MEDS Clinical Medicine (2026)
Clausius Scientific Press, Canada

DOI: 10.23977/medsc.2026.070219
ISSN 2616-1907 Vol. 7 Num. 2

Massive Heparin Resistance During Cardiopulmonary Bypass for Left Atrial Myxoma Resection Complicated by Postoperative Coagulopathy

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Keywords: Heparin resistance; Left atrial myxoma; Cardiopulmonary bypass; Fresh frozen plasma; Video-assisted thoracoscopic surgery

Abstract: Heparin resistance during cardiac surgery is uncommon, and its occurrence in patients with left atrial myxoma is rare. The mechanism likely involves glycosaminoglycans released from myxomatous tissue competing with heparin for antithrombin III binding, combined with possible antithrombin III deficiency. We describe a 60-year-old woman who developed severe heparin resistance during video-assisted thoracoscopic resection of a left atrial myxoma. After standard unfractionated heparin dosing, her activated clotting time remained below 480 seconds despite a cumulative dose of 717 IU/kg. Rapid transfusion of 450 mL fresh frozen plasma achieved a therapeutic activated clotting time of 497 seconds, and cardiopulmonary bypass proceeded without complication. On postoperative day 1, she had transient coagulopathy with prolonged activated partial thromboplastin time and prothrombin time, low fibrinogen, and mildly reduced antithrombin III, but no clinical bleeding. These abnormalities resolved by postoperative day 2 without treatment. She was discharged on day 7 in stable condition. Anesthesia teams should anticipate heparin resistance in cardiac myxoma surgery and have blood products available before heparin administration. Fresh frozen plasma can serve as effective rescue therapy when heparin alone does not achieve therapeutic anticoagulation.

1. Introduction

Cardiac myxoma is the most common primary cardiac tumor in adults, accounting for approximately 50% of all benign cardiac neoplasms[1]. These tumors typically arise in the left atrium (75% of cases), with a predilection for the interatrial septum near the fossa ovalis[1,2]. Although histologically benign, cardiac myxomas carry serious clinical risk because of embolization, intracardiac obstruction, and constitutional symptoms[2,3]. Surgical resection under cardiopulmonary bypass (CPB) remains the definitive treatment and offers excellent long-term outcomes with recurrence rates below 5% for sporadic cases[1].

Heparin resistance during cardiac surgery is defined as failure to achieve a target activated

clotting time (ACT) greater than 480 seconds despite standard unfractionated heparin (UFH) dosing (typically 300 to 400 IU/kg)[4,5]. The overall incidence of heparin resistance in cardiac surgery ranges from 4% to 26%, but its occurrence during cardiac myxoma surgery is rare and poorly characterized[4,6]. The pathophysiology is multifactorial: myxomatous tissue is rich in glycosaminoglycans (GAGs), which competitively inhibit the heparin-antithrombin III (AT-III) complex, and chronic consumptive processes or hepatic dysfunction may cause AT-III deficiency[4,7].

Failure to achieve adequate anticoagulation before CPB risks serious thrombotic complications, including oxygenator clotting, cerebral embolism, and disseminated intravascular coagulation[5,8]. Management strategies include supplemental heparin dosing, AT-III concentrate, fresh frozen plasma (FFP) transfusion, and alternative anticoagulants such as bivalirudin or argatroban[9,10]. The best approach remains controversial, especially when blood products must be thawed urgently during a time-sensitive cardiac procedure.

Only one comparable case has been reported in the English literature: Houston et al. described a patient with massive atrial myxoma requiring 2400 IU/kg UFH and emergency CPB, in whom AT-III concentrate proved ineffective[11]. Our case represents the second documented instance of severe heparin resistance during cardiac myxoma surgery and the first successful use of FFP as rescue therapy in this setting. We also report a previously undescribed transient postoperative coagulopathy after massive heparin exposure, which resolved without intervention.

2. Case Presentation

A 60-year-old woman, weighing 61 kg with a height of 160 cm (BMI 23.8 kg/m²), was admitted with progressive chest tightness and exertional dyspnea of one month's duration. She was a retired school teacher, a lifelong non-smoker, and drank alcohol only occasionally. She denied any family history of cardiac disease, bleeding disorders, or thromboembolic events. Her past medical history included only an appendectomy performed more than 10 years ago under general anesthesia, from which she recovered uneventfully. She had no known drug allergies.

Her symptoms began four weeks before admission with vague chest discomfort and a non-productive cough. She first visited a local clinic where community-acquired pneumonia was diagnosed and empirical antibiotics were prescribed for 10 days. When her symptoms persisted and worsened, progressively limiting daily activities, she was referred to our hospital.

On admission, she was conscious, well-nourished, and in no acute distress. Vital signs were as follows: temperature 36.8° C, heart rate 80 beats per minute, respiratory rate 18 breaths per minute, blood pressure 110/64 mmHg, and peripheral oxygen saturation 98% on room air. Cardiovascular examination revealed a regular rhythm at 80 beats per minute with a low-pitched diastolic rumbling murmur (grade 2/6) best heard at the cardiac apex. There was no pericardial rub, gallop rhythm, or jugular venous distension. Respiratory examination showed bilateral symmetric chest movement with clear breath sounds and no adventitious sounds. The abdomen was soft and non-tender without organomegaly. Extremities showed no peripheral edema, cyanosis, clubbing, or signs of embolic phenomena. Neurological examination was grossly intact.

