Case report

A Case of Antithrombin III Deficiency Diagnosed and Treated During Mitral Valve Replacement

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Abstract

Objective: To assess the risk of acquired antithrombin III (AT III) deficit before heart surgery and consider countermeasures.

Patient: A 50-year-old gentleman who suffered from congestive heart failure due to mitral valve regurgitation.

Methods: We replaced the mitral valve with cardiopulmonary bypass. Activated clotting time (ACT) was not long enough even after general heparinization (300 U/Kg) for cardiopulmonary bypass. We measured the activity of antithrombin III and added a total 50000 units of heparin until ACT was over 400 sec. We noted low AT III activity (36.8%) and transfused 4 U of fresh frozen plasma (FFP) during surgery.

Results: After administration of protamine (0.3 ml/Kg), ACT reached 137 sec. The hemostasis procedure was uneventful and the patient recovered well without a bleeding incident.

Conclusion: Measurement of AT III activity just before the initiation of cardiopulmonary bypass is necessary to avoid insufficient anticoagulation such as antithrombin III deficit.

Key words: antithrombin III deficit, cardiopulmonary bypass, surgery, heparin

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Introduction

Insufficient anticoagulation during heart surgery with cardiopulmonary bypass could result in a fatal complication such as myocardial infarction, and bleeding during and after surgery^{1,2)}. Antithrombin III (AT III) deficit is known to be one of the main reasons for insufficient anticoagulation in heart surgery²⁾.

We report a case diagnosed with antithrombin III (AT III) deficit during mitral valve replacement. The activated clotting time (ACT) is a good monitor of heparin. In our case, even after a sufficient dose of heparin infusion, ACT was not long enough (133 sec). Because of this, we measured AT III activity during surgery (36.8%), and

administered additional heparin and fresh frozen plasma (FFP).

Our patient recovered well and was discharged without any complications. We believe that AT III activity should be evaluated before initiation of cardiopulmonary bypass in heart surgery.

Patient and Methods

The patient, a 50 year-old Japanese male, visited the cardiology department of our hospital because of dyspnea on minor exercise. Examination revealed congestive heart failure due to mitral valve regurgitation and atrial fibrillation. A cardiologist prescribed warfarin to prevent stroke and diuretics for control of heart failure. After improvement of heart failure, the patient entered our hospital for mitral valve replacement and Maze's procedure. After admission, warfarin was changed to heparin until surgery (subcutaneous injection, target ACT 150 – 200 sec). The patient had no significant medical history or family history such as coagulopathy, liver disease, or denutrition. The results of his blood test including coagulation on admission are shown in Table 1 and were within the normal range except for the prothrombin time (he was taking warfarin).

After satisfactory induction of general anesthesia, 16,500

Table1 Laboratory data on admission

Parameter	Result	Normal range
White blood cells (WBC)	4300	3500–8500 (/μL)
Red blood cells (RBC)	454	430–570 × 10 ⁴ (/μL)
Platelet (Plt)	23.4	15.0–35.0 × 10 ⁴ (/μL)
Prothrombin time (PT)-INR*	1.98	
Activated partial thromboplastin time (APTT)	32.2	23.2–35.3 (sec)
Total protein (TP)	7.3	6.7–8.3 (g/dl)
Albumin	4.2	4.0–5.0 (g/dl)
Aspartate aminotransferase (AST)	24	13–33 (IU/l)
Alanine aminotransferase (ALT)	21	8–42 (IU/l)

* INR: international normalized ratio.

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Figure 1 Vertical axis indicates AT III activity (normal range; 80 – 130%). Horizontal axis indicates time from the start of operation. ACT; activated clotting time (sec). FFP: fresh frozen plasma.

unit (U) of heparin was infused and cannulation for cardiopulmonary bypass was undertaken (control ACT was 147 sec). On initiation of cardiopulmonary bypass, ACT dropped to 133 sec. We took a blood sample for ACT again and clamped the ascending aorta to stop the heart. ACT was still 123 sec, 2 min after clamp of the aorta. Immediately additional heparin (15,000 U) was infused and ACT rose to 305 sec. Infusion of heparin was repeated until ACT was over 400 sec. Mitral valve replacement and Maze's procedure were finished in 68 min. Weaning from cardiopulmonary bypass was uneventful and 16,000 U of protamine was given. AT III activity sampled just after the initiation of cardiopulmonary bypass was measured with the photometric method (commercial kit L-system AT III, Sysmex Ltd., Kobe, Japan) in the hospital laboratory and the activity was 36.8% (Figure 1). Four units of FFP were transfused in order to raise the low AT III (we ordered AT III administration, but there was no AT III agent in the operation room). ACT after the protamine infusion was 137 sec. We could stop bleeding without any difficulty. AT III activity measured after leaving the intensive care unit (ICU) had recovered to 67% and reached to 99% before the hospital discharge (Figure 1). The patient recovered well and had no trouble with coagulation such as bleeding or embolism. The patient was discharged 23 days after surgery (average duration of hospital admission for open heart surgery in Japan) with satisfactory control of warfarin.

Discussion

AT III deficit can be either hereditary or acquired²⁾. Most acquired AT III deficit cases are asymptomatic until cardiopulmonary bypass and most patients are more than 50 years-old²⁾. DeBois describes, in his review, that the incidence of acquired AT III deficit varies between 5–6% in heart

surgery²⁾. The precise mechanism is unclear, but heparin and nitroglycerin given before the surgery are known to be one of the risk factors of acquired AT III deficit. Our patient received low doses of heparin (target ACT, 150 – 200 sec) instead of warfarin after hospital admission. A case report of coronary artery bypass with cardiopulmonary bypass reported AT III deficit which was followed by fatal myocardial infarction¹⁾. When we checked the cardiopulmonary bypass circuit, we found a significant amount of thrombus in the circuit filter.

When ACT is not long enough, even after the first administration of heparin, additional heparin should be given until ACT exceeds 400 sec, and immediate blood sampling for AT III activity measurement is essential. Additional heparin administration should precede the repeat ACT measurement. An AT III agent (if an AT III agent is not available, FFP should be given as a substitute) should be administered once AT III activity is less than 70%, in order to minimize the risk of complications. Our experience with this case encouraged us to measure AT III activity just after the induction of anesthesia and use a routine anticoagulation sensitivity test to detect AT III deficit¹⁾.

In conclusion, we diagnosed and treated acquired AT III deficit during mitral valve replacement. Immediate additional heparin and measurement of AT III activity played a key role in the prevention of a fatal complication.

References

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