Heliyon 9 (2023) e23210

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Treatment of malignant airway stenosis with extracorporeal membrane oxygenation under low-dose anticoagulation: A case report

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ARTICLE INFO

Keywords:
ECMO
Cancer
Airway obstruction
Anticoagulation
Procedure

ABSTRACT

The occurrence of airway obstruction due to severe stenosis from lung cancer poses a significant risk of asphyxia. Although the placement of a metallic stent may relieve the obstruction, the procedure is associated with a high risk of asphyxia. To mitigate this risk, extracorporeal membrane pulmonary oxygenation (ECMO) has been proposed to temporarily substitute for cardiopulmonary function during the procedure. However, the use of systemic anticoagulation with heparin during ECMO may increase the likelihood of bleeding during surgery. This case report describes a successful treatment of a patient with malignant central airway obstruction through low-dose heparin veno-venous ECMO. This approach resulted in reduced intraoperative bleeding and invasive operation time, allowing for prompt postoperative withdrawal and recovery.

1. Introduction

Malignant central airway obstruction can occur as a result of infiltration, metastasis, or compression of malignant lesions in the airway lumen or in adjacent organs. Common culprits include lung cancer, esophageal cancer, and thyroid cancer. Immediate relief of airway obstruction is the primary treatment goal. Extracorporeal membrane oxygenation (ECMO) is a technique that can serve as a temporary substitute for cardiac and/or pulmonary function for an extended period, ensuring tissue oxygenation and providing a bridge to rescue therapy.

It is worth noting that current guidelines for extracorporeal life support (ECLS) state that maintaining the activated clotting time (ACT) between 160 and 180 seconds or the activated partial thromboplastin time (APTT) between 50 and 70 seconds, in patients receiving anticoagulation therapy during ECLS, may unexpectedly elevate the oxygenator failure rate [1]. On the contrary, studies have indicated that adult patients undergoing veno-venous ECMO treatment may not necessarily require prolonged systemic anticoagulation, with no significant increase in thrombotic complications or mortality rates compared to the standard anticoagulation group, while experiencing lower probabilities of gastrointestinal bleeding and transfusion events [2].

Given the unique context of this case report, focusing on late-stage cancer patients with notably elevated D-dimer levels indicative

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https://doi.org/10.1016/j.heliyon.2023.e23210
Received 7 June 2023; Received in revised form 24 November 2023; Accepted 29 November 2023
Available online 2 December 2023

of hypercoagulability, a cautious approach was adopted, favoring low-dose anticoagulation over a non-anticoagulated regimen, resulting in a favorable patient outcome. It is imperative to highlight the critical role that hemostatic strategies and appropriate anticoagulation management play in the patient's recovery process. This case report bridges a crucial paradox: while standard-dose anticoagulation can potentially increase bleeding during stent implantation and heighten the risk of mechanical trauma related to intratracheal electrocoagulation, these factors substantially reduce the likelihood of a swift ECMO decannulation. Conversely, low-dose anticoagulation minimizes bleeding, diminishes exogenous resource consumption, and enhances the probability of expeditious ECMO weaning. This perspective holds promise, particularly for cancer patients.

2. Case report

A 58-year-old male with a height of 172cm, weight of 61kg, and a BMI of 20.6 kg/m^2 developed progressive dysphagia one year ago. After gastroscopy and histopathological examination, he was diagnosed with esophageal carcinoma. A color doppler ultrasound suggested liver metastasis, and he underwent radical esophagectomy after 2 cycles of neoadjuvant chemotherapy but refused further therapy. Recently, he presented to our emergency department with cough and shortness of breath and received continuous non-invasive ventilator treatment. CT scan revealed multiple enlarged lymph nodes in both hilum and mediastinum, an enlarged bilateral cervical lymph node, and severe luminal narrowing of the trachea and opening of the left and right main bronchi caused by the esophageal cancer (Fig. 1). Fibrobronchoscopy showed nodular changes and narrowing of the tracheal lumen from the proximal trachea to both right and left main bronchi. The stenotic segment of the left main bronchus was approximately 4 cm in length, and the right main bronchus stenosis was 2.5 cm. During the procedure, nodular tissue caused significant mucosal hemorrhage (Fig. 2). The position of the stenosis involved the carina and bilateral main bronchi, which could lead to difficulty in oxygenation and ventilation in acute airway collapse. Endotracheal intubation and tracheotomy could not relieve mechanical airway obstruction. After multidisciplinary consultation, we decided to use veno-venous extracorporeal membrane oxygenation (VV-ECMO) for temporary respiratory support during self-expandable metallic Y stent placement.

