

Pheochromocytoma induced fulminant cardiogenic shock following laparoscopic salpingectomy, successfully managed with extracorporeal membrane oxygenation

Tiberiu Ezri, MD^{1*} Abraham Golan, MD, FRCOG², Lior Sasson, MD³, Yoseph Rozenman MD⁴

¹Associate Professor & Head, Department of Anesthesia, ²Professor & Head, Department of Obstetrics & Gynecology, ³Lecturer and Head, Department of Cardiothoracic Surgery, ⁴Associate Professor & Head, Department of Cardiology, the Edith Wolfson Medical Center, Holon, Israel, Affiliated to Sackler Medical School, Tel Aviv University, Israel and *Outcomes Research Group, Cleveland, OH

Summary

Pheochromocytoma is a rare disorder caused by functioning tumor composed of chromaffin cells that secrete catecholamines. Patients with undiagnosed pheochromocytoma may have a high mortality. We present a young female patient with a preoperative diagnosis of asymptomatic neurofibromatosis who underwent laparoscopic salpingectomy for ectopic pregnancy. She subsequently developed a severe acute catecholamine-induced toxic cardiomyopathy presenting with cardiogenic and noncardiogenic pulmonary edema and shock. Intra-aortic balloon pump (IABP) support, combined with inotropic therapy, was unsuccessful in restoring hemodynamic stability. As a desperate measure, the patient was connected to an extracorporeal membrane oxygenation (ECMO) device. Within a few days, her condition gradually improved and she was weaned from ECMO and mechanical ventilation. A left adrenal pheochromocytoma was subsequently diagnosed and successfully removed laparoscopically, after two weeks of patient preparation.

The patient was discharged home with no serious complications.

We discuss the clinical presentation and treatment of catecholamine-induced cardiomyopathy.

Keywords: pheochromocytoma, cardiopulmonary failure, salpingectomy, anesthesia, extracorporeal membrane oxygenator

J Rom Anest Terap Int 2009; 16: 154-158

Case report

A 32 y.o. female was admitted to our gynecology department with a seven week asymptomatic ectopic pregnancy (EP). Two years before she had a contralateral EP successfully managed with methotrexate (MTX).

The patient was previously diagnosed of having an asymptomatic neurofibromatosis Type I. She was

otherwise healthy and had a good functional capacity. Transvaginal sonography (TVS) examination showed a 13 mm gestational sac in the left adnexae, with no free fluid in the pelvis. She had no known allergies and received no chronic medication. Upon admission, her heart rate and blood pressure were normal as were the laboratory results except for a mild leukocytosis (13,300/mL).

Intravenous methotrexate treatment was subsequently started.

Twenty four hours after admission the patient complained of acute abdominal pain. Physical examination revealed peritoneal irritation. Blood pressure was 140/80 mmHg and heart rate, 64 bpm. Transvaginal sonography confirmed a ruptured left EP with blood and clots (appreciated at 1000-1500 ml) in the pelvis. The contralateral tube was normal.

Adresa pentru corespondență: Tiberiu Ezri MD
Department of Anesthesia
Wolfson Medical Center
Holon 58100, Israel
E-mail: tezri@netvision.net.il

The patient was hemodynamically stable and was taken to the operating theatre for laparoscopic salpingectomy.

Anesthesia was induced with rapid sequence technique with etomidate and succinylcholine. Following an easy endotracheal intubation, for no apparent reason, the patient suddenly developed a supraventricular tachycardia of 170 bpm that was successfully managed with 6 mg i.v. adenosine. Surgery was uneventful; left salpingectomy was performed. Blood loss during surgery was approximately 1000 mL.

At the end of surgery the SpO₂ dropped to 92%, while abundant pink, frothy sputum was noticed to leak from the endotracheal tube. The patient was taken intubated to the PACU and was managed for pulmonary edema with furosemide and morphine. Her blood pressure and heart rate were unstable. Hemodynamic data are presented in Table 1.

Table 1. Hemodynamic measurements & SvO₂

Measurement Timing	Heart rate	Systolic blood pressure	CVP	CI	SVR	PVR	PAP	PCWP	SvO ₂
Preoperative	64	140							
PACU	120-140	100-70	7-10	1.8	1800	140	20/10	12	55
CICU	160	100-40	10-12	1.7	3000	141	22/13	13	50-40
ECMO	80-90	90-190	10						

Laboratory data are presented in Table 2. At this stage, the arterial blood gases showed a combined metabolic acidosis and severe hypoxemia. A twelve-lead ECG revealed sinus tachycardia with no myocardial ischemia.

Table 2. Blood gases

Measurement Timing	pH	PaCO ₂	Bicarbonate	Base excess	PaO ₂
PACU	7.17	54	17	-11	54
CICU	7.22-7.00	49	16	13	40

Blood gases taken with full ventilatory support, FiO₂ 1 and PEEP 5-10 cmH₂O

The chest X-ray showed widespread pulmonary edema with no cardiomegaly.

Subsequently, a pulmonary artery catheter was placed through the right internal jugular vein showing normal pulmonary and wedge pressures, and low cardiac index (CI) and mixed venous oxygen saturation (SvO₂) (Table 1).

A transthoracic echocardiography revealed severe global left ventricular hypokinesis with an ejection fraction of 10-15%, normal right ventricular contraction and normal cardiac valves.

A running diagnosis of combined pump failure and hyperpermeability pulmonary edema was considered.

Since the blood pressure and heart rate were unstable, treatment with inotropes and vasoactives (see Table 3) was started with no improvement. Despite the severe pulmonary edema the only means that temporarily succeeded to maintain an acceptable blood pressure and SvO₂ was the administration of repeated fluid boluses.

Three hours after surgery, the patient was transferred from the PACU to the coronary ICU for further treatment and investigations. She was sedated, and mechanically ventilated. She continued to be hemodynamically unstable with severe metabolic acidosis and worsening hypoxemia (Table 2). Her systemic vascular resistance was very high (Table 1). Her ECG continued to show only sinus tachycardia and her liver and kidney tests were normal. A four chamber transesophageal

Table 3. Medication

Location	PACU	CICU	ECMO
Medication	Morphine Furosemide Dopamine, Epinephrine Norepinephrine	Morphine Furosemide Bicarbonate Albumin Digoxin Methylprednisolone Rocephine, Clindamycine Amikacin Dopamine, Epinephrine Norepinephrine	Esmolol Norepinephrine Milrinone

echocardiography view showed an almost immobile but small left ventricle (estimated EF = 9%); only the apex was moving, with normal right ventricular contraction and normal cardiac valves (Fig. 1).

Several differential diagnoses were considered at this stage, including anaphylaxis, septic shock, hyperthyroidism and pheochromocytoma (PCC) due to the history of neurofibromatosis. Samples were sent for blood and urine cultures and serological tests such as thyroid function tests and blood and urine catecholamines.

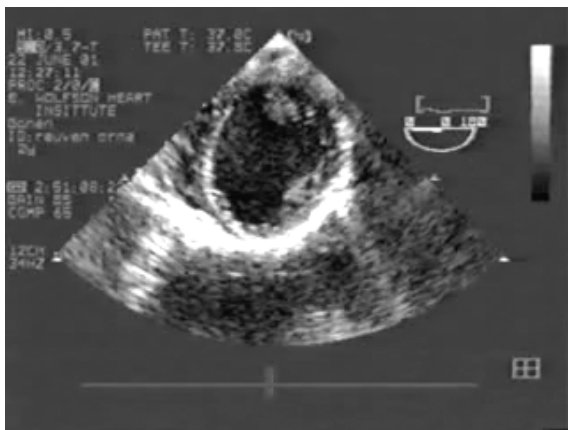


Fig. 1 Four-chamber view TEE showing an almost immobile left ventricle (Estimated EF = 9%)

The patient was managed with a wide range of supporting medications (Table 3).

In spite of the intensive treatment 12 hours after surgery, the patient became anuric, with her systolic blood pressure, PaO₂ and SvO₂ equalizing at 40. The patient was virtually dying!

An intra aortic balloon pump (IABP) inserted through the femoral artery was ineffective in restoring normal hemodynamics. As a desperate, last resort measure, the patient was connected to an Extra Corporeal Membrane Oxygenator (ECMO) machine. The procedure performed by the cardiac surgeons was laborious since the patient had a very low systolic blood pressure. The venous and arterial cannulae were inserted into the femoral vein and femoral artery. Hemodynamics and medication of the patient while on ECMO are presented in Tables 1 and 3. An abdominal ultrasound performed at this stage showed a small retroperitoneal hematoma with no intra-abdominal space occupying lesion. The patient developed coagulopathy and severe hemolysis requiring the administration of 13 units of blood during a 48 hour period. Thrombocytopenia (20 000) and leukocytosis (45 000) were also recorded. The patient also received fresh frozen plasma, platelets and cryoprecipitate.

Due to persistent tachycardia (despite normal cardiac output) esmolol therapy was initiated and the patient required supra-pharmacological doses to control the heart rate. We elected to use beta blocker therapy trying to give the heart as much “rest” as possible when hemodynamic control was maintained using the ECMO.

On the third postoperative day, while on ECMO, the patient started to improve gradually. With a LVEF of 35-40%, milrinone was started to try to wean the patient from IABP and ECMO. Urinary output and arterial blood gases were normal, however, surprisingly, large swings of blood pressure were observed (90 to

190 mmHg systolic blood pressures), reinforcing our suspicion of pheochromocytoma.

On the fourth postoperative day the IABP was removed and on day seven, the patient was disconnected from the ECMO and her trachea was extubated. At this stage, the echocardiography showed normal LV function with an EF of 60%.

An abdominal CT scan and MIBG (Meta-iodobenzylguanidine scintiscan) imaging confirmed the diagnosis of a 4 cm, left adrenal pheochromocytoma. The diagnosis was further confirmed by the results of catecholamines levels. Urinary catecholamines were: epinephrine – 1470 µg/24 h (normal = 0-20) and norepinephrine – 1651 µ/24 h (normal = 0-40);

Serum catecholamines levels were: epinephrine – 502 pg/ml (normal = 20-30) and norepinephrine – 2048 pg/ml (normal = 250-500).

Surgery for resection of the PCC was carefully planned.

The patient was prepared for two weeks with alpha & beta blocker agents along with hydration and was taken to laparoscopic adrenalectomy after she was considered fit for surgery [1].

Anesthesia for laparoscopic adrenalectomy consisted of propofol, fentanyl and rocuronium. Magnesium, phentolamine (regitine) and norepinephrine were pre-prepared for treatment of severe hypertension or hypotension episodes, would they occur.

Intraoperative monitoring consisted of transesophageal echocardiography, pulmonary artery catheterization and radial artery catheterization.

Throughout surgery and tumor resection, the patient was hemodynamically stable. The histopathology result definitively confirmed the diagnosis of pheochromocytoma.

A few days later, the patient was discharged home with only a mild left leg weakness.

Discussion

Pheochromocytoma is usually a benign tumor of the sympathetic system that may be present in various regions of the body from the skull to the urinary bladder. 90% of them however are located in adrenals [2].

The majority (85%) of patients with PCC present with hypertension. Hypotension may occur owing to a predominant secretion of epinephrine (instead of norepinephrine) or a peptide called adrenomedulline, vascular or cardiac smooth muscle cell down-regulation or to catecholamine-induced toxic myocarditis [2, 3].

Toxic catecholamine-induced myocarditis associated with PPC may manifest with multifocal necrosis, interstitial fibrosis. Overstimulation of adrenergic

receptors leads to Ca^{++} influx, ATPase activation resulting in decrease ATP stores which in turn causes intracellular accumulation of calcium and FFA, permeability disorders and cellular death [2].

Severe toxic cardiomyopathies have been described in patients with pheochromocytoma, manifesting as pulmonary edema and dilated cardiomyopathy with often grim outcome [2]. A case of graft "rejection" has been described in a heart transplanted patient, manifested with dilated cardiomyopathy despite the transplantation. After finding the tumor and its surgical removal, the patient's heart was able to function normally [4].

Other cardiac complications associated with PPC include life-threatening arrhythmias, acute myocardial infarction and non-cardiogenic pulmonary edema [2, 5]. Our patient presented with a combined cardiogenic and noncardiogenic pulmonary edema. This was caused by a combination of severe LV failure, normally functioning right ventricle and pulmonary capillary hyperpermeability manifested by severe widespread pulmonary edema with normal cardiac filling pressures.

Extremely high maternal and fetal mortality rates (58% and 56% respectively) were reported in undiagnosed pheochromocytoma during pregnancy [6].

In our patient, PPC was suspected because she had a history of neurofibromatosis. Neurofibromatosis may be complicated by pheochromocytoma in 5-15% of cases [2].

The various and unpredictable manifestations of PCC are described in a recent review by Manger [7].

Catecholamine induced toxic cardiomyopathy of PCC manifesting with cardiogenic shock should be considered in the differential diagnosis in patients with no other apparent reason for shock [7]. Thyroid storm may also cause cardiogenic shock [8]. We excluded these and other causative factors which possibly contributed to shock such as anaphylaxis and sepsis before we finally diagnosed PCC.

The only effective treatment in managing the broad spectrum clinical manifestations of pheochromocytoma is detection and resection of the tumor [7].

However, temporary life-support by management of hypertension or hypotension crises and cardiogenic shock with pulmonary edema may be crucial to maintain the patient alive until the PCC is detected and removed.

In such situations, sustaining the cardiac output by beta and alpha agonistic agents might be ineffective [9] since the receptors are saturated with the catecholamines secreted by the PPC and in some cases the altered hemodynamic condition might be secondary to the secretion of other substances (i.e. adrenomedulin). Alternative pressure support medications such as phosphodiesterase-5 inhibitors (milrinone, amrinone), calcium or glucagon which do not work through beta

and alpha receptors should be administered. Consequently, all vasoactives and inotropic agent given to our patients were ineffective, except for milrinone.

An intra-aortic balloon pump may be a temporary means in sustaining the patient's life, however, it can be ineffective [9] as it was in our case, supposedly owing to the fact that the heart was almost immobile at the stage the IABP was inserted. As a last resort and a desperate trial, we connected our patient to ECMO and this proved to be life-saving.

ECMO is a mobile variation of cardio-pulmonary bypass enabling complete functional replacement of the heart and lungs inside and outside the operating theatre (non-pulsatile flow, lowers preload, maintains afterload) (Fig. 2). Although ECMO may be life saving, one should be aware of its several disadvantages such as high maintenance cost and requirement for a specialized team. Complications are frequent [10] and are related to patient's condition prior to the connection to ECMO, catheters insertion and the use of cardiac-pulmonary bypass and include hemorrhage and coagulopathy, renal failure, infection, hemolysis, system (ECMO machine) failure and others. Our patient experienced retroperitoneal hemorrhage from difficult femoral cannulation with coagulopathy, hemolysis and ischemia of her left leg which almost completely resolved before her discharge from the hospital.

