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CASE REPORT
Heart failure

Tissue plasminogen activator for axillary Impella 5.0 with heparin-induced thrombocytopenia as a treatment of choice for acute Impella thrombosis: a case report

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Background Patients with cardiogenic shock requiring temporary support with percutaneous ventricular assist device, such as Impella (Abiomed, Inc.), can develop heparin-induced thrombocytopenia (HIT) which requires use of alternative purge solution anticoagulation. There are limited recommendations on use of anticoagulation other than standard Unfractionated Heparin in 5% dextrose solution.

Case summary This case describes 69-year-old female who presented with symptoms of decompensated systolic heart failure and was found to be in cardiogenic shock and despite use of inotropes and vasopressors maintained low systolic blood pressure and low mixed venous oxygen saturation which lead to use of axillary Impella 5.0 (Abiomed, Inc.) who developed HIT. Purge solution anticoagulation was switched to Argatroban, but due to increased motor pressures, tissue plasminogen activator (tPA) was successfully used to maintain proper motor pressures. Ultimately, patient was transferred to an outside facility for a transplant evaluation.

Discussion This case demonstrates successful and safe use of tPA as an alternative purge solution although more data needed to support this finding.

Keywords Impella 5.0 • Anticoagulation • Alteplase • Heparin-induced thrombocytopenia • Case report

ESC Curriculum 6.2 Heart failure with reduced ejection fraction • 6.4 Acute heart failure • 7.1 Haemodynamic instability
7.3 Critically ill cardiac patient

Learning Points

- To emphasize the increased risk of heparin-induced thrombocytopenia (HIT) in the critically ill patients in cardiogenic shock who require Impella (Abiomed, Inc.) therapy.
- To understand different types of Impella 5.0 (Abiomed, Inc.) purge solution anticoagulation when patient develops HIT.
- To explore the effectiveness and safety of tissue plasminogen activator (tPA) Alteplase use as a purge solution anticoagulation in a patient who developed HIT.

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Introduction

Since 2008, the use of percutaneous ventricular assist devices (pVADs) in patients with cardiogenic shock has grown significantly.[1] Recent data reported the increased incidence of heparin-induced thrombocytopenia (HIT) with the heparin-based Impella (Abiomed, Inc.) device.[2] As blood flows through the catheter, a purge solution runs counter current to the patient's blood from entering the Impella (Abiomed, Inc.) motor. The purge solution requires heparin to maintain the patency of the purge pathway in the event blood enters the motor. Anticoagulation in patients with pVADs can often be complicated due to unpredictable flow rates, pre-existing coagulopathy, or heparin allergies.[3] Few cases have described the use of tissue plasminogen activator (tPA) as an alternative to Unfractionated Heparin (UFH) with a 5% dextrose purge solution. We present a case of a patient with cardiogenic shock who required support with Impella 5.0 (Abiomed, Inc.) and developed HIT-related axillary venous thrombosis. Alteplase was used to avoid clotting of the circuit and maintain proper motor pressures. The patient was successfully transferred to an outside facility for a transplant evaluation.

Timeline

Timeline	Sequence of Events
Day 1–2	Patient developed symptoms of decompensated systolic heart failure
Day 3	Patient admitted to Cardiac Care Unit for Pulmonary catheter placement and further management
Day 4–6	Worsening hemodynamics, increasing inotropes and vasopressors requirements
Day 7	Impella 5.0 (Abiomed, Inc.) placement
Day 9	Revision of Impella 5.0 (Abiomed, Inc.) due to malfunctioning. Purge solution anticoagulation with Unfractionated Heparin initiated. Systemic anticoagulation: Unfractionated Heparin
Day 12	Thrombocytopenia. HIT panel positive
Day 13	Systemic and Impella purge solution switched to Argatroban
Day 14	Ongoing thrombocytopenia with increasing Impella motor pressures. Purge solution switched from Argatroban to Tissue Plasminogen Activator Alteplase. Systemic anticoagulation continued with Argatroban.
Day 15	Ongoing thrombocytopenia. Axillary Deep Venous Thrombosis. Disseminated Intravascular Coagulation panel is negative, purge solution switched back to Argatroban.
Day 16	Patient transferred to transplant center