On October 19th, 2021, the patient underwent ECMO using the PLS (permanent life support) system with rotaflow devices (MAQUET cardiopulmonary AG, hirrlingen, Germany).

Considering that he is a long-term bedridden oncology patient with a padua score of 7, a preoperative coagulation function suggesting a D-dimer of 4.15 mg/L (normal range 0.0–0.5 mg/L), belongs to the group of people with high coagulation status or prone to thrombosis, and the high risk of surgical bleeding, a low loading dose of heparin (20 U/kg) was administered intravenously. After the Activated Clotting Time of whole blood (ACT) reached 148 seconds, an outflow cannula via the right femoral vein (using 21-Fr) and an inflow cannula via the right internal jugular vein (using 15-Fr) were placed. The ECMO flow was maintained at 4.0–4.5 L/min with a rotation speed of 4000 rpm, an oxygen concentration of 0.8, and an oxygen flow rate of 4 L/min, while the PaO2 remained at 95–99 % without mechanical ventilation. After confirming stable vital signs, bronchoscopic treatment was performed using a high-frequency electric knife to cut the tumor tissue, cryotherapy to ablate, and a Y-shaped airway metallic stent under rigid bronchoscopy followed by argon plasma coagulation to achieve hemostasis (Fig. 3). Due to the significant bleeding during the procedure, topical thrombin and norepinephrine were applied in the endotracheal tube without the maintenance of the heparin pump. The activated clotting time, oxygen saturation, and clot in the oxygenator were closely monitored and recorded. The PaO2 levels were maintained at 80–120 mmHg, the PaCO2 was 35–45 mmHg, and ACT was maintained at 108–135 seconds. The operative time was 80 minutes, with 100 ml of intraoperative bleeding.

After the operation, the patient's vital signs were stable with invasive mechanical ventilation (mode SIMV, PSV 14cmH2O, PEEP 5cmH2O, FiO2 100 %). ECMO parameters were reduced (rotation rate 3000 rpm, flow 4.0L/min, oxygen concentration 0, and oxygen flow 0L/min). However, the patient's oxygen saturation could not be maintained, and arterial blood gas analysis indicated PaO2 56

Fig. 1. CT scan revealed multiple enlarged lymph nodes in both hilum and mediastinum, an enlarged bilateral cervical lymph node, and severe luminal narrowing of the trachea and opening of the left and right main bronchi caused by the esophageal cancer.

Fig. 2. The proximal trachea was occluded by neoplasma in bronchoscopy. Carina and bilateral apertures of bronchus were not visible.

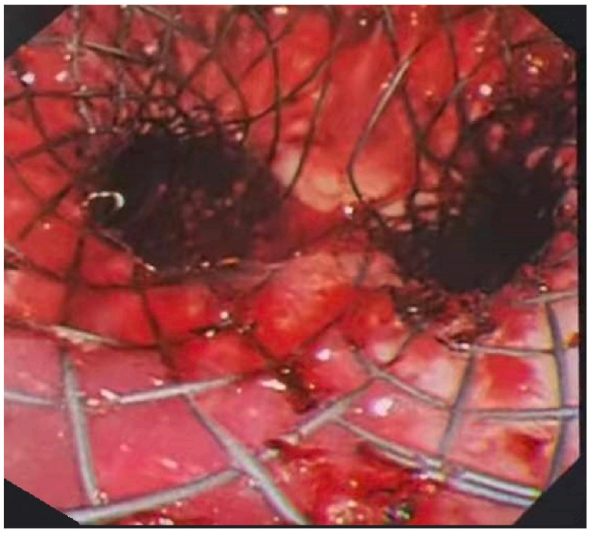

Fig. 3. Opening of the Carina and bilateral apertures of bronchus after implantation of a Y-shaped overlapping stent.

