

## SURGICAL APPROACH OF HYPERTENSION: PHEOCHROMOCYTOMA CASE REPORT

Adriana Ion<sup>1</sup>, I. Bostaca<sup>1</sup>

<sup>1</sup>The University of Medicine and Pharmacy “Gr. T. Popa”, Iași, Romania

Corresponding author: Adriana Ion

Phone no. 0040741089910

E-mail: adriana.ion@hotmail.com

### Abstract

*Pheochromocytoma is present in about 1% of hypertensive patients. It has a 90% cure potential, but a high mortality rate if left untreated. Complications include malignant hypertension, heart failure, myocardial infarction, ventricular arrhythmias, stroke or metastasis (malignant pheochromocytoma). We present the case of a 47-year-old hypertensive female patient who was admitted to hospital in 2014 with excessive fluctuations in blood pressure (300/140 mmHg to 90/50 mmHg), rapid pulse not responding to medication, profuse night sweats, palpitations, vertigo, nausea, and vomiting. The patient had a history of high arterial pressure dating back to 1996, following complex anti-hypertensive treatment, and frequent episodes of paroxysmal atrial fibrillation in the previous four years, reduced by external electric shock. Laboratory and imaging investigations revealed a solid-type formation with mixed structure in the right adrenal gland, indicating pheochromocytoma. Surgery with resection of the right adrenal gland was proposed. Preoperative preparation to combat the risks of large variations in blood pressure and hypovolemia started 1–3 weeks before surgery, consisting of an alpha-blocker to control blood pressure, a beta-blocker to prevent arrhythmic events, and hydration to prevent postoperative hypotension. A right adrenalectomy was performed. Histopathology of the resected piece confirmed the diagnosis of pheochromocytoma. After surgery, the large variations in blood pressure, arrhythmic events and tumor symptoms were all reduced, and blood pressure returned to within normal range. Follow-up treatment consisted of Carvedilol 12.5 mg, 1 cp / day and a low-salt, hypolipidaemic diet was recommended. The case is notable for the late diagnosis made about 18 years after the onset of the hypertensive symptoms, treated with excessive medication.*

**Keywords:** *secondary hypertension, pheochromocytoma, surgery*

---

### Introduction

Secondary hypertension is identified in approximately a quarter of all cases of hypertension with a significant percentage of misdiagnosis, leading to problems of treatment and control of blood pressure. Pheochromocytoma is present in about 1% of all

hypertensive patients, with cure potential of 90% and a high rate of mortality in untreated cases with complications of malignant hypertension, heart failure, myocardial infarction, ventricular arrhythmias, stroke or metastasis (malignant pheochromocytoma).

Pheochromocytoma is a tumor originating in the chromaffin tissue of the adrenal gland and

other tissues as: periaortitis sympathetic chain, bladder wall, Zuerkandl body, with an increase in catecholamine activity and clinical manifestations specific to the sympathetic nervous system hyperactivity: tachycardia, resistant hypertension, orthostatic hypotension, anxiety, palpitations, excessive sweating, headache, weight loss, hyperglycemia, hyperlipemia. The tumor may have familial causes or may be associated with other diseases like neurofibromatosis, parathyroid adenoma, thyroid carcinoma. In most cases it is benign but can become malignant in 10% of cases. The incidence is predominant in the third to fifth decade of life and evenly distributed between males and females.

---

## Material and Methods

A 47-year-old hypertensive female patient was admitted to hospital in June 2014 describing palpitations, vertigo, nausea, vomiting, and heavy sweating. The patient had been diagnosed in 1996 at a routine check with essential hypertension (BP=160/80 mmHg) without other symptoms for which treatment with enalapril 10 mg/day was recommended. The patient did not follow the treatment or monitor blood pressure periodically, and did not notice any significant increases of her blood pressure. In 2006, during a consultation for knee pain, her blood pressure indicated a value of 240/120 mmHg, and the patient was prescribed enalapril 10 mg/day, which she took daily and the hypertension reduced. In the same year, the medication was replaced with amlodipine and nebivolol to treat a cough, a side effect of the antihypertensive treatment. There were no other observations for two years. In 2008, the first episode of paroxysmal atrial fibrillation occurred in the context of a total hysterectomy and bilateral ovariectomy for uterine fibroids, reduced pharmacologically, and the medication for hypertension was changed with propafenone 150 mg t.i.d, bisoprolol 5 mg o.d.

In 2010, the patient presented with a second episode of paroxysmal atrial fibrillation and received emergency external electric shock. Since 2010, the patient reported frequent

episodes of paroxysmal atrial fibrillation at home, pharmacologically reduced by adding 1 capsule of bisoprolol 5 mg to the standard medications.

In 2013, the symptoms increased (with related emotional stress) and included an excessive rise in blood pressure values up to SBP of 330 mmHg, refractory to previous treatment, fast heart rate of 280 bpm, agitation and profuse night sweats. Medication adjustments were made with propafenone 300 mg t.i.d, bisoprolol 5 mg o.d., perindopril 5 mg aspirin 75 mg.

On admission (in 2013), the cardiovascular evaluation revealed on electrocardiogram: sinus rhythm=70/min,  $\hat{A}QRS=49^\circ$ , left ventricular hypertrophy. The patient was readmitted (in June 2014) with paroxysmal atrial fibrillation, very large fluctuations in blood pressure values (300/140 mmHg to 90/50 mmHg) and emergency treatment with external electric shock was administered. Transthoracic echocardiography revealed normal heart size and contractions, important concentric left ventricular hypertrophy, aortic cusps atheroma, calcifications of the mitral ring that stretches from the cusps generating a moderate mitral regurgitation (grade 2+), the absence of pericardial fluid or intracavitary thrombus. Blood pressure on admission was 280/130 mmHg. The recommended treatment consisted of lercanidipin 10 mg b.i.d, rilmenidinum 1 mg b.i.d, furosemid 20 mg, bisoprolol 5 mg b.i.d, enalapril 1,26 mg every six hours or valsartan 160 mg b.i.d. The antihypertensive medication had lowered blood pressure values but excessive fluctuations in blood pressure values were recorded while the patient was in hospital dropping to 85/60 mm Hg and rising to 300/120 mmHg. The patient also presented with fever (38,8-39,1° C) treated with perfalgan. ECG monitoring detected an episode of torsade de pointes (Figure 1) and an episode of atrial flutter 1/1 with frequency of 300 bpm, converted to sinus rhythm by DC electric shock (Figure 2). Antiarrhythmic treatment with propafenone 900 mg/d and carvedilol 50 mg/d stopped the arrhythmia recurrence.

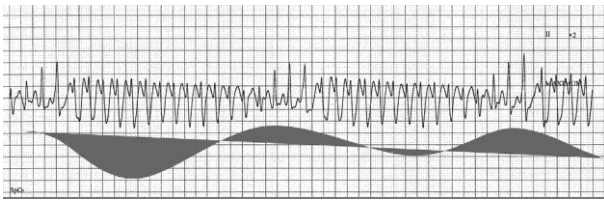


Figure 1 - Monitoring ECG in "crisis" of pheochromocytoma: torsade de pointes - a condition of polymorphic ventricular tachycardia

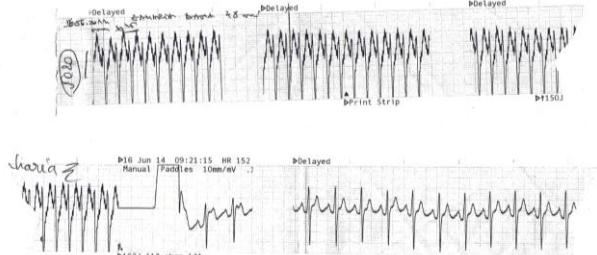


Figure 2 - ECG recording of atrial flutter with 1:1 a-v conduction and sinus rhythm conversion by DC shock

Biochemical analysis blood: glucose=147 mg/dl, BUN = 59 mg/dl creatinine=1.97 mg/dl, uric acid= 9.8 mg/dl, cholesterol = 318 mg/dl LDL = 243.4 mg/dl HDL = 43 mg/dl SGOT=59 IU/L SGTP = 108 IU/L, GGTP = 73 IU/L LDH = 332 IU/L CK=65 IU/L CKMB=32 IU/L.

