

Surgical adrenalectomy during rescue Extracorporeal Life Support for pheochromocytoma induced cardiogenic shock: a case report

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Abstract: *Introduction :* Pheochromocytoma, a rare catecholamine-producing tumor, has been described to provoke stress-induced Takotsubo-like cardiomyopathy and even severe refractory cardiogenic shock. In this case report, venoarterial extracorporeal membrane oxygenation (VA-ECMO) was used for hemodynamic stabilization and was continued during the resection of a large neuroendocrine tumor.

Description : A 69-year old male, recently diagnosed with a pheochromocytoma, was referred to our center because of severe cardiogenic shock after induction of anesthesia for resection of the mass. Despite adequate alpha- and beta-adrenergic blockade for one month, he developed malignant hypertension with subsequently hemodynamic collapse. After successful cardiopulmonary resuscitation he developed pulmonary oedema with severe hypoxemia and persistent hemodynamic lability. On arrival in our hospital, echocardiography revealed significant left ventricular impairment. Decision was made to commence him on VA-ECMO for a refractory cardiogenic shock with severe pulmonary oedema. Because of persistent blood pressure swings despite VA-ECMO and beta-adrenergic blockade, we decided to remove the tumor on mechanical circulatory support by an open surgical approach the next day. After clamping of the adrenal circulation, the patient experienced profound hypotension requiring high doses of epinephrine and a methylene blue infusion. Surgical resection was successful but complicated by a postoperative bleeding for which the patient underwent an emergent endovascular embolization of an adrenal artery. Over the next days, there was progressive cardiac recovery and the patient was weaned off VA-ECMO on the fourth postoperative day. The patient was discharged from the intensive care 27 days after admission and left the hospital on day 30.

Discussion: VA-ECMO seems to be a feasible last resort therapy in refractory cardiogenic shock induced by pheochromocytoma crisis as suggested by a high survival rate in literature. Despite its support benefit during this type of shock, surgical removal of the tumor is rarely done with mechanical circulatory support and heparinization.

Keywords: Cardiogenic shock, ECMO, Pheochromocytoma, Adrenalectomy, Methylene blue.

INTRODUCTION

Pheochromocytoma is a rare catecholamine-secreting tumor arising from chromaffin cells of the adrenal gland. Its annual incidence is estimated 8 per 1 million. However its true incidence might be underestimated due to diagnostic difficulties (1). Clinical symptoms of pheochromocytoma include arterial hypertension, headache, palpitations and sweating. In addition, pheochromocytoma associated stress-induced Takotsubo-like cardiomyopathy and life-threatening cardiogenic shock have been described (2-5). Besides medical therapy to control heart rate and blood pressure, a surgical approach is typically warranted for curative disease control.

We present the case of a 69-year old male patient who was transferred to our facility for evaluation of mechanical support for cardiogenic shock shortly after induction of anaesthesia for elective pheochromocytoma resection. Upon arrival to our hospital, veno-arterial extracorporeal membrane oxygenation circuit (VA-ECMO) was initiated for hemodynamic stabilization. Due to persistent hemodynamic instability, surgery was performed under extracorporeal life support (ECLS).

CASE PRESENTATION

A 69-year old male patient with history of non-insulin dependent diabetes mellitus, arterial

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Conflict of interest: None.