Case presentation

This is a 69-year-old female with a past medical history of coronary artery disease post coronary artery bypass grafting 10 years ago, myocardial infarction four years ago requiring percutaneous coronary intervention with multiple stents placement, New York Heart Association functional class IV (stage D SCAI Classification) systolic heart failure on home milrinone, and ischemic cardiomyopathy with left ventricular ejection fraction 25% on most recent echocardiogram, as well as Type II diabetes mellitus, hyperlipidemia, obesity, and chronic kidney disease (Stage 3B), who initially presented with fatigue and worsening dyspnea on exertion. Relevant home medications included aspirin 81 mg daily, atorvastatin 80 mg nightly, carvedilol 25 mg every 12 h, Clopidogrel 75 mg daily, hydrochlorothiazide 25 mg daily, insulin Lantus 30 units daily, insulin (short-acting) 15 units three times a day before meals, spironolactone 25 mg daily, and torsemide 20 mg twice/day. The patient underwent treatment for a urinary tract infection five days before admission. On admission, the patient's blood pressure was 92/59 mm Hg, heart rate 70 b.p.m., respiratory rate 18 breaths/min, temperature 36°C, and oxygen saturation 93% on room air. Physical exam was significant for positive jugular venous distension, bibasilar crackles on auscultation, normal heart sounds without a murmur, rub or gallop, soft bowel sounds with a distended abdomen, and soft pitting edema +2 of lower extremities bilaterally. Initial laboratory values are shown in Supplementary material online, *Tables S1–7*. Moreover, her chest X-ray imaging showed pulmonary vascular congestion. Therefore, she was admitted for treatment of acute on chronic congestive heart failure, which acutely decompensated despite treatment with furosemide and chlorothiazide. The patient was transferred to cardiac critical care unit (CCU) for Swan Ganz catheter placement and monitoring. In the CCU, continuous veno-venous hemodialysis was started due to oliguria in the settings of acute kidney injury (Creatinine is 5.8, increased from 3.8 two days prior). She required initiation of Dobutamine, Furosemide, Milrinone, and Norepinephrine continuous infusions for hemodynamic support. Despite an increase in inotrope and vasopressors requirement, she remained persistently hypotensive to 84/52 with worsening lethargy. The blood gas mixed venous O_2 saturation at that time was 40%, warranting a decision to initiate mechanical circulatory support via an axillary Impella 5.0 (Abiomed, Inc.) Unfortunately, the Impella device required revision two days later due to a broken pin in the manifold (i.e. structural damage of the blood outlet component of the Impella catheter outlet, pumping blood out of the Impella device into the aorta). Subsequently, the pulmonary vascular congestion and hemodynamics improved, with a decrease in inotropes and vasopressor requirement. Laboratory values pre- and post-Impella placement are reported in Supplementary material online, *Table S7*. She was initially placed on UFH 25 units/mL in dextrose 5% purge solution post pVAD placement and systemic UFH anticoagulation.