mmHg and PaCO2 48 mmHg. The ECMO parameters were adjusted to rotation speed 3000 rpm, flow rate 3.5L/min, oxygen concentration 0.6, and oxygen flow rate 4L/min. After 50 minutes of support, the oxygen concentration and flow rate were gradually adjusted downward until the patient was kept on the invasive ventilator with PSV 14cmH2O, PEEP 5cmH2O, FiO2 60 %, and ECMO parameters with rotation rate 3000 rpm, flow 3.5L/min, oxygen concentration 0, and oxygen flow 0L/min. Concurrent review of arterial blood gas analysis showed an PaO2 of 88 mmHg and PaCO2 of 39 mmHg. Subsequently, ECMO was safely withdrawn after 60 minutes with an PaO2 of 91 mmHg and PaCO2 of 41 mmHg. On October 20, 2021, the patient was successfully weaned from ECMO and transferred back to the general ward on October 22, 2021. As of the date of publication, the patient is surviving well and is undergoing radiotherapy and systemic chemotherapy in the oncology department.

3. Discussion

Central airway stenosis refers to the narrowing of the vocal cords, main airways, and main bronchi. Transbronchoscopic intervention is currently the preferred method for effectively relieving malignant airway stenosis caused by various tumors [3]. However,

the trachea serves not only as a surgical site but also to ensure ventilation and maintain oxygenation. For some patients, an artificial airway must be established to enable further treatment. When tracheoscopy or CT shows an endotracheal diameter of less than 5 mm, it is recommended to consider surgical treatment with ECMO support [4].

To support the complex airway surgery, the use of ECMO in airway surgery has gained increasing attention in recent years. ECMO offers several advantages, including facilitating complex reconstructions, maintaining gas exchange, and enabling precise surgical dissection by eliminating the need for crossing ventilation tubes [5]. The study based on real-world cases have shown the successful implementation of ECMO in major airway surgery, both in adult and pediatric patients [5]. Furthermore, ECMO has been proven effective in managing central airway obstruction caused by neck and chest tumors, providing adequate ventilation and supporting emergency surgical interventions [6]. The adoption of ECMO in these cases has demonstrated feasibility and safety, enabling successful airway management and surgical procedures.

ECMO is a modified form of cardiopulmonary bypass, and therefore, shares some similarities in anticoagulation strategies [7,8]. During ECMO treatment, blood comes into contact with the non-endothelial surface of the extracorporeal circuit, triggering a blood biosurface reaction that activates a systemic inflammatory response and coagulation cascade, platelets, vWF, and fibrinolytic system [9]. To prevent thrombosis in ECMO circuits, anticoagulants are administered. However, inadequate anticoagulation significantly increases the risk of thrombosis and its related complications [10].

The Extracorporeal Life Support Organization (ELSO) guidelines recommend systemic anticoagulation with heparin during ECMO support, with a target range of 180–220 seconds for activated clotting time (ACT) [11]. However, there is no consensus on the target value of ACT, and guidelines vary among different centers. With advances in centrifugal pumps, newer polymethylpentene oxygenators, and the biocompatibility of heparin-coated tubing, the risk of thrombosis and its complications have been reduced [12].

Despite these advances, bleeding due to anticoagulation has become the most common complication of ECMO, including intracranial bleeding, surgical site bleeding, and gastrointestinal bleeding, with fatal consequences [13,14]. Studies have shown that the incidence of bleeding in adults treated with ECMO ranges from 27 to 60 % [15], and that a higher activated partial thromboplastin time (aPTT) in the preoperative 24 hours is associated with the complication of bleeding [14].

To reduce bleeding on ECMO, low-dose anticoagulation (LA) strategies have been proposed [16–18]. For instance, Arlt et al. reported that in disastrous trauma patients, initiating treatment without heparin and subsequently administering continuous low-dose heparin anticoagulation can reduce the incidence of bleeding [19]. Some studies have also shown that lowering anticoagulation standards and maintaining the coagulation system may benefit ECMO-assisted patients [17,20]. A meta-analysis found that the LA group had a similar risk of deep vein thrombosis but a lower incidence of gastrointestinal and surgical site bleeding compared to the standard-dose anticoagulation (SA) group. Meanwhile, the incidence of intracranial bleeding, pulmonary bleeding, and ECMO cannulation site bleeding was not significantly different, and the probability of successful withdrawal and oxygenator replacement was similar between the two groups [8].

