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Case Report

Diagnosis and Treatment of Disseminated Intravascular Coagulation: A Case Report

Rasoul Ferasatkish MD*, Hossein Naddafnia MD•**, Seyed-Mostafa Alavi MD*, Mohammad-Hassan Naseri MD***

Disseminated intravascular coagulation is a pathologic syndrome with different medical disorders. Diagnosis and treatment of this syndrome is one of the difficult managements in medical science. Thromboelastogram is the only guide for early diagnosis and precise management of this syndrome. We describe a patient who developed disseminated intravascular coagulation due to endocarditis and spleen abscess. She was diagnosed by thromboelastography and treated successfully.

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Introduction

Disseminated intravascular coagulation (DIC) is a pathologic syndrome characterized by laboratory evidence of consumptive and proteolytic degradation components.[1] The clinical expression varies and maybe manifested by laboratory abnormality alone or in combination with hemorrhagic and thrombotic complications.[2, 3] The major event in the pathogenesis of DIC is the unregulated and excessive generation of thrombin, and overexpansion of proteases, such as fibrinogen, factor 5, and factor 8.[4] Thrombin, binds to thrombin receptors on platelets and endothