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Recurring Extracorporeal Circuit Clotting During Continuous Renal Replacement Therapy Resolved after Single-Session Therapeutic Plasma Exchange

Tibor Fülöp, M.D.^{1,*}, Adrian Cosmin, M.D.¹, and Luis A. Juncos, M.D.^{1,2}

¹Department of Internal Medicine, Division of Nephrology; University of Mississippi Health Care and University of Mississippi Medical Center, Jackson, MS, United States of America

²Department of Physiology and Biophysics, University of Mississippi Medical Center, Jackson, MS, United States of America

Abstract

We report a case of a 17 year old white male with multiple fractures and multi-organ failure who developed oliguric acute renal failure requiring continuous renal replacement therapy. Repeated clotting of the extracorporeal circuit (ECC) prevented delivery of a minimally acceptable dose of renal replacement therapy despite adequate anticoagulation and dialysis catheter exchanges. Evaluation for a primary hypercoagulable state was negative, but his fibrinogen was elevated (1,320 mg/dL, normal range: 150–400 mg/dL), likely induced by his severe inflammatory state. A single session of therapeutic plasma exchange (TPE) with albumin and normal saline replacement was performed with subsequent drop in fibrinogen to 615 mg/dL. No further episodes of premature ECC clotting occurred, suggesting plasma factor(s) removed may have contributed to the clinical hypercoagulable state. TPE may play an adjunctive role in select cases of recurrent ECC clotting refractory to current anticoagulation techniques.

Keywords

anticoagulation; clotting; continuous renal replacement therapy; fibrinogen; therapeutic plasma exchange

Introduction

Most patients on continuous renal replacement therapy (CRRT) require anticoagulation to prevent clotting of the extracorporeal circuit (ECC). A wealth of methods for anticoagulation have been described, including unfractionated heparin, low molecular weight heparin[1], regional citrate anticoagulation[2] and argatroban,, among others. Activation of the coagulation cascade is most often attributed to either filter and vascular access problems or lack of sufficient anticoagulation. Patient-specific characteristics, such as acquired elevation of coagulation factors, are rarely considered in the differential.

Case Report

A 17 year old otherwise healthy white male was admitted to the Intensive Care Unit due to a motor vehicle accident with multiple fractures of femur, tibia and fibula. Following surgical

*Corresponding author: Tibor Fulop, M.D., Division of Nephrology, University of Mississippi Medical Center, 2500 North State Street, L 504; Jackson, Mississippi 39216-4505, USA, Tel. (601) 984-5670, Fax (601) 984-5765. tfulop@umc.edu.

repair he experienced an episode of massive emesis with aspiration, resulting in respiratory distress and hypoxemia, requiring intubation and positive pressure ventilation with high frequency oscillator ventilation. While his blood pressure stabilized and vasoactive agents were discontinued after fluids and broad spectrum antibiotics were instituted, he gained large amount of edemas and remained anuric. His creatinine rose rapidly from 0.8 mg/dL on admission to 3.5 mg/dL by the 3rd hospital day.

Nephrologists were consulted, and diagnosed oliguric acute kidney injury secondary to sepsis and ischemic-hypotensive injury. Continuous veno-venous hemofiltration (CVVH) with an AN69 filter and regional citrate anticoagulation (RCA) was initiated as follows:

- blood flow rate of 150 mL/minute,
- Anticoagulant Citrate Dextrose Solution-A (ACD-A) solution at 250 mL/hour for RCA,
- prefilter calcium-free replacement fluid (Prismasol) rate of 3000 mL/hour, and
- net ultrafiltration rate of 150 mL/hour.

Systemic ionized calcium concentration was normalized with simultaneous calcium infusion via central triple lumen catheter. He did well for 3 days, when repeated episodes of ECC clotting started, with the average filter life being approximately 3.5 hours (filter life varied between 1 hour and 6.5 hours). Escalating citrate infusion rate, adding low-dose heparin (500 Unit/hour) to the circuit and repeatedly exchanging the dialysis catheter failed to extend the filter life. Intermittent conventional hemodialysis using full dose heparin (1,000 Units/hour maintenance) also failed due to premature ECC clotting. Consequently, even the minimal acceptable doses of renal replacement therapy could not be delivered to this critically ill patient.

Extensive work-up for primary hypercoagulable state returned negative with normal homocysteine, IgG and IgM anticardiolipin antibodies, beta₂glycoprotein IgG and IgM, prothrombin G and M, total/free protein S and protein C. He had persistently low INR at 0.9, but his platelet counts and PTT remained within normal limits. We noted, however, that his fibrinogen was very high at 1,320 mg/dL (normal range: 150–400), likely induced by his severe inflammatory state.

After careful consideration of the difficult and unusual circumstances, a single-session total plasma exchange (TPE) was performed, during which we removed 4006 mL of “dark golden” plasma (1.1 times estimated plasma volume), and replaced 2 liters of 5% albumin and 1.75 liters of normal saline. This resulted in an acute drop in fibrinogen to 615 mg/dL, and we restarted continuous renal replacement therapy with identical AN69 filter and RCA anticoagulation. While the fibrinogen level slightly rebounded the next day to 827 mg/dL, no further episodes of premature ECC clotting occurred, suggesting that the elevated fibrinogen, or perhaps another plasma factor removed by TPE, was responsible for premature ECC clotting. He was discharged home on the 39th day hospital with normalized kidney function.

Discussion

Markedly elevated fibrinogen levels are associated with increased blood viscosity[3,4] and a tendency for pathologic clot formation[5]. Markedly elevated acute phase reactants, including fibrinogen, may represent a little explored cause of recurrent premature ECC clotting. Fibrinogen is depleted very effectively during plasma exchange procedures, along with multiple other coagulation factors[6,7]. Decreasing the circulating levels of these

factors with TPE may help to decrease the “hypercoagulable state”, reduce filter and ECC consumption, and improve efficiency of renal replacement therapy.

To effectively reduce fibrinogen level the replacement fluid should not deploy fresh frozen plasma but rather 5% albumin, with or without additional normal saline, to achieve a measured (40–50%) drop of fibrinogen level. We successfully tested this novel concept and identified elevated fibrinogen as one possible marker for an acquired procoagulant state. Selective fibrinogen removal systems may offer an additional option in the future[8,9]. Major limitations of this case are that we have not assessed plasma viscosity, von Willebrand factor activity, or markers of systemic inflammation (plasminogen activator inhibitor type-1, procalcitonine). However, AT-III deficiency was unlikely to explain our case: first, he also failed heparin-independent, citrate-based anticoagulation; and second, TPE would have been expected to further decrease AT-III activity [10]. Additional studies are needed to identify patient-specific characteristics leading to recurrent ECC clotting on CRRT, and to explore the adjunct role of TPE in these cases.

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