Hemorrhagic pheochromocytoma presenting as severe hypertension with myocardial infarction

Phéochromocytome hémorragique. Présentation clinique par hypertension artérielle sévère et infarctus du myocarde

1. Case report

A 50-year-old man, presented to the emergency department of our tertiary care hospital complaining of sudden right hypochondrial pain extending to the back, followed with an abrupt frontal-occipital cephalgia and intense diaphoresis and nausea. He had no medical history of note except for being a smoker of 30 cigarettes a day. Over the last year, the patient’s history was remarkable for intermittent episodes of cephalgia, diaphoresis and palpitations lasting some minutes with spontaneous recovery, in a frequency of 3–4 times per week. They were not provoked by physical activity. There were not any records of blood pressure during the episodes. He did not undergo any diagnosis procedure since he did not consult any doctor before emergency admission. On arrival paramedics found him diaphoretic and tremulous, with heart rate of 110 beats per minute and blood pressure of 201/117 mmHg. ECG showed 2 mm ST-segment depression in leads II, III, aVF, and V4 to V6, consistent with inferior and lateral wall myocardial ischaemia. Paroxysms of ventricular tachycardia were controlled with intravenous nitroglycerin. The patient was treated initially with aspirin, clopidogrel, enoxaparin and urapidil. In the emergency department, chest radiography showed no evidence of acute cardiopulmonary disease. Initial laboratory work-up revealed elevated troponin-T of 1.16 ng/mL (normal < 0.04) with myoglobin of 211.9 ng/mL (normal < 70 ng/mL), elevated white cells count (37,700 mil/mm³, normal 4–11 mil/mm³), serum glycemia of 345 mg/dL (normal < 106 mg/dL) and haemoglobin of 15.1 g/dL (normal 13–17.4 g/dL). Contrast enhanced computed tomography scan of abdomen showed a right hemorrhagic adrenal mass. Antiplatelet and antithrombotic therapy was discontinued. The patient was transferred to the intensive care unit with the initial impression of myocardial infarction (MI) caused by hypertensive emergency and right adrenal hemorrhage. Over the next 24 hours, the patient’s clinical status improved. Repeat laboratory results showed that his white blood cell count had fallen. Successive electrocardiograms showed the presence of asymmetrical peaked T waves in leads V2 to V4 with no ischemia signs or Q waves. Serum levels of troponin peaked at 24 hours (9.16 ng/mL) with myoglobin levels of 671 ng/mL. A transthoracic echocardiography performed 24 hours after the initiation of the symptoms revealed mild mitral regurgitation with a normal ejection fraction (70%). He was discharged from the intensive care unit three days later. Because of his medical history of headache and diaphoresis a 24-h urine collection for metanephrines was ordered. It returned with marked elevations in metanephrines (6,057 µg, normal < 374 µg), normetanephrines (1,218 µg, normal < 778 µg) and vanillylmandelic acid (23 mg, normal < 7.3 mg) levels. All the rest of the laboratory findings were normal. Both 123-I-metaiodobenzylguanidine scan and Single-Photon Emission Computed Tomography (SPECT) demonstrated a pathological uptake in the same location as the hemorrhage in the right adrenal gland (Fig. 1). On the basis of the clinical findings, laboratory reports and image procedures, the patient was suspected of having pheochromocytoma. Initially, cardiac angiography was not performed as it was strongly suspected that myocardial ischemia was secondary to the acute release of catecholamines from hemorrhagic pheochromocytoma. A decision was made to postpone the procedure after surgery except the patient experienced cardiac symptoms again. Before discharge the patient was started on aspirin. Because he maintained stable hemodynamic parameters, surgery was deferred to optimize preoperative adrenergic blockade. The patient was given oral doxazosin 4 mg for alpha-blockade for 2 weeks. Thereafter laparoscopic right adrenalectomy was performed successfully. During surgery, blood pressure was well controlled, although a few episodic rises required intravenous nitroglycerin. The patient was discharged home on the third postoperative day. The pathology report confirmed that the tumor was a pheochromocytoma with residual necrosis. At 2-month follow-up blood pressure remained normal off all medications. Metanephrine urine testing returned to within reference range. Eventually cardiac angiography was performed after surgery. It revealed no coronary atherosclerotic disease; left ventricular remained normal (ejection fraction 70%) and no mitral regurgitation was found. In view of these results, the final diagnosis was MI secondary to hemorrhagic pheochromocytoma and hypertensive emergency, with reversal myocardial ischaemia after tumor resection.

