A Case of Heparin Resistance during AVR

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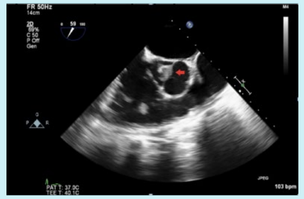
Introduction

Abstract

A 61-year-old male, ASA 4 inpatient presented for AVR due to aortic insufficiency caused by the presence of a vegetation on the AV. The vegetation was a result of bacteremia and sepsis. Intraoperatively, the patient required a total of **69,000 units of UFH** and **1,000 units of Antithrombin III** to achieve an ACT > 400 seconds to initiate cardiopulmonary bypass, demonstrating heparin resistance.



Kadado J, Grewal V, Feghali K, Hernandjez-Montfort J. (2018). *TEE 2-D image showing a large vegetation on the aortic valve.* ResearchGate. https://www.researchgate.net/figure/Fig-2-TEE-2-D-image-showing-a-large-vegetation-on-the-aortic-valve_fig2_325316436

Learning Objectives

- Understand the role of Heparin in cardiopulmonary bypass
- Discuss the definition, incidence, and causes of heparin resistance
- Outline the proposed treatment options for heparin resistance

Background

HEPARIN (UFH)

- MOA**:** inhibition of coagulation factors IIa (thrombin) and Xa via potentiation of Antithrombin III (AT3)
- Clinical use in CPB*:* prevention of thrombosis (goal ACT > 400 seconds)

HEPARIN RESISTANCE

- Definition: requiring a much greater than expected dose of Heparin to achieve a target ACT
- Incidence: 4-26% of patients
- Potential causes: AT3 or other coagulation factor deficiency, ***sepsis***, pregnancy, Nitroglycerin, extremes of age, high platelet count, preoperative administration of Heparin

Case Management

Preoperative Course

Preoperative TEE and cardiac catheterization revealed that the vegetation was causing severe dysfunction of the AV, resulting in aortic insufficiency, CHF with pulmonary edema, and paroxysmal atrial fibrillation with appropriate biventricular function. Proposed procedures included AVR, pulmonary vein isolation, and LAA clipping.
Upon arrival to the OR, induction of anesthesia, intubation, and line placement took place as normal. Baseline ABG and ACT were performed.

Anticoagulation Timeline

0728	Baseline **ACT 108s**
0743	Upon surgeon's request, **39,000 units UFH** (400 units/kg) administered
0751	**ACT 322s** **10,000 units UFH** administered
0800	**ACT 368s** **500 units AT3** and **10,000 units UFH** administered
0820	**ACT 393s** **500 units AT3** and **10,000 units UFH** administered
0835	**ACT 422s**
0844	Initiation of CPB

Postoperative Course

Cardiopulmonary bypass was terminated at 1106 and the patient was transported to CVICU intubated and sedated. He was extubated later the same day.

Discussion

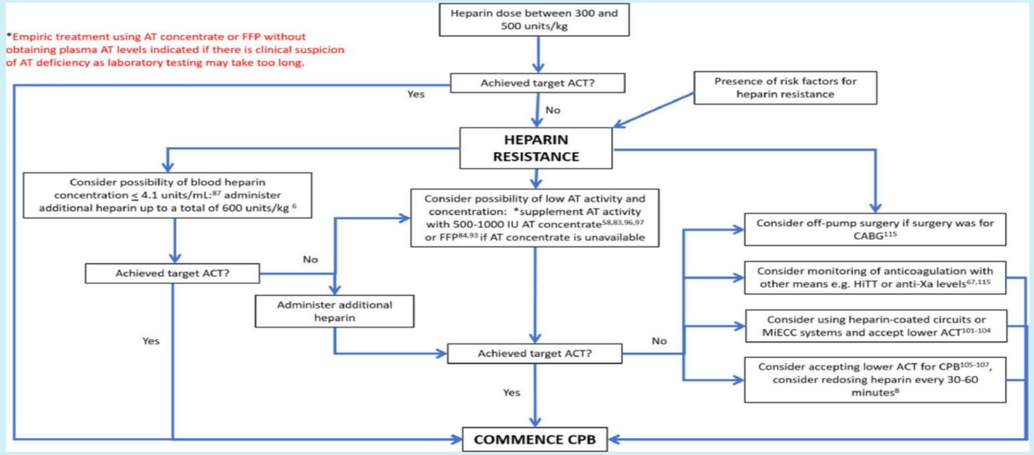
Sepsis and Heparin Resistance

Sepsis can cause acquired AT3 deficiency related to upregulated hemostasis and altered quantities of proteins in the body that bind UFH.

Excessive Heparin Administration

The most common first action taken when encountering heparin resistance is to administer more Heparin. However, it is generally recommended to avoid exceeding 600 units/kg of UFH due to risk of heparin rebound (reappearance of heparin in the blood after neutralization by protamine) and postoperative bleeding. There is also a recognized ceiling effect of Heparin, exerting limited additional effects on ACT at > 4.1 units/mL of Heparin in the blood.

Proposed Treatment of Heparin Resistance



Chen Y, Hui Yi Phoon P, Chih Hwang N. (2022). Fig 2 Algorithm for treatment of heparin resistance. Flow chart adapted from Finley and Greenberg.8 ACT, activated clotting time; AT, antithrombin; CABG, coronary bypass graft surgery; CPB, cardiopulmonary bypass; FFP, fresh frozen plasma; HiTT, high-dose thrombin time; MiECC, minimally invasive extracorporeal circulation. *Journal of Cardiothoracic and Vascular Anesthesia*. https://www.jcvaonline.com/article/S1053-0770(22)00463-3/fulltext

Important alternatives to administering more Heparin to consider:

- 500-1000 units of AT3 or 2-4 units of FFP (if no AT3 available)
- Choosing a different UFH lot number
- Final and potentially catastrophic option is to proceed with initiation of CPB despite subtherapeutic ACT

References

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