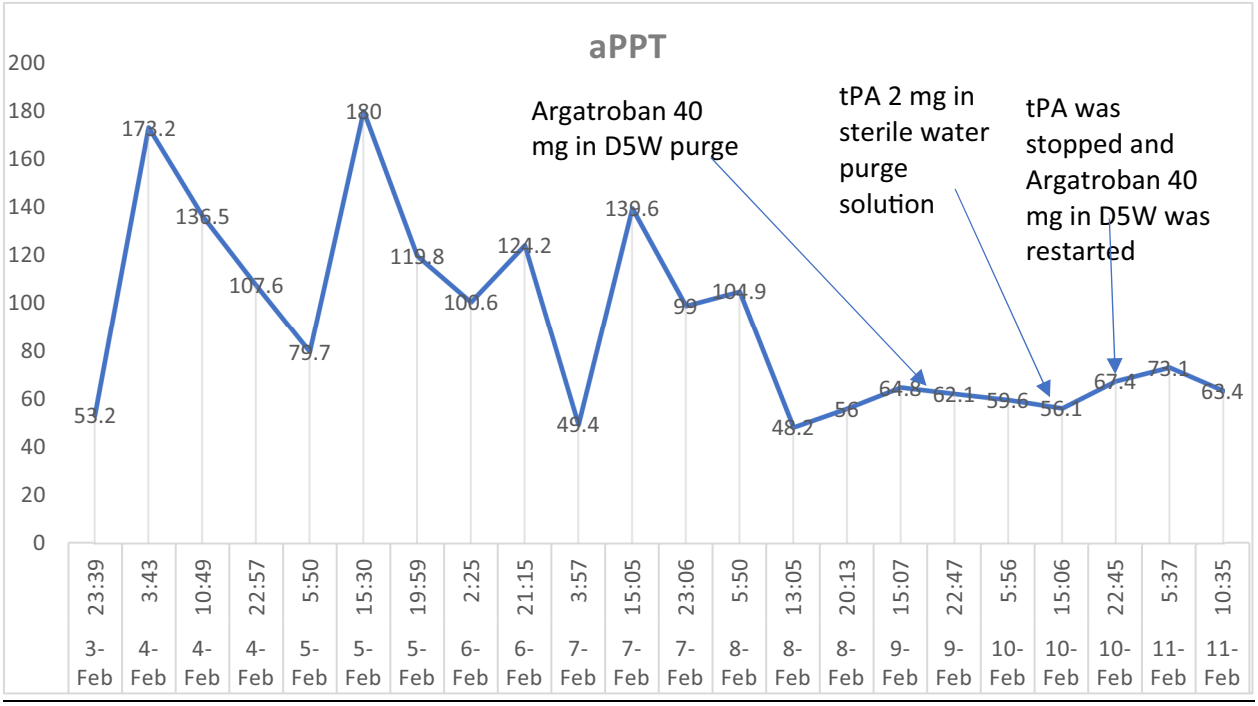
Of note, UFH was used for two days prior to Impella (Abiomed, Inc.) insertion as deep venous thrombosis (DVT) prophylaxis dose (5000 units every 8 h). She became febrile, pan culture was sent, and empiric

Table 1 Hemodynamic parameters pre- and post-tPA purge solution use

Hemodynamics	Pre-tPA	Post-tPA
Pulmonary Artery Pressure	53/18 mmHg	58/19 mmHg
Pulmonary Artery Pressure (mean)	30 mmHg	33 mmHg
Central Venous Pressure (mean)	5 mmHg	7 mmHg
Pulmonary Capillary Wedge Pressure	19 mmHg	14 mmHg
Venous Oxygen Saturation (SVO_2)	60%	61%
Cardiac Output (L/min)	5.7	6.5
Cardiac Index (L/min/m^2)	3.3	3.7
Systemic Vascular Resistance	1136	899
Peripheral Vascular Resistance	238	185

Abbreviations: tPA: tissue plasminogen activator Alteplase

Table 2 Activated partial thromboplastin clotting time trend before and after switching heparin purge to Argatroban and tissue plasminogen activator Alteplase



antibiotics, Vancomycin, and Meropenem were started. On day four following Impella 5.0 (Abiomed, Inc.) placement, the patient developed acute thrombocytopenia (platelet count dropped from 115 to 90 to 56) with a positive HIT panel (HIT Antibody-IgG 0.659). The decision was made to switch UFH to Argatroban for the purge anticoagulation of Impella 5.0 (Abiomed, Inc.). Systemic anticoagulation was changed to Argatroban as well. Due to the higher viscosity of Argatroban 60 mg in 5% dextrose water (D5W) in the purge fluid, motor pressures were escalating. After discussions with multiple specialists and a trial of Argatroban 40 mg in D5W, the decision was made to transiently use tPA as purge fluid to relieve the pressures (*Table 1*). Alteplase was used for 11 h with a 2–3 mL/h purge solution infusion. *Table 2* illustrates the trend of activated partial thromboplastin and clotting time before and after switching UFH 50 000 units in D5W to Argatroban 40 mg in D5W and tPA Alteplase afterward. Laboratory values before and after tPA use are reported in Supplementary material online, *Table S6*.