Preoperative laboratory tests revealed mild anemia with hemoglobin 86 g/L. Platelet count was 308 × 10^9/L. Coagulation studies showed prothrombin time (PT) 11.5 seconds, activated partial thromboplastin time (APTT) 28.4 seconds, international normalized ratio (INR) 1.0, and fibrinogen 3.2 g/L. Cardiac biomarkers were largely unremarkable (cardiac troponin I 0.01 ng/mL), though B-type natriuretic peptide was mildly elevated at 156 pg/mL. Thyroid function, renal function, liver enzymes, and electrolytes were all within normal limits.

Transthoracic echocardiography identified a large, mobile echogenic mass measuring

approximately 4.5 × 3.2 cm within the left atrium, attached to the interatrial septum at the fossa ovalis. The mass prolapsed through the mitral valve orifice during diastole, causing functional mitral stenosis with a mean transmitral pressure gradient of 12 mmHg. Color Doppler showed turbulent diastolic flow across the mitral valve. Contrast-enhanced chest computed tomography confirmed a left atrial filling defect consistent with myxoma and excluded pulmonary embolism or metastatic disease. The preoperative diagnoses were: (1) left atrial mass, suspected myxoma; (2) mitral valve orifice obstruction secondary to left atrial mass; (3) history of pulmonary infection; and (4) status post appendectomy. The prognosis was anticipated to be favorable given the benign histology of cardiac myxoma and the curative potential of complete surgical resection.

Surgical resection was performed via a video-assisted thoracoscopic approach[12]. The patient was positioned in left lateral decubitus with right chest elevation. Femoral arteriovenous cannulation was established for CPB. Anesthetic induction consisted of midazolam 4 mg, etomidate 2 mg, sufentanil 40 μg, and cisatracurium 12 mg. Anesthesia was maintained with sevoflurane 1% to 2%, propofol 2 to 5 mg/kg/h, and remifentanil 0.1 to 0.3 μg/kg/min. Invasive arterial blood pressure, central venous pressure, pulse oximetry, ACT, and transesophageal echocardiography were monitored throughout.

The critical intraoperative event occurred during heparinization for CPB. After baseline ACT measurement (177 seconds)[13], an initial prophylactic dose of UFH 1 mg/kg was administered for cannulation, followed by a full heparinization dose of 2 mg/kg. Despite these standard doses, the ACT remained below the target of 480 seconds. Incremental boluses of UFH were given sequentially: 60 mg, 20 mg, 30 mg, and 60 mg, bringing the cumulative total to approximately 350 mg (~717 IU/kg). At 25 minutes after initial heparinization, the ACT was still subtherapeutic. Severe heparin resistance was formally diagnosed, and the blood bank was urgently contacted for FFP. During the 10-minute thawing period, the patient developed transient hypotension requiring norepinephrine infusion. At 45 minutes post-heparinization, 450 mL of rapidly thawed FFP was transfused along with an additional 60 mg UFH, achieving a therapeutic ACT of 497 seconds. CPB was successfully initiated. The aortic cross-clamp time was 46 minutes, and total CPB time was 78 minutes.

Intraoperative findings included a friable, gelatinous, pedunculated mass measuring 4.5 × 3.2 × 2.8 cm attached to the interatrial septum. The mass was completely resected with a small margin of surrounding septal tissue. The mitral valve apparatus was preserved intact. Pathological examination confirmed cardiac myxoma. Heparin was reversed with protamine 200 mg, returning the ACT to baseline of 177 seconds.

The patient was transferred to the intensive care unit intubated and hemodynamically stable on low-dose norepinephrine. On postoperative day 1, she was successfully extubated. Laboratory evaluation at that time revealed unexpected coagulopathy: APTT 72 seconds, PT greater than 120 seconds, AT-III activity 70.4% (reference range 75% to 125%), D-dimer 12.4 mg/L, and fibrinogen 1.8 g/L. Despite these abnormal values, no active bleeding was observed from the chest drains or surgical sites, and no blood product transfusion was administered. On postoperative day 2, coagulation parameters had normalized spontaneously (APTT 35 seconds, PT 13.2 seconds, AT-III 82%, fibrinogen 3.5 g/L). The remainder of the postoperative course was unremarkable, and the patient was mobilized on postoperative day 4. She was discharged home on day 7 in stable condition with complete resolution of her preoperative symptoms.

At three-month outpatient follow-up, transthoracic echocardiography showed no residual intracardiac mass and normal mitral valve function. The patient reported complete recovery with return to all daily activities. At six-month telephone follow-up, she remained asymptomatic with no evidence of tumor recurrence, bleeding, or thrombotic complications. Annual echocardiographic surveillance was recommended for five years.