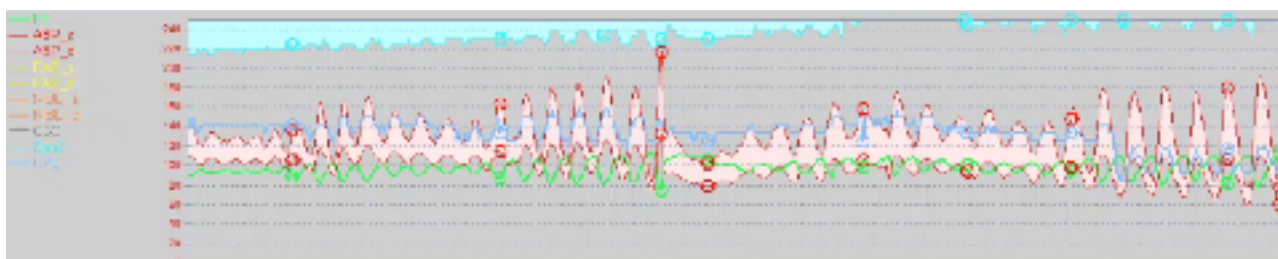


Fig. 1. — Blood pressure fluctuations of the patient before surgery during VA-ECMO and medical support. The red curve presents blood pressure and blood pressure pulsatility. HF indicates heart rate; ABP_s, systolic arterial blood pressure; ABP_d, diastolic arterial blood pressure, SpO₂, saturation and CVD, central venous pressure.

hypertension, paroxysmal atrial fibrillation and non-STEMI, was diagnosed with right adrenal gland pheochromocytoma. After diagnostic work-up, the patient was initiated alpha-blocking agents (prazosin) and shortly after beta-blocking drugs (bisoprolol). After one month, adrenergic suppression was reached and the patient was scheduled for elective surgery in a peripheral center. Prior to the start of surgery, an epidural catheter was placed and general anesthesia was initiated using fentanyl 150 µg, propofol 160 mg and rocuronium 50 mg followed by endotracheal intubation. Shortly after induction of anesthesia, the patient developed malignant hypertension followed by hemodynamic collapse necessitating cardiopulmonary resuscitation and administration of epinephrine. Despite continuous infusions of vasoactive drugs, ongoing hemodynamic lability and severe hypoxemia secondary to pulmonary oedema persisted. Surgery was cancelled and the patient was transferred to our center for evaluation for mechanical circulatory support. Chest X-ray showed severe pulmonary oedema and subsequent transesophageal echocardiography (TEE) revealed significant left ventricular systolic dysfunction with an estimated ejection fraction of 10%. Diagnosis of cardiogenic shock was confirmed and the patient was started on VA-ECMO for hemodynamic and hypoxic failure. Despite infusions of milrinone, epinephrine, norepinephrine, molsidomine, labetalol and orally titrated beta-blocking drugs, the patient still suffered from severe hemodynamic lability (Fig. 1). Therefore we multidisciplinary decided to remove the pheochromocytoma while heparinized on mechanical circulatory support, 24 hours after ECLS initiation. The surgical team opted for an open approach by right subcostal laparotomy. After clamping of the surreal vein, the patient experienced abrupt profound hypotension requiring boluses of epinephrine. TEE showed biventricular akinesia, only partially recovering with epinephrine. Even with an epinephrine drip up to 1 µg/kg/min, a

methylene blue loading dose of 1mg/kg was needed to compensate for vasoplegia. To prevent ECMO circuit clotting, anticoagulation with heparin was continued targeting an activated clotting time (ACT) of 180 seconds throughout the surgical procedure. The pheochromocytoma was successfully resected and the patient was transferred to the ICU.

A combination of VA-ECMO and medical support was continued postoperatively for hemodynamic support. Despite high doses of norepinephrine up to 0,3 µg/kg/min and epinephrine up to 2 µg/kg/min, the patient suffered from profound hypotension for which a second loading dose of methylene blue (0.5 mg/kg) was given and continuous infusion was started at 0.3125 mg/kg/h. Subsequently, a Swan-Ganz catheter was placed in an attempt to optimize vasopressor doses. This confirmed SVR's in the lower range (930-970 dyn x sec x cm⁻⁵).

Furthermore, the immediate postoperative course was complicated by excessive blood loss from the abdominal drains. Urgent CT scan revealed a bleeding focus from an adrenal artery for which endovascular embolization was performed. Heparin was ceased shortly and a titrated transfusion strategy was used to correct coagulation deficits.