The patient developed right upper extremity swelling. A duplex was performed, which was positive for axillary DVT. Coagulation laboratory values were obtained and reported in Supplementary material online, *Table S7*. Purge anticoagulation was then switched back to Argatroban. Broad spectrum antibiotic coverage with Vancomycin and Meropenem was discontinued in light of possible contribution to thrombocytopenia, following the Infectious Disease Specialist's recommendations. Shortly after, she was transferred to an outside facility for a heart transplant evaluation. Ultimately, the patient underwent a successful heart transplant operation but lost to follow up with our health system.

Discussion

Our case of a 69-year-old female with a history of ischemic cardiomyopathy with reduced ejection fraction admitted for management of acute decompensated congestive heart failure, required placement of axillary Impella (Abiomed, Inc.). HIT complicated her hospital course, requiring the replacement of UFH systemic and purge anticoagulation with Argatroban. However, Impella purge pressures were increasing, and Alteplase was used in the purge solution with successfully restoring purge pressures.

Prevalence of HIT in critically ill patients is reported to range under 1%, while some studies have shown that the incidence of HIT in patients with acute cardiogenic shock under Impella 5.0 (Abiomed, Inc.) support is 10.7%.[4] Argatroban, a direct thrombin inhibitor, offers a therapeutic alternative for patients who developed HIT. Lewis *et al.* demonstrated the use of Argatroban therapy in significantly reducing the risk of new thrombosis and thrombosis-associated mortality without an increased risk of bleeding, compared to UFH discontinuation and/or oral anticoagulation.[5] Indeed, microaxial flow pumps are associated with an increased risk of major bleeding and vascular complications.[6] A meta-analysis of 17 studies with a total of 3933 cardiogenic shock patients requiring microaxial flow pumps reported vascular complications and major bleeding in 7.4% and 15.2% of patients, respectively.[6] Currently, UFH is the agent of choice in patients requiring pVAD support, while other alternatives include Bivalirudin or Argatroban.[6] In our case, the use of Argatroban was complicated by pVAD circuit clotting and increased motor pressure. In the setting of HIT as a contraindication for UFH and increased viscosity and circuit clotting with the use of Argatroban, the transient use of tPA has shown to be as effective with microaxial pumps. More importantly, serial activated partial thromboplastin clotting time (aPTT) monitoring is crucial in assessing the effectiveness of such an approach. One of the limitations of this study is the lack of recorded data on Anti-Factor Xa plasma-free hemoglobin or triglycerides since high levels can disturb the correct analysis of aPTT.[6]

Moreover, systemic anticoagulation might have affected the aPTT—levels during the initial period of Impella use. The data on using tPA is

scarce, and only a few case reports and one case series describe substituting standard purge fluid for a solution containing tPA resulting in the resolution of low purge flow in most cases. Tunney *et al.* reported successful use of tPA for 48 h[7] vs. 11 h in our case, and Succar *et al.* reported in a case series of five patients the use of Impella purge solution (0.04 or 0.08 mg/mL tPA in sterile water) for Impella pump thrombosis.[8] Based on this data, purge-delivered fibrinolytic therapy may be an option in selected patients if replacement of the Impella 5.0 (Abiomed, Inc.) is not feasible.[9]

Even though more data is warranted on the effectiveness and safety of tPA use as a purge solution, this case demonstrates that it can be utilized as a valid alternative in select cases.

Lead author biography

Dr. Elena Merino is a PGY2 Internal Medicine resident at Morristown Medical Center. She graduated from St. George's University School of Medicine in 2021. Aspiring cardiologist with special interest in cardiac critical care and adult congenital heart disease.

Supplementary material

Supplementary material is available at *European Heart Journal – Case Reports*.

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Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

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Data availability

The data underlying this article are available in the article and in its online supplementary material.

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