CASE REPORT

Magnesium sulphate and 123I-MIBG in pheochromocytoma: Two useful techniques for a complicated disease

M. Vendrell a,*, N. Martín a, A. Tejedor a, J.T. Ortiz b, À. Muxí c, P. Taurà a

a Servicio de Anestesiología, Reanimación y Tratamiento del Dolor, Hospital Clinic Barcelona, Spain
b Servicio de Cardiología, Hospital Clinic Barcelona, Spain
c Servicio de Medicina Nuclear, Hospital Clinic Barcelona, Spain

Received 30 October 2014; accepted 2 April 2015
Available online 27 May 2015

Abstract Pheochromocytoma is a tumour of the chromaffin tissue. It may, through catecholamine release, have deleterious effects on myocardial structure.

A 48-year-old woman with a history of hypertension and type II diabetes mellitus (ASA II) was diagnosed of pheochromocytoma-induced myocarditis, which caused severe cardiogenic shock, with an ejection fraction of 20%. Extreme blood pressure swings required aggressive therapy with vasoactive drugs (norepinephrine and dopamine) and an intra-aortic balloon pump, despite which severe haemodynamic instability persisted. Finally, the use of magnesium sulphate allowed for cardiovascular stabilization and weaning off vasoactive drugs prior to surgery.

123I-metaiodobenzylguanidine scintigraphy helps not only to functionally confirm tumour tissue, but also to assess severity and prognosis of cardiac failure.

Prognosis of pheochromocytoma-induced heart failure can be very poor. The use of these two well-known and relatively simple ‘tools’ for treatment and prognosis is a helpful option to keep in mind.

© 2014 Sociedad Española de Anestesiología, Reanimación y Terapéutica del Dolor. Published by Elsevier España, S.L.U. All rights reserved.

PALABRAS CLAVE
Feocromocitoma;
Sulfato de magnesio;
Gammagrafía

Resumen Los feocromocitomas son tumores del tejido cromafín. Pueden, a través de la secreción de catecolaminas, causar efectos deletéreos sobre el miocardio.
MgSO₄ and ¹²³I-MIBG in pheochromocytoma

Introduction

Pheochromocytoma is a tumour of the chromaffin tissue which affects around 1 in every 2500–6500 individuals. It produces systemic effects via release of catecholamines. Its main symptoms are headache and sustained hypertension, but paroxysmal hypertension and arrhythmias may happen. Pheochromocytoma crisis, with severe myocardial damage such as life-threatening cardiomyopathies, has a reported incidence of up to 26%.¹ These are probably caused by autonomic imbalance when there is an elevated secretion of catecholamines coming from the pheochromocytoma.² Paroxysmal episodes are unpredictable.

In such a setting, two particularities must be recalled. Firstly, and regarding therapeutic approach, magnesium sulphate (MgSO₄) is a well-known, safe agent, which helps in improving cardiovascular stability, as it inhibits catecholamine release, blocks catecholamine receptors, and has antiarrhythmic properties, both atrial and ventricular, related to calcium channel antagonism.³,⁴

Secondly, the use of ¹²³I-metaiodobenzylguanidine (¹²³I-MIBG) scintigraphy technique is not only useful to functionally confirm tumour tissue, but it can also assess severity and prognosis of cardiac failure. Also, it can be a helpful tool in establishing a differential diagnosis in case heart function fails to improve after pheochromocytoma removal.⁵

Case report

A 48-year-old woman with hypertension and type 2 diabetes mellitus consulted at her community hospital complaining of abdominal pain, nausea and vomiting. Initial exploration revealed marked hypertension (180/130 mmHg) and acute-onset dyspnoea with pulse oximeter saturation of 88% (despite rebreathing mask at 40% oxygen). During general screening, supra-ventricular paroxysmal tachycardia with haemodynamic instability occurred (60/40 mmHg), requiring cardioversion with adenosine (18 mg administered in two boluses) and amiodarone (bolus of 150 mg), as well as treatment with 1.5 μg/kg/min norepinephrine and 10 μg/kg/min dopamine.

Chest X-ray compatible with pulmonary oedema, electrocardiogram with sinus tachycardia of 130 bpm and ST-segment elevation in the anterolateral side, and elevated troponin levels suggested acute myocardial infarction Killip IV. However, emergency coronary angiography showed normal coronary arteries with normal coronary flow. Echocardiogram demonstrated a global hypokinesia of the heart with normal chamber size. Ejection fraction (EF), calculated using a biplane Simpson formula, was 20%, with an E/A ratio = 2.154 (Fig. 1). Cardiac index, measured by thermodilution method with a pulmonary arterial catheter, was 0.9 Lmin⁻¹m⁻². Despite vasoactive therapy with norepinephrine and dopamine, she remained hemodynamically unstable and an intra-aortic balloon pump (IABP) was placed.