Further hemodynamic stabilization was obtained and repeat echocardiography confirmed improving cardiac function. Vasoactive drugs and inotropes could be reduced and the patient was successfully weaned off ECMO on the fourth postoperative day. TEE guidance during the weaning process, showed full recovery of his cardiac function. Eventually, epidural catheter was safely removed on the fifth postoperative day, after normalization of coagulation parameters.

Complete resection of the adrenal pheochromocytoma with dimensions of 11 x 9 x 6,5 cm was confirmed by the histopathological report (Fig. 2). The patient was discharged from ICU 27 days after admission and left the hospital on postoperative day 30.



Fig. 2. — Adrenal pheochromocytoma with dimensions of 11 x 9 x 65.5 cm and a weight of 358 grams.

DISCUSSION

We describe a case of refractory cardiogenic shock after induction of anaesthesia for scheduled pheochromocytoma resection. Despite medical therapy, ECLS was essential as a rescue strategy. A French retrospective study found that ECMO was used in 41% of all patients admitted to the ICU with pheochromocytoma crisis (2). This study also demonstrated that ECMO is not a risk factor for increased mortality (2). Surgical removal of the pheochromocytoma is however rarely performed under mechanical circulatory support (2, 3, 6, 7). Most centers prefer awaiting cardiac function to recover before proceeding with surgical adrenalectomy (2, 8, 9). A more recent systematic review of Matteucci et al. reported 62 cases of patients suffering from pheochromocytoma-induced cardiogenic shock requiring ECLS (9). The overall in-hospital survival rate for those patients was 87%. In 10 patients the tumor was removed while receiving ECLS with an in-hospital survival rate of 100% (9). However, a publication bias may partially explain this high survival rate.

Our patient suffered major hemodynamic instability during resection of the mass, despite having been optimized medically before surgery and continuous ECMO flow. Total hemodynamic collapse after clamping of the surreal vein however might suggest suboptimal treatment. Surprisingly, our surgeons found a clot in the surreal vein. The latter is typically more prevalent in malignant pheochromocytoma, and might have contributed to pulsatile release of catecholamines declaring blood pressure swings (10).

Despite high doses of norepinephrine and epinephrine, increase in mean arterial pressure

was achieved with administration of methylene blue after clamping of the surreal vein. Methylene blue is considered a rescue vasopressor drug (11). However, successful use of methylene blue to treat hypotension occurring after vein ligation in pheochromocytoma surgery has been described earlier (12). Alpha- and beta-adrenergic receptor down regulation is a known contributor to post isolation hypotension (13). It interferes with NO-cyclic guanosine monophosphate pathway on many levels, inhibiting NO-mediated vasodilatation. Omitting alpha- and beta-adrenergic receptor pathways by administration of methylene blue might be an attractive alternative for use of catecholamines in catecholamine-resistant hypotension (14). Therefore, methylene blue therapy has already been proven to be successful in catecholamine resistant septic shock as well as in anaphylactic shock states (15, 16).

This case was also complicated by a post-operative bleeding under heparin therapy, solved by an endovascular procedure and correction of coagulation, leaving no comorbidity. In a similar case by Van Dang, the patient developed retroperitoneal hematoma despite heparin was started only after the adrenalectomy (3).

CONCLUSION

We present a successful case of open surgical adrenalectomy under salvage extracorporeal life support for a pheochromocytoma-induced cardiogenic shock. Although this life-threatening presentation of the neuroendocrine tumor is rather rare, ECLS use can be life-saving. In the majority of the cases in the literature, surgical resection is done after stabilization and weaning from ECLS. If however tumor resection cannot be delayed in case of persistent hemodynamic instability, it can be performed during ECLS despite the necessity of anticoagulant therapy. This strategy should be carefully considered since the risk of bleeding and other complications. Furthermore, we confirm the efficacy of methylene blue on mean arterial pressure in pheochromocytoma post vein ligation hypotension, in line with one earlier case report.

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