

Case Reports

Cardiopulmonary Bypass in a Patient with Factor XII Deficiency

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Abstract: The performance of cardiopulmonary bypass (CPB) in the factor XII-deficient patient is challenging in that the normal method for monitoring anticoagulation is ineffective as a result of an impaired contact activation system. We report the case of a factor XII-deficient patient who underwent surgical revascularization on CPB. His factor XII level was replenished with fresh-frozen plasma immediately before surgery. This management strategy lowered the baseline activated clotting time

(ACT) to near normal, providing a meaningful ACT value for CPB. Factor XII is also a key component in the fibrinolytic system and its deficiency is associated with increased thrombosis. Because the factor XII level quickly returns to baseline postoperatively, perioperative care must include strategies to avoid postoperative thromboembolic events. **Keywords:** cardiopulmonary bypass, factor XII, anticoagulation, fibrinolysis. *JECT. 2014;46:251–253*

Severe factor XII (Hageman factor) deficiency occurs rarely (one in 1,000,000 individuals) and is an autosomal-recessive disorder (1). A deficiency of this serine protease does not predispose the patient to an increased risk of bleeding but is associated with an increased partial thromboplastin time (PTT) and activated clotting time (ACT), because these tests require the activation of factor XII for accurate results. For this reason, monitoring the anticoagulation status of a patient undergoing cardiopulmonary bypass (CPB) is a challenge.

In addition, activated factor XII is an integral part of the fibrinolytic system, aiding in the conversion of plasminogen to plasmin and prekallikrein to kallikrein, both of which aid in fibrinolysis (2). The impaired fibrinolytic system puts the deficient patient at risk of thrombosis. It is therefore important to avoid the use of any antifibrinolytic agents intraoperatively and to closely monitor the patient postoperatively for any embolic events.

This report describes the case of a factor XII-deficient patient undergoing CPB for coronary artery disease. We

describe the strategy used for normalizing the factor XII level and the avoidance of any antifibrinolytic drugs to safeguard against any thrombotic events.

DESCRIPTION

A 66-year-old, 79-kg man with three-vessel coronary artery disease and no other cardiac risk factors presented for coronary artery bypass grafting. When taken to the operating room (OR), a sample for blood gas, electrolyte, and ACT analysis was drawn from the radial arterial line and run on an i-STAT analyzer (Abbott Point of Care Inc., Abbott Park, IL). Blood gas and electrolyte results were normal, but the ACT registered >800 seconds (normal 74–137 seconds). A second sample was obtained through the cordis of the Swan-Ganz catheter. The second ACT was run on a different analyzer and also measured >800 seconds. Preoperative prothrombin (PT) and PTT had not been ordered on this patient, as per protocol, but laboratory analysis now revealed a normal PT (14.8 seconds, normal 12.0–15.4 seconds) and an elevated PTT (>150 seconds, normal 23–38 seconds). A one-to-one mix of the patient's blood with donor plasma in the laboratory led to near normalization of the PTT (47 seconds). Prolongation of these clotting studies and uncertainty as to their etiology coupled with the inability to determine adequate

Received for publication May 28, 2014; accepted August 19, 2014.
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The senior author has stated that the authors have reported no material, financial, or other relationship with any healthcare-related business or other entity whose products or services are discussed in this paper.

anticoagulation on CPB led to a delay in the performance of the patient’s operation.

A subsequent hematological workup revealed that the patient had a factor XII deficiency (<5%, normal 50–200%) as measured by assay. A perioperative management strategy was developed and the patient’s surgical date was rescheduled for 2 weeks from the original surgical date. On the day of his operation, 2 hours before the patient’s entry into the OR, two units of fresh-frozen plasma (FFP) were transfused in an attempt to replenish the patient’s deficient factor XII level and obtain a meaningful ACT value for CPB. A PTT and factor XII level were determined following FFP administration (Table 1). Before heparinization, the ACT was 177 seconds. Epsilon-aminocaproic acid, a plasminogen inhibitor that suppresses fibrinolysis, was not administered as a result of the increased risk of coagulation and graft thrombosis. The CPB circuit consisted of a Sorin Apex membrane oxygenator (Sorin Group, Arvada, CO) and SMARxT coated tubing (Sorin Group). The heparin loading dose was 32,000 units (400 units/kg) of heparin with 5000 units added to the pump prime. The ACT before going on CPB was 848 seconds. CPB was initiated and a three-vessel coronary artery bypass performed under moderate hypothermic cardioplegic arrest. Cross-clamp time was 84 minutes with a total CPB time of 99 minutes. ACTs remained above 600 seconds throughout the procedure (Figure 1). No additional heparin was administered. On termination of bypass, protamine (320 mg) was administered for a one-to-one heparinization reversal, as per standard protocol. The subsequent ACT was 149 seconds.