In this condition, she was remitted to our hospital and into the cardiology intensive care unit. Due to important blood pressure swings (varying from 170/120 mmHg to 60/35 mmHg), fluctuating from need of vasoactive (1.8 μg/kg/min norepinephrine, 25 μg/kg/min dobutamine) to hypotensive drugs (8 μg/kg/min nitroprusside), as well as persistent abdominal pain, pheochromocytoma was suspected. A bedside abdominal echography revealed a right suprarenal tumour of 60 mm × 52 mm, confirmed by abdominal computed tomography. In order to establish the definitive diagnosis, a ¹²³I-MIBG scintigraphy showed a low-uptaking infraphepatic image, suggestive of pheochromocytoma necrosis. Levels of plasma metanephrines of 352 pg/mL (normal <90) and normetanephrines 7249 pg/mL (normal <200) corroborated the diagnosis. Cardiac sympathetic denervation was also assessed, by measuring the heart-to-mediastinum activity ratio at 4 h post ¹²³I-MIBG injection in the anterior view. The ratio of 1.5 (normal >1.8) demonstrated low myocardial uptake (Fig. 2).

At this point, the anaesthesiology team was contacted in order to optimize the patient prior to surgery since, despite aggressive pharmacological treatment with vasoactive drugs and IABP support, persistent haemodynamic instability did not allow for introduction of α blocker therapy. MgSO₄ infusion was considered valuable as a bridge for α-blocker treatment. Thus, on day 3, MgSO₄ infused at 1 g/h after priming dose of 2 g was added. Twenty-four hours later, the
patient showed gradual stabilization (blood pressure around 100/70 mmHg, heart rate 80 bpm), with no further hypertensive crisis weaning off of vasoactive drugs, removal of IABP, and volume overload in order to refill the depleted vascular space. A bedside echocardiogram demonstrated a non-dilated left ventricle (LV), with normal motility and no segmentary alterations. Calculated EF was 45%.

This favourable evolution allowed for removal of the IABP and initiation of alpha blockade on day 9, with phenoxybenzamine 10 mg thrice a day, scheduling the patient for resection of the right adrenal mass. Laparoscopic surgery was performed on day 18 after admission. Prior to surgery, echocardiogram showed a slightly hypertrophic LV, with no dilation and normal global motility. Heart valves and right side of the heart were normal. Estimated EF had increased up to 60% with complete restoration of left ventricular systolic function with light diastolic dysfunction (Doppler transmitral flow velocity E/A ratio = 0.8) (Fig. 3).

Prior to anaesthesia induction, which was performed with midazolam and etomidate, to avoid severe blood pressure drops and reflex tachycardia, as well as fentanyl and cisatracurium, invasive arterial monitoring via left radial artery was obtained. As established in our hospital’s protocol, a bolus (4 g) plus infusion (1 g/h) of MgSO₄ was initiated before anaesthesia induction and maintained throughout surgery, which lasted 85 min. Suprarenal gland was removed without incidences. Anaesthesia was maintained with desflurane, fentanyl and cisatracurium. Intra-operatively, a modified pulmonary arterial catheter (Swan-Ganz thermodilution ejection fraction/volumetric catheter, continuous cardiac output/continuous end diastolic volume/EF and SvO₂, model 777FB, Baxter, American Edwards L, Irvine, CA), and invasive arterial monitorisation were used.

No inotropes or vasoconstrictors were needed intraoperatively, and the patient remained stable, with blood pressure around 110/70 and heart rate around 80 bpm. At this time, haemodynamic profile showed a significant CI increase (2.4–3.64 L/min·m⁻²) with normal right ventricular function (end-diastolic ventricular index: 156 mL·m⁻²; ejection fraction index: 51%). The patient was extubed in the operating room and transferred to the reanimation ward for 24-h-control where she made an uneventful recovery. Tramadol and dexketoprophen were used for postoperative analgesia. She was discharged home 4 days after surgery with no drug therapy. The histopathological study

**Figure 1** (a) Transmitral flow Doppler shows the early ventricular filling (E) and atrial contraction (A). Basal E/A relationship shows an E/A ratio of 2.154. (b) M mode echocardiography in the left ventricle reveals the improvement of heart contractility.
confirmed the diagnosis of pheochromocytoma, 85% of which was necrosed. At nine months follow-up, the patient was clinically asymptomatic, hemodynamically stable, with an echocardiogram that showed normal contractility with an estimated EF of 65%.

This case report was performed in a university hospital setting, based on patient data acquired during care-as-usual. The data were analyzed retrospectively, and all requirements for patient anonymity are in agreement with the regulations of the ethical committee of our hospital for publication of patient data.

Discussion

We report the case of a patient presenting with spontaneous haemorrhagic necrosis of pheochromocytoma, with sudden release of catecholamines. This caused what is known as a catecholamine storm or "attack", with myocardial stunning, pulmonary oedema and heart failure.

The patient had to undergo surgery for tumour removal. Prior to surgery, it is essential to block \( \alpha \)-adrenergic receptors, since emergency surgery in absence of preparation is associated to poor survival rates. However, the patient’s unstable haemodynamic condition did not allow for introduction of alpha-blockade. After ensuring there were no other treatable causes of acute-onset heart failure, such as coronary artery lesions, magnesium sulphate was used as bridge therapy for weaning off vasoactive drugs and initiation of alpha-blockade treatment.

The successful use of magnesium sulphate for prevention of catecholamine storms during surgical removal of pheochromocytoma has been known for quite a long time.\(^6\) However, MgSO\(_4\) is also useful for treating pheochromocytoma crisis, and it has been recognized as such since James et al.\(^7\) presented three cases of life-threatening crisis in which MgSO\(_4\) was particularly beneficial.

MgSO\(_4\) has a generally marked anti-adrenergic effect, inhibiting catecholamine release and storage and mainly blocking extra-cellular and intra-cellular sites of calcium action. It is mostly well known for treatment of ventricular arrhythmias such as Torsades de Pointes because of its aforementioned action on calcium channels, but it may also be used for auricular arrhythmias, since it acts on sodium and potassium currents that affect membrane potentials in the heart’s conductive system.\(^7,4,8\)

The haemodynamic behaviour observed in our patient suggested the protective cardiac effects of MgSO\(_4\), improving the contractile response of stunned myocardium with a decrease of systemic vascular resistance and an increase in cardiac index without changes in heart rate or arterial pressure.

Another interesting consideration derived from this case is the use of \(^{123}\)I-MIBG scintigraphy. Being a norepinephrine analogue, MIBG demonstrates a high uptake in sympathetically innervated tissues, and it has been in use for diagnostic assessment of tumours that arise from neural crest cells since the 1980s. Its main goal is to functionally confirm tumour tissue that has been localized via computerized tomography scan or magnetic resonance imaging, and to diagnose extra-adrenal pheochromocytomas and remaining tumour tissue after surgery, being a useful tool for follow-up.\(^5\)

However, and as in our case, once this was performed, cardiac sympathetic denervation was also assessed. \(^{123}\)I-MIBG scintigraphy can also be used for the assessment of cardiac sympathetic function in heart failure. In chronic heart failure, there is a reduction in NE uptake, with an accelerated spillover in the myocardial adrenergic nerve terminals (increase in pre-synaptic activity). MIBG, with the same uptake and storage methods as NE, allows for autonomic cardiac function characterization.\(^9\) This technique can also be used in acute heart failure syndromes. As a direct effect of excessive catecholamines, myocardial injury and myocardiocyte degeneration have been reported.\(^3\)

In our patient, \(^{123}\)I-MIBG scintigraphy showed a low myocardial uptake, as demonstrated by a low heart-to-mediastinum ratio (1.5, normal >1.8) (Fig. 1). This ratio correlates with the severity of heart failure and outcome.\(^10\) When \(^{123}\)I-MIBG scintigraphy for pheochromocytoma is performed, it is useful to have myocardial uptake measured by an experienced radiologist, in order to assess the influence of catecholamines on the heart.\(^9\)

After pheochromocytoma removal, catecholamine over-stimulation is discontinued. Accordingly, tumour removal prompts a reversal of cardiomyopathy and associated symptoms. Heart function should improve, with the myocardium returning to normal within months.\(^1\)

If heart function fails to improve, again \(^{123}\)I-MIBG scintigraphy proves useful. A continued heart-to-mediastinum ratio alteration may be due to a permanent remaining lesion on the heart after the insult; but it may also be because of persistent adrenergic influence on the heart, due to
incomplete tumour removal, contra-lateral pheochromocytoma, or extra-adrenal paragangliomas.

In conclusion, we believe that the use of these two well-known ‘devices’ – magnesium as a therapeutic one and 123I-MIBG scintigraphy as a diagnostic and prognostic one – is a relatively simple and extremely useful approach to keep in mind when facing pheochromocytomas, helping us to better manage cardiovascular alterations caused by this tumour.

Conflict of interest

None of the authors have declared conflict of interest related to the case.

Ethical responsibilities

The information in this case was collected during the usual process of diagnosis and treatment of a patient. The authors have followed the protocols established by the Hospital Clinic of Barcelona to access data from medical records. The patient gave permission by informed consent for the usage of such data.

References

