Use of Extracorporeal Membrane Oxygenation for Mechanical Circulatory Support in a Patient With 5-Fluorouracil Induced Acute Heart Failure

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Extracorporeal life support has evolved to become a viable support option in patients with acute cardiac failure. Tailored mechanical circulatory support (MCS) can now be provided to patients using existing extracorporeal life support devices. We report the successful use of peripheral venoarterial extracorporeal membrane oxygenation (ECMO) to provide MCS to a patient with acute 5-fluorouracil (5-FU)–induced cardiomyopathy. 5-FU is a key component of adjuvant chemotherapy for colorectal cancer. It is also frequently used in the treatment of gastric, esophageal, pancreatic, breast, bladder, and prostate cancer. There is a wide range of cardiotoxicity with this 5-FU, including ischemia, vasospasm, arrhythmia, hypertension, Q-T interval prolongation, and acute cardiomyopathy and 5-FU–induced cardiac complications are not rare. This case illustrates the crucial place of ECMO as a bridge to recovery in chemotherapy, cardiomyopathy, or decision making.

Case Report

A 32-year-old man began adjuvant treatment for colorectal adenocarcinoma with 5-FU continuous infusion after presumed curative bowel resection. He experienced stuttering chest pain from day 1 of therapy with progressive shortness of breath. His risk factors for cardiovascular disease included a positive family history of ischemic heart disease and previous methamphetamine use. He presented to the emergency department in a peripheral hospital on completion of his first cycle, with inferolateral ST elevation. Cardiac troponin was mildly elevated and a presumptive diagnosis of 5-FU–induced cardiomyopathy was made. Sublingual glyceryl trinitrate, oral atenolol, and amloidipine were administered. After this, the patient became hypotensive, with cool and clammy peripheries. He was commenced on dobutamine and noradrenaline infusions for cardiogenic shock despite intra-aortic balloon counterpulsation and high doses of dobutamine (10 μg/kg per minute), noradrenaline (0.25 μg/kg per minute), and adrenaline (0.25 μg/kg per minute). There was evidence of end-organ malperfusion with increasing lactate, altered mentation, and early hepatic and renal dysfunction. In the face of impending circulatory collapse, peripheral venoarterial ECMO was instituted as a bridge to recovery. He was deemed unsuitable for cardiac transplantation because of underlying malignancy requiring chemotherapy.

Under controlled light sedation and local anesthesia the patient was placed on venoarterial ECMO by percutaneously inserting a 25 Fr multistage cannula positioned in the right atrium via the left femoral vein for access and a 16 Fr cannula (Maquet) via right femoral artery for return of oxygenated blood. A retrograde arterial blood flow cannula was inserted in the right femoral artery distally to maintain limb perfusion. ECMO flows were set at 3.5 L/min. Unfractionated heparin was initiated by bolus 1000 U followed by 800 U/h, targeting an Activated Partial Thromboplastin Time 80 to 100 seconds. The patient was awake and spontaneously breathing for the duration of MCS.

Soon after peripheral venoarterial ECMO was commenced, there was rapid improvement in hemodynamics; in addition, markers of end-organ perfusion (lactate, renal, and hepatic indices) improved. This enabled prompt weaning of vasoactive agents. The intra-aortic balloon pump was removed day 3 in intensive care unit. Anti failure therapy was introduced (ramipril, spironolactone) and doses slowly increased as tolerated. Serial transthoracic echocardiograms revealed improvement in cardiac function. MCS support was ceased on day 6.
in intensive care unit, and the patient was transferred to the cardiology ward day 7. Cardiac MRI confirmed improvement in cardiac function with ejection fraction of 48% with appearances consistent with chemotherapy-related myocarditis.

Discussion

In our case with unclear pathogenesis of cardiogenic shock, we decided to use mechanical hemodynamic support (intra-aortic balloon counterpulsation and ECMO) to avoid the above-mentioned disadvantages of sympathomimetics. Early use of ECMO for hemodynamic stabilization allows the possibility of myocardial recovery after improvement of the initial stunning. An aggressive strategy, including the use of mechanical support as a bridge to transplant or recovery, has been associated with improvement in survival compared with conservative treatment. The delay in MCS of such patients with clinically advanced respiratory, hepatic, or renal failure for consideration of implantable or more permanent therapy is associated with poor outcomes. In our case with progressive cardiogenic shock, the most effective and a relatively easily inserted extracorporeal life support was necessary. Therefore, we decided to use ECMO to obtain rapid resuscitation, stabilization, and subsequent triage to a more permanent treatment strategy. This concept, known as a bridge-to-decision or bridge-to-bridge may optimize patient survival and resource utilization.

5-FU is associated with a wide range of adverse side effects, most commonly diarrhea, mucositis, myelosuppression, and thrombophlebitis if administered via peripheral cannulae. Less commonly, but more severe, is the spectrum of cardiac complications ranging from acute coronary syndrome, vasospastic angina, cardiomyopathy (including Tako-Tsubo cardiomyopathy), myopericarditis, coronary thrombosis and dissection, malignant arrhythmias, cardiogenic shock, and sudden cardiac death. The mechanism of 5-FU cardiotoxicity is not fully understood. Proposed mechanisms include coronary artery vasospasm, endothelial dysfunction, and thrombus formation independent of vasoconstriction, direct myocardial injury, accumulation of toxic metabolites such as α-fluoro-β-alanine, alteration of erythrocyte membrane with conversion to echinocytic shape leading to diminished oxygen delivery and ischemia, and the Kounis syndrome, an allergic insult resulting in vasospasm. The mainstays of therapy include immediate discontinuation of 5-FU, nitrates, and nondihydropyridine calcium-channel blockers and monitoring of patients with positive cardiac biomarkers for ≥72 hours. Once stable, antifailure therapy is recommended.

Our patient did not report any angina and obstructive coronary lesions were excluded by angiography. Echocardiography did not reveal apical ballooning to suggest Tako-Tsubo–like syndrome. Treatment of cardiogenic shock remains a therapeutic challenge, especially if coronary artery disease has been excluded. Sympathomimetics (dopamine, dobutamine, adrenaline, and noradrenaline) are usually used as first-line therapeutics, but several disadvantages in their use must be taken into account. Sympathomimetic-induced vasoconstriction can lead to perfusion mismatch or microcirculatory deficits; increased oxygen demand and subsequent metabolic acidosis are regularly observed. In addition, some experimental studies suggest that sympathomimetics are directly linked to enhanced systemic inflammatory response because of an increase in interleukin-6 expression.

Conclusions

Cardiogenic shock is a recognized complication of 5-FU. We present a case where ECMO support enabled short-term extracorporeal life support, allowing the heart to recover from a reversible cause of cardiomyopathy. Together with medical therapy for heart failure, near-complete recovery of cardiac function was possible. Although recent or ongoing immunosuppression per se is a predictor of poor outcome in ECMO patients, early use of ECMO as a bridge to recovery in patients with acute chemotherapy–induced heart failure may be a viable alternative in carefully selected cases.

Disclosures

None.

References


Keywords: acute heart failure – drug-related side effects and adverse reactions – extracorporeal life support – extracorporeal membrane oxygenation support – shock, cardiogenic
Figure 1. Cardiac catheterization. A, Left coronary artery and (B) right coronary artery. No coronary artery disease visualized.

Figure 2. Transthoracic echocardiogram. Apical 4-chamber view on day of admission. Of note, there are no regional wall motion abnormalities and no evidence suggestive of chronic cardiomyopathy.
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