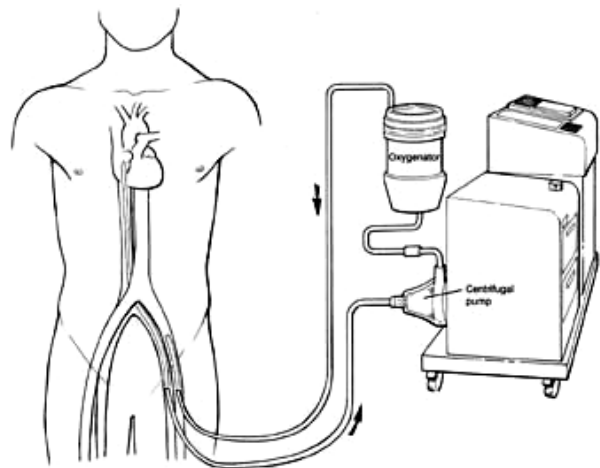


Fig. 2. Schematic description of an ECMO machine

ECMO proved to be life saving in patients with PCC related cardiogenic shock [11, 12].

Preoperative preparation for resection of PCC should include a 2-3 week treatment with alpha blockers and hydration. Beta blockers are added if necessary.

After adequate preparation our patient successfully underwent laparoscopic adrenalectomy that today is

the standard clinical approach for resection of adrenal tumors [13].

Patients are considered to be fit for surgery/anesthesia if [1]:

1. BP: < 165/90 and > 80/45
2. ECG: No ST-T changes
3. No more than 1 PVC every 5 min

Intraoperative management requires a smooth induction of anesthesia and intubation, blunting of surgical stimulation, preservation of normocarbica and avoiding hypoxemia and preservation of normovolemia.

The following drugs should be prepared for prompt administration: esmolol, regitine, magnesium, nitroglycerine, milrinone, etc.

Monitoring may include an arterial line, central venous pressure and eventually pulmonary artery catheter measurements.

Postoperatively there is a risk of hypotension which should be managed with vasopressors and i.v. fluids.

One question still remains unanswered: what was the trigger for the massive catecholamine surge that eventually caused the severe toxic cardiomyopathy and cardiogenic shock. One could speculate that the trigger might be the stress caused by the either endotracheal intubation the abdominal inflation with CO₂ for laparoscopy or subsequently the abdominal deflation.

In conclusion, our case demonstrated that pheochromocytoma should be considered in the differential diagnosis in a patient with unexplained tachycardia, arrhythmia, cardiogenic shock, hypertension or pulmonary edema in previously healthy, young patients. In spite of the grave condition, salvage of this patient was possible by an efficient cooperation of a multidisciplinary medical team.

The use of ECMO may be life saving as a last resort therapy.

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Șoc cardiogen fulminant indus de un feocromocitom după salpingectomie laparoscopică, tratat cu succes prin oxigenare extracorporală de membrană

Rezumat

Feocromocitomul este o afecțiune rară cauzată de funcția unei tumori de celule cromafine care secretă catecolmine. Pacienții cu feocromocitom nediagnosticați pot avea o mortalitate ridicată.

Prezentăm cazul unei femei tinere cu diagnosticul preoperator de neurofibromatoză la care s-a efectuat o salpingectomie laparoscopică pentru o sarcină ectopică. Postoperator, pacienta a dezvoltat o cardiomiopatie acută toxică indusă de catecolamine, cu tabloul unui edem pulmonar cardiogen și necardiogen și stare de șoc.

Terapia inotropică asociată cu aplicarea balonului intraaortic de contrapulsatie nu au reușit realizarea stabilității hemodinamice. Ca măsură disperată pacienta a fost conectată la un aparat de oxigenare extracorporală cu membrană (ECMO). În câteva zile starea pacientei s-a ameliorat progresiv și a fost desprinsă de ECMO și de ventilația mecanică. S-a diagnosticat un feocromocitom la nivelul suprarenalei stângi care după două săptămâni de pregătire a fost rezecat laparoscopic. Pacienta a fost externată fără complicații. Este discutat tabloul clinic și tratamentul cardiomiopatiei induse de catecolamine.

Cuvinte cheie: feocromocitom, insuficiență cardiopulmonară, salpingectomie, anestezie, aparat de oxigenare extracorporală cu membrană