Pheochromocytoma was suspected based on large fluctuations in blood pressure values and related symptoms of sweats, palpitations, headache. The dosage of urinary metanephrines came out normal: 84 µg/24 h (reference value = 25-312 µg/24 hours) and urinary AVM were slightly elevated: 13.68 mg/24h.

Abdominal ultrasound examination revealed a solid type of mixed structure formation in the right adrenal gland measuring 62 /38mm, bilobate (Figure 3), with an impression on the inferior vena cava and net separation limit to the kidney, left adrenal gland normal.

A CT scan identified an enlarged right adrenal gland, heterogeneous, with dimensions of 47 x 40 x 32 mm, with polynodular aspect and some coarse cortical calcifications; inside was a hypodense area (Figure 4). The formation exerted compression on the vena cava. The left adrenal gland CT appeared normal. The CT concluded a solid expansive formation of the right adrenal gland with malignancy characteristics.



Figure 3 - Pheochromocytoma imaging at abdominal ultrasonography



Figure 4 - CT imaging of right adrenal gland with pheochromocytoma

Following the laboratory and imaging investigations, the patient was diagnosed with malignant tumor of the right adrenal gland – pheochromocytoma and secondary hypertension with the indication for surgery. The surgical recommendation was right adrenalectomy.

Morphology described macroscopic resection piece: tumor formation of 4.5/3/3 cm, encapsulated, coating on the slope of 2/1 cm of adrenal gland, the section had a non-homogeneous appearance with yellowish areas alternating with brown or hemorrhagic areas and necrosis (Figure 5). Microscopic examination of tumor fragments presented aspects of pheochromocytoma (Figure 6) with predominantly solid pattern. Tumor cells were polygonal with abundant granular cytoplasm,

with reduced nuclear pleomorphism, without significant mitotic activity, isolated voluminous, hyperchromatic nuclei. Areas of bleeding with conjunctiva organization in progress could be seen. The capsule was integrated. No vascular invasion was found in sections examined. The remaining cortical of the adrenal gland showed a normal morphology, the adjacent areas of the pheochromocytoma nodule presenting compression atrophy. No confirmation for malignancy pattern.



Figure 5 - Exeresis piece of right adrenal gland with pheochromocytoma

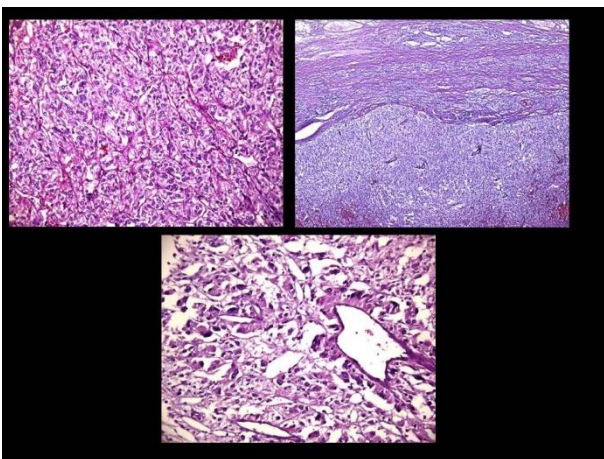


Figure 6 - Adrenal gland (right), pheochromocytoma, high and low power microscopic

Postoperatively, ABPM monitoring indicated a non-dipper profile tension with a blood pressure with average values of 133/80 mmHg, 152/97 mmHg maximum, minimum of 90/60 mmHg, normal hypertensive load. The Holter monitoring indicated the absence of arrhythmic events, sinus rhythm = 65 bpm.

A low-salt, hypolipidaemic diet was recommended, and treatment with carvedilol 12.5 mg/d.

## Discussion

Secondary hypertension has a relatively low incidence in the population. Our case study is notable for its late diagnosis made about 18 years after the onset of the hypertensive symptoms, treated with excessive medication. After an intensive and aggressive antihypertensive treatment, mainly symptomatic, once the generating symptoms tumor is discovered, the therapeutic strategy is radically changed, becoming curative. An important aspect may be the masking of the adrenergic phenomena by the drug therapy, preventing an early diagnosis, and the effects of this unnecessary and ineffective chronic treatment on the body. Thus, the importance of recognizing the limits of medical treatment and of opening to new diagnostics perspectives.