A timeline of the key clinical events is summarized in Table 1.

Table 1: Clinical timeline of the patient's course.

Time point	Event
Preoperative	Admission with chest tightness and dyspnea; echocardiography confirmed left atrial myxoma
Intraoperative	Standard UFH dosing failed to achieve therapeutic ACT; cumulative dose 717 IU/kg
Intraoperative (45 min post-heparinization)	450 mL FFP transfused; ACT reached 497 seconds; CPB initiated
Postoperative day 1	Extubated; coagulopathy observed (APTT 72 s, PT >120 s, fibrinogen 1.8 g/L); no bleeding
Postoperative day 2	Coagulation parameters normalized spontaneously without treatment
Postoperative day 4	Patient mobilized
Postoperative day 7	Discharged home in stable condition
Three-month follow-up	Echocardiography normal; patient asymptomatic
Six-month follow-up	Telephone follow-up; no recurrence or complications

3. Discussion

This report describes a rare case of severe heparin resistance during video-assisted thoracoscopic resection of a giant left atrial myxoma, successfully managed with FFP transfusion, and a previously unreported transient postoperative coagulopathy.

The mechanism of heparin resistance in cardiac myxoma surgery likely involves competitive inhibition of the heparin-AT-III complex by GAGs present in myxomatous tissue[4,7]. Cardiac myxomas produce mucopolysaccharide-rich extracellular matrix containing heparan sulfate and chondroitin sulfate, which share structural homology with heparin and can bind AT-III [1]. Chronic consumptive coagulopathy or subclinical hepatic dysfunction may also deplete AT-III levels[4,5]. In our patient, the postoperative AT-III level of 70.4% supports this hypothesis, although preoperative AT-III measurement was not obtained.

Management of heparin resistance in cardiac surgery remains debated. Current options include escalating UFH dosing, AT-III concentrate, FFP infusion, and direct thrombin inhibitors[8,9]. Houston et al. reported the only other comparable case: a patient with massive atrial myxoma required 2400 IU/kg UFH for emergency CPB, and AT-III concentrate failed to achieve therapeutic anticoagulation[11]. In our case, cumulative dosing of 717 IU/kg was insufficient, but FFP transfusion achieved a therapeutic ACT within minutes. This difference reflects the heterogeneity of heparin resistance presentations and suggests that FFP may be particularly effective when multifactorial deficiency underlies the resistance. FFP contains approximately 1 IU/mL of AT-III alongside other coagulation factors, potentially offering broader repletion than purified AT-III concentrate alone[5]. The time required for FFP thawing (approximately 10 minutes in our case)

remains a limitation in emergent scenarios, during which transient hemodynamic compromise may occur.

A novel observation in our case was the transient postoperative coagulopathy on postoperative day 1, characterized by markedly prolonged APTT and PT, mildly reduced AT-III, elevated D-dimer, and hypofibrinogenemia, without clinical bleeding. This pattern, which resolved spontaneously by postoperative day 2, has not been previously described after massive heparin exposure in myxoma surgery. We think this represents a rebound consumptive coagulopathy triggered by AT-III depletion and the resumption of endogenous coagulation factor production after heparin clearance[14]. The self-limiting nature of this disturbance suggests that expectant management without additional blood product transfusion may be appropriate in clinically stable patients.

The strengths of this report include detailed intraoperative documentation of heparin dosing and ACT responses, providing a clear pharmacodynamic profile of heparin resistance, and comprehensive postoperative coagulation monitoring that captured a previously undescribed phenomenon. The limitations include the absence of preoperative AT-III levels, lack of intraoperative anti-Xa or heparin concentration monitoring, and the inability to exclude all confounding factors for postoperative coagulopathy given its occurrence in a complex surgical context. Future cases should include preoperative AT-III assessment and systematic anti-Xa activity measurement.

4. Conclusions

Severe heparin resistance can complicate cardiac myxoma surgery even when tumor dimensions are moderate rather than massive. Anesthesiology and surgical teams should anticipate this possibility, ensure immediate availability of FFP or AT-III concentrate, and establish communication with the blood bank before heparin administration. FFP is an effective rescue therapy when conventional and supplemental heparin dosing fails to achieve CPB-ready anticoagulation. The transient postoperative coagulopathy we observed suggests that massive heparin exposure may induce a self-limiting consumptive coagulopathy in myxoma patients, warranting careful postoperative monitoring but not necessarily aggressive intervention. We recommend four practical measures for clinical teams: anticipate heparin resistance in left atrial myxoma surgery, prepare blood products before heparin administration, consider FFP when AT-III concentrate is unavailable, and monitor for transient postoperative coagulopathy after large heparin doses.

Declaration

This case report was prepared in accordance with the CARE guidelines.

Author Contributions: Conceptualization: KD; Writing - original draft: KD; Writing - review and editing: KD.

Institutional Review Board Statement: Ethical review and approval were waived for this study due to the retrospective nature of the case report.

Informed Consent Statement: Informed consent was obtained from the patient for publication of this case report.

Data Availability Statement: The data presented in this study are available within the article.

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