2. Discussion

Pheochromocytomas are rare catecholamin-producing tumors derived from chromaffin cells of the adrenal medulla or
extra-adrenal paraganglioma. The classical triad symptom, is directly the consequence of the over secretion of catecholamines. It consists of palpitations, headaches and sweating lasting from minutes to hours, occurring episodically, and it is attended by hypertension [1]. Sustained or paroxysmal hypertension is commonly associated in 80–90% of patients with pheochromocytoma. Blood pressure can reach dangerously high values of over 200 mmHg in some patients as a consequence of the rapid and marked tumoral release of catecholamines, compromising the function of vital organs [2]. Some data have shown the relatively high incidence of cardiovascular complications in subjects with pheochromocytoma and concomitant hypertensive emergency [3]. MI and severe arrhythmia are among the most frequent heart complications. The specific association between pheochromocytoma and MI has been documented over many decades [4–6] and pheochromocytoma is associated with a wide variety of ischaemia-type ECG changes [4,5]. Monomorphic ventricular tachycardia and MI have been described as part of pheochromocytoma-induced cardiomyopathy [6]. Interestingly, most of these patients with myocardial ischemia, did not show coronary atherosclerosis in cardiac catheterization in contrast to classic atherosclerosis-mediated ischaemia [4,5]. For this reason, it is essential to rule out pheochromocytoma in an acute coronary syndrome presenting with hypertensive crisis and not relevant cardiovascular meal history. The increase routine use of echocardiogram has identified specific patterns of wall motion abnormalities in pheochromocytoma-induced cardiomyopathy similar to those reported in Takotsubo cardiomyopathy [4,7]. In our patient, the suspicion of pheochromocytoma-induced Takotsubo cardiomyopathy could not be confirmed and a formal diagnosis of MI was performed. Typical Takotsubo wall motion abnormalities were not present on echocardiogram. Moreover, the peak troponin level was 9 ng/mL. The critical value of troponin in Takotsubo cardiomyopathy has been reported to be as a mean 0.18 ng/mL [8], significantly less than that observed in MI. In general, a troponin level of more than 6 ng/mL is very likely to be associated to MI rather than to Takotsubo cardiomyopathy [9]. If there is clear evidence of myocardial ischemia, it is important to perform a prompt cardiac angiography. In our patient initially cardiac angiography was not initially performed because of hemodynamic instability and evidence of partially necrotic adrenal mass. A decision was made to postpone the procedure after the removal of pheochromocytoma when cardiac enzymes and ST-segment deviations normalised. However, this approach is debatable. Indeed, early diagnosis is mandatory to prevent severe cardiovascular complications in pheochromocytoma, since cardiac dysfunction is generally reversible after curative surgery [10].

Plasma free metanephrines or urinary fractionated metanephrines offer the highest sensitivity for diagnosis of pheochromocytoma [11]. In general, plasma concentrations of free normetanephrine higher than 430 μg/L or of free metanephrine higher than 220 μg/L unequivocally confirm a pheochromocytoma [9]. In those patients with clinical cardiomyopathy, plasma metanephrine levels are even substantially elevated. Therefore, if the metanephrine levels are normal or borderline, pheochromocytoma-induced cardiomyopathy can generally be ruled out [12]. Once the diagnosis of pheochromocytoma is considered, management must be initiated with fluid, and drug resuscitation and α-blockade. It is recommended that patients should not proceed to laparoscopic curative surgery unless they have been adequately treated with α-blockade for at least 10 days [1]. Urgent surgery is not indicated even in the presence of hemorrhagic pheochromocytoma because it has been shown that delayed surgery is associated with fewer intraoperative and postoperative complications but also with lower mortality rate [13].