Surgical resection of the tumor is the only curative therapeutic approach for pheochromocytoma. The indication for surgery by right adrenalectomy is given according to the location, size and degree of tumor invasiveness. Preoperative preparation of the patient diagnosed with pheochromocytoma is essential to combat the risks of large variations in blood pressure and hypovolemia. The preparation is initiated 1–3 weeks before surgery with alpha-blockers such as phenoxybenzamine administration in doses of 10 mg b.i.d. Preoperative administration of alpha-blockers prevents severe hypovolemia and variations of blood pressure during intraoperative manipulation of the tumor. Simultaneously, a beta-blocker is added to control heart rate and an increased consumption of liquids or intravenous fluids is recommended to avoid postoperative hypotension. The surgery intervention allows

the removal of the specific symptoms and a complete cessation of the previous antihypertensive treatment.

## Conclusions

Pheochromocytoma is a very curable form of secondary hypertension but, remains a late diagnosed etiological condition (label "extended" by the "primary/essential" Hypertension). Delayed diagnosis results in expensive and ineffective drug treatment and high risk of severe non-fatal or fatal complications of hypertension.

Our case study demonstrates the cumulative effect of severe hypertension caused by pheochromocytoma (SBP = 330 mmHg, adrenergic cardiomyopathy with severe arrhythmias: 1/1 atrial flutter, torsade de pointes), and the reduced effectiveness of drug treatment over time. The blood pressure values normalization and the elimination of symptoms after tumor resection certify that the surgical intervention remains the only optimal therapeutic decision.

## References

- [1] Negoită CI., Hipertensiunea arterială secundară, Ed. Junimea Iași, 1975.
- [2] Bostaca I., Cheile diagnosticului în clinica medicală, Ed. Polirom Iași, 1999.
- [3] Bostaca Tamara, Găleşanu R., Bostaca I., Cioară Olga, Rare Causes of Secondary Arterial Hypertension Identified by Abdominal Echography as First Intention Diagnostic Method, *Journal of the American College of Cardiology* (suppl. B), 2002, vol. 39, 176B.
- [4] Bostaca Tamara, Cioară Olga, Bostaca I.: Abdominal echography as a Screening Imagistic Method for the Diagnosis of the Secondary Endocrine Arterial Hypertension, 2nd Virtual Congress of Cardiology International Congress of Cardiology on Internet September 1<sup>st</sup> – November 30<sup>th</sup> 2001, [www.fac.org.ar/scvc/scviresp/areas\\_es/tlhtae.htm](http://www.fac.org.ar/scvc/scviresp/areas_es/tlhtae.htm).
- [5] Prejbisz A., Lenders J.W., Eisenhofer G., Januszewicz A., Cardiovascular manifestations of pheochromocytoma, *J Hypertens*. Nov 2011; 29(11):2049-60.
- [6] Young W.F. Jr., Adrenal medulla, catecholamines, and pheochromocytoma. In Goldman L, Schafer AI, eds. *Cecil Medicine*, 24th ed. Philadelphia, Pa: Saunders Elsevier; 2011:chap 235.
- [7] Young W.F. Jr., Adrenal causes of hypertension: pheochromocytoma and primary aldosteronism, *Rev Endocr Metab Disord* 2007; 8:309.
- [8] Bruynzeel H., Feelders R.A., Groenland T.H. et al., Risk Factors for Hemodynamic Instability during Surgery for Pheochromocytoma, *J Clin Endocrinol Metab* 2010; 95:678-685.
- [9] Kinney M.A., Narr B.J., Warner M.A., Perioperative Management of Pheochromocytoma, *J Cardiothorasc Vasc Anesth*. 2002;16:359–369.
- [10] Favia G., Lumachi F., Polistina F., D'Amico D.F. (1998) Pheochromocytoma, a rare cause of hypertension: long-term follow-up of 55 surgically treated patients, *World J Surg* 22 (7): 689–693; discussion 694