However, some studies suggest that microembolic events may occur in ECMO patients, and the clinical significance of this potential microembolic burden is still unclear [21]. Therefore, in patients with contraindications to therapeutic anticoagulation, short-term heparin-free veno-venous ECMO may be an effective treatment modality without thromboembolic complications [18,22].

Prolonged epidural bronchoscopy for airway narrowing can cause rapid hypoxia or even death due to airway spasm, bleeding, and pulmonary edema during treatment [23]. However, ECMO can effectively prevent these complications. In this case, despite the patient's malignant airway stenosis, preoperative assessments of pulmonary function, vascular ultrasound, cardiac ultrasound, CT, and other tests were completed to evaluate the patient's general condition. Since the patient's preoperative organ function was satisfactory and tissue oxygen supply could be maintained postoperatively with an invasive ventilator, low-dose anticoagulation was chosen to minimize the ECMO machine run time. Although the feasibility or superiority of low-dose anticoagulation versus standard anticoagulation remains controversial, we decided to use high-flow (>3.5 L/min) short-term ECMO without a maintenance heparin pump during treatment. Despite postoperative hypoxemia, the patient was successfully weaned from ECMO after a brief period of support, with an ECMO turnaround time of 190 minutes and no significant embolus formation on postoperative inspection of the circuit and oxygenator. In addition, postoperatively, we performed another fibrinoscopic exploration, which did not show persistent bleeding, but a small amount of cigar coverage. The patient developed hypoxemia after lowering the ECMO parameters, and this was considered to be related to the repeated use of electrocoagulation for haemostasis after intraoperative bleeding, thus triggering airway hyperreactivity.

We acknowledge that cases of esophageal cancer with airway metastasis, and successfully performed bronchoscopic guided tumor resection and stent implantation with ECMO support have been reported in the literature. However, the unique aspect of our study lies in our approach to resolving a critical contradiction. By employing low-dose anticoagulation, we aim to minimize bleeding complications, reduce the need for external blood products, and increase the likelihood of a swift ECMO wean. This novel strategy holds promise, particularly for cancer patients.

Based on this case, we recommend comprehensive preoperative assessments, prediction of the ECMO duration, and reasonable choices of low-dose anticoagulation to effectively reduce bleeding and invasive operation time in central airway surgery. This approach can also prevent consumption and over-activation of procoagulant and anticoagulant components and reduce complications associated with prolonged ECMO.

While this case report provides an interesting application of low-dose anticoagulation ECMO to manage malignant airway obstruction during stent placement, there are some limitations worth noting. As a single case study, the results may not be widely generalizable without further research comparing outcomes to standard anticoagulation protocols. Additionally, long-term outcomes were not reported, so it is unclear if the low-dose anticoagulation contributed to complications like stent thrombosis later on. Finally, the rationale for the chosen low-dose heparin regimen is not extensively justified by existing literature. More rigorous studies are

needed to optimize anticoagulation protocols that balance clotting and bleeding complications in complex ECMO cases. Overall, this report provides a helpful proof of concept, but requires more rigorous investigation to establish evidence-based guidelines for anticoagulation management with ECMO during airway procedures in cancer patients.

Funding

None.

Data availability statement

Data will be made available on request.

Ethics statement

Informed consent was obtained from the patient for the publication of all images, clinical data and other data included in the main manuscript.

CRediT authorship contribution statement

Jingsha Zhao: Writing – original draft, Methodology, Data curation, Conceptualization. **Peng Cui:** Writing – review & editing, Conceptualization. **Ziwei Zhou:** Writing – review & editing, Supervision, Project administration. **Bin Niu:** Writing – review & editing, Supervision. **Chuanliang Pan:** Writing – review & editing, Project administration, Methodology.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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