Disclosure of interest

The authors declare that they have no competing interest.

References

Partial hypopituitarism in a female patient with a 45,X/46,XY mosaicism

Hypopituitarisme partiel chez une patiente avec un mosaïcisme 45,X/46,XY

1. Observation

A 20-year-old female patient was referred to our department for short stature and primary amenorrhea. She was the sixth child of a non-consanguineous marriage. Her past medical history was unremarkable. There were no physical complaints or symptoms.

On examination, she had a body weight of 44 kg, a height of 138 cm (−4 standard deviations), a body mass index of 23.1 kg/m², a supine and standing blood pressure of 120/60 mmHg, a round face with a low posterior hairlines and multiple cutaneous nevi. She had a female phenotype with female external genitalia (Tanner stage: breast development: stage 3 and pubic hair: stage 2). Her bone age was delayed (<17 years).

Laboratory tests revealed hypergonadotropic hypogonadism with FSH level of 115 mIU/mL (normal ranges: 3.35–21.63 mIU/mL), LH level of 38.33 mIU/mL (normal ranges: 2.39–6.6 mIU/mL) and estradiol level <9 pg/mL (normal ranges: 18–147 pg/mL). Thyroid function and prolactin level were normal.

L-dopa stimulating test showed growth hormone deficiency (peak GH = 3.89 ng/mL, normal response > 10 ng/mL) and insulin-induced hypoglycemia test confirmed this diagnosis (peak GH = 1.25 ng/mL, normal response > 10 ng/mL). IGF1 concentration was beyond the normal range (100 ng/mL, normal ranges: 220–850 ng/mL). The peak cortisol level in response to insulin-induced hypoglycemia test was 212 nmol/L (normal response > 550 nmol/L). ACTH level was lower than normal (<10 pg/mL) indicated corticotropin deficiency.

Pelvic ultrasonography and magnetic resonance imaging (MRI) scan showed hypoplastic uterus with no visualized ovaries. MRI of the hypothalamic and pituitary region was normal. Echocardiography and renal sonography were normal. The bone mineral density showed osteoporosis.

Cytogenetic analysis of peripheral blood revealed a karyotype with mos 45,X/46,XY[41].

Molecular analysis of SRY gene was positive.

Patient was treated with hydrocortisone. Growth hormone substitution therapy was prescribed but coverage has not been accepted by the national insurance system.

Laparoscopy showed apparently complete Müllerian structure with streak gonads. Because of the high risk of gonadoblastoma and dysgerminoma among subjects with 45,X/46,XY mosaicism, bilateral prophylactic gonadectomy was performed to our patient. Later, sex steroid replacement therapy was started.

2. Discussion

Turner syndrome is the most common chromosomal anomaly in females occurring in 1/2500 live born females. This syndrome is caused by a partial or complete absence of one sex chromosome. Out of all the patients diagnosed with Turner syndrome, about 2% to 5% are individuals with 45,X/46,XY [1]. In our country, the prevalence of 45,X/46,XY mosaicism among patients with Turner syndrome varies from 3% to 4.3% [2,3].

This extremely rare condition with an estimated incidence of 1.5/10,000 newborns is characterized by a wide phenotypic spectrum. In fact, patients with 45,X/46,XY mosaicism ranged from women with or without Turner syndrome stigmata, to men apparently normal, passing by the ambiguous phenotypes [4]. Such phenotype variability is thought to be related to the tissue distribution and relative proportions in the developing gonads of the respective cell lines, particularly those with functional copies of the SRY gene [5].

The most common presentation for individuals with a 45,X/46,XY karyotype is sexual ambiguity, accounting for ~60%, and the least common phenotype consists of those with bilaterally descended testes, found in 11–12% [6].

Our patient presented with a phenotypically Turner-like female despite the small proportion of 45,X cells found in blood karyotype. In fact, mosaicism found in lymphocytes does not