later, she presented with no complains. Repeated biochemical test showed normal level 2 and 3 months following surgery, and we re-addressed the patient to the endocrinologist for follow-up. Histopathology report revealed a proliferation of round granulated cells forming papillae and layers with cytonuclear atypia. A scanty fibrous stroma, associated with numerous congestive vessels and the capsule appeared non-infiltrated by the tumor. Informed consent to report this case was obtained from the patient for publication purposes.

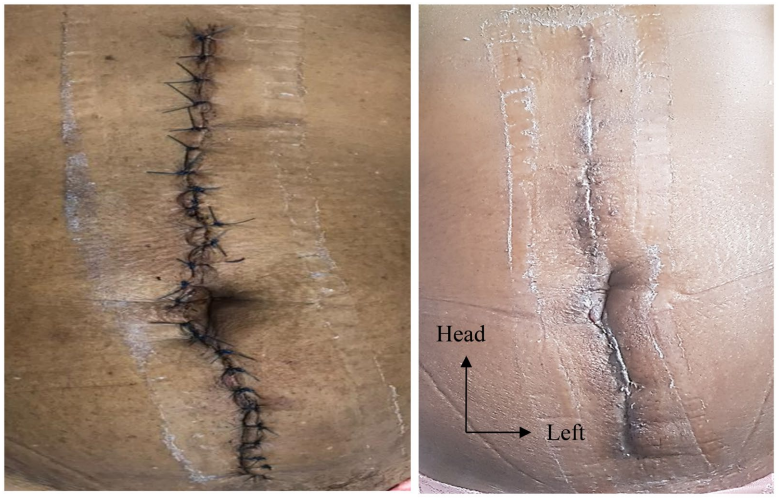

Figure 8. Wound dressing and on day 7 (A) and day 14 post-operative (B).

5. Discussion

Adrenal Pheochromocytoma is potentially lethal if undetected and is associated with long-term morbidity. It is a rare catecholamine-secreting, vascular, neuroendocrine tumor arising from chromaffine cells of the adrenal medulla, with prevalence ranging from 0.1% to 0.6% [1] [2]. in a case series study carried out in two tertiary hospitals in Yaoundé Cameroon, 7 cases of symptomatic adrenal masses were diagnosed between 2009 and 2019, demonstrating the scarcity of adrenal tumors [3]. Furthermore, Angwafo III *et al.* reported an overall of 18 patients operated for adrenal tumors in three tertiary hospital in Yaounde Cameroon, over a 15 year period, corresponding to an incidence of 1.2 cases per year [4].

In a systematic review of 200 cases, the mean age of patients was 43.8 ± 15.5 years. Nonhereditary cases of Pheochromocytoma were most often diagnosed in the fourth and fifth decades of life, while familial tumors tended to occur at a younger age [5]. Our patient was aged 56 years, and presented with non-secondary location on extension workup. Researches on sex ratio for Pheochromocytoma have been so far inconclusive, and however, there seem to be a slight tendency for females in our context [4].

A study conducted in Cameroon by Nouedoui *et al.* in 1990-1997, at the Yaounde General Hospital reported the diagnosis of 7 adrenal incidentaloma following abdominal imaging among which two were benign [6]. Our patient presented with the classic symptoms of Pheochromocytoma namely the triad of headache, episodic sudden perspiration, and tachycardia, known as the Menard's triad, as reported by Bravo and Tagle, in 2003 [7]. Additionally, she was followed-up for Type 2 diabetes and Hypertension for the past 6years. The persistency of recurrent spontaneous paroxysmal hypertension with the presence of a painless right iliac fossa mass prompted a urologic re-evaluation. One reason for this delay in urologic consultation could be explained by the recent recommendations of the American Endocrinologist Association, which states that, Although frequently in-

vestigated as a secondary cause of hypertension, because of its rarity, routine testing for Pheochromocytoma is not recommended unless indicated by clinical suspicion [8]. Despite this recommendation, diagnosis of Pheochromocytoma is often delayed and undiagnosed in our context because of low resources and low socio-economic incomes.

We completed our diagnosis with positive metabolic testing for plasma free metanephrines, and the CT-scan showed an adrenal mass, demonstrating an enhancement of 60 seconds following an intravenous contrast bolus with no evidence of neighbouring structures involvement. Both biochemical tests and CT-Scan imaging are determinant for excluding or confirming Pheochromocytoma [9] [10]. Based on the above picture, we indicated a right adrenalectomy.

Considering preparatory assessment, as we sought out for a positive outcome within and after intervention we followed the American Association of Endocrine Surgeons guidelines for adrenalectomy [11]. Our patient had no absolute exclusion criteria on preoperative assessment, and after excluding electrolyte imbalance, we initiated α-adrenergic blockade 02 weeks prior to surgery with *α*-Methyldopa orally, alternatively to Phenoxybenzamine. We could not reach the targeted systolic arterial blood pressure probably because of the unavailability of Phenoxybenzamine in our context. We preferred opened surgery to laparoscopy based on low resources for laparoscopy, and low socio-economic incomes in our context. Also, the patient had a history of abdominal surgery, which could be a possible source of adherences and a tumor size above 6 cm, considered a relative contraindication for laparoscopic adrenalectomy [12]. We did a Transperitoneal laparotomy for a better exposure, given the size of the tumor, and for optimal great vessel and retroperitoneal access. Tumorectomy was done in a unique block and arterial blood pressure closely monitored along surgery accordingly to resuscitation protocol for adrenalectomy [13]. In the series of Angwafo III *et al.*, all patients had open total adrenalectomy using the anterior sub-coastal approach in 16 (88.9%) patients and the anterior midline approach in 2 (11.2%) patients. The surgeon's approach was extra peritoneal among 10 (56.6%) patients and transperitoneal with 8 (44.4%) patients [4]. We encountered bleeding and Hypertension as main operative complications, which were further stabilized with transfusion of 01 pint of blood and antihypertensive drugs. This was probably due to major vessels trauma and intraoperative manipulation of the adrenal mass. Bleeding and hypotension were reported as most frequent complications in yaounde, with a mean duration of surgical intervention of 165.3 ± 43.1 mins, compaired to 180mins in our case [4].

Hydrocortisone supplementation is recommended post-operatively to prevent adrenal insufficiency. Our patient did not received hydrocortisone supplement, as the cortisol level was normal.

The average hospitalization days post-surgery was 4 days higher than that reported by Musina *et al.* This was probably due to the fact that in other studies, the laparoscopic approach was associated with early recovery.

Our patient was deemed as cure clinically and biochemically two weeks later, as compared to results of current studies. However, we encouraged our patient to take genetic testing, as one third of pheochromocytomas initially benign turn to be malignant post-operatively.

Retrospective studies demonstrate a clear advantage of laparoscopic surgery over open surgery in terms of analgesia, hospital stay, blood loss, and complication rate. However, laparoscopic surgeries typically showed longer operative time than open surgery did. There are no randomized prospective studies comparing laparoscopic with open adrenalectomy [13].

6. Conclusion

Pheochromocytoma is a rare neuroendocrine tumor, treatment is surgical, open surgery still has a place in our context. Laparoscopic adrenalectomy, which is still pending in our hospitals then, is alleged to have better outcomes in trained and tested hands.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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