The patient received two units of packed red blood cells postoperatively after dropping below our institution’s criteria for transfusion (hemoglobin <8.0 g/dL). His post-operative drug regimen included antiplatelet therapy with aspirin (81 mg orally daily). His recovery was uneventful and he was discharged home on postoperative day 4.

COMMENTS

The detection of the factor XII-deficient patient involves asymptomatic prolongation of laboratory tests that rely on the presence of contact factors, namely ACT

Table 1. PTT and factor XII levels in the factor XII-deficient patient.

	PTT (23–38 seconds)	Factor XII (50–200%)
Baseline	>150	<5
After FFP administration	37	19
Postprotamine	41	Not drawn
24 hours post-FFP administration	57	<5

PTT, partial thromboplastin time; FFP, fresh-frozen plasma.

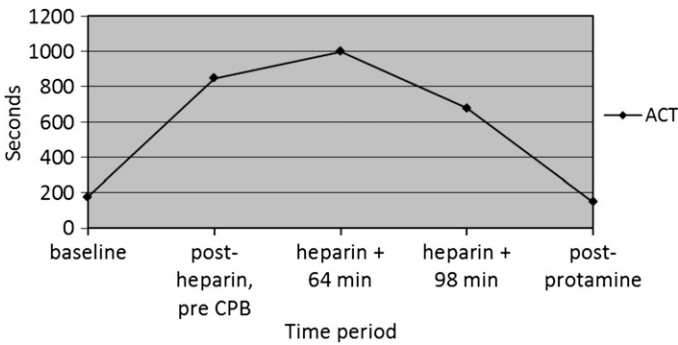


Figure 1. Activated clotting time (ACT) results after fresh-frozen plasma administration in a factor XII-deficient patient.

and PTT. A preoperative coagulation panel, including PT and PTT, may have been useful in this case, but are not routinely run at our institution because they rarely contribute any meaningful information. An ACT before bringing the patient to the OR would have indicated a clotting disorder, but the rarity of such an event precludes the necessity of a protocol change.

Performance of CPB in a factor XII-deficient patient is challenging in that traditional heparin monitoring is impaired. A review of the literature shows at least four management strategies have been used in such factor-deficient patients. One previous study proposed empiric heparin administration followed by a confirmatory rise in the ACT above a baseline level (3,4). With this strategy the ACT is of questionable value, because the baseline reading already indicates an anticoagulative state. Other authors recommend FFP administration, which will increase the *in vivo* levels of factor XII (1,2,5–7). The resultant ACT value is meaningful and can be used to monitor anticoagulation, although the patient is exposed to the inherent risks of allogeneic transfusions of FFP. These risks include acute lung injury, circulatory overload, allergic and/or anaphylactic reactions as well as other associated transfusion reactions (8). Another study recommended adding a calculated amount of donor FFP to the patient’s own blood sample before ACT testing (9). This is a time-consuming, patient-specific titration. In addition, variations between the patient and donor plasma protein and antithrombin III levels could affect the validity of the ACT determination. A final study recommended monitoring patient anti-Xa levels as an indication of anticoagulation (10). Although this approach limits the patient’s blood exposure, it is costly and labor-intensive. Turn-around time for assay performance makes this approach nonapplicable at this time.

We elected to transfuse the patient with two units of FFP immediately before surgery to restore factor XII levels and obtain a meaningful ACT for CPB. This is a simple and relatively safe method of replenishing the patient’s clotting factor, although it is not without risk, as

previously stated. The infusion did not result in complete normalization of factor XII levels, but raised levels enough to provide a normal PTT value and a reasonable baseline value for the ACT. Protamine administration brought the ACT back to a baseline level. The measurement of heparin concentration could have been a useful adjunct to the FFP administration, but the technology was unavailable at our institution. What has not been reported previously is the timing of the rise and fall in factor XII levels after FFP administration for a factor XII-deficient patient. As seen in Table 1, this increase in factor XII proved to be quite transient. The PTT began to rise 24 hours posttransfusion, and the factor XII level had returned to its baseline value at that time point. This is slightly sooner than expected with factor XII having a reported half-life of 40–50 hours.

The patient was also closely monitored postoperatively for any embolic events resulting from the impaired fibrinolytic system. The first reported patient with factor XII deficiency died of a pulmonary embolism after a fall (2). Graft thrombosis has also been reported after CPB in a factor XII-deficient patient who underwent coronary revascularization (3). We did not administer any antifibrinolytic drugs intraoperatively to our patient because of concern for increased thrombotic risk. We did use the typical venous thromboembolism avoidance techniques postoperatively, which included lower extremity compression devices and subcutaneous heparin administration, in addition to protecting the bypass grafts with antiplatelet therapy.

Anticoagulation monitoring in the factor XII-deficient patient who requires CPB can be challenging. The trans-

fusion of FFP provides a safe, quick, and effective means of factor replacement, enabling normal ACT measurements during the procedure. Healthcare providers should also be cognizant of the time course and decline in factor XII level after FFP administration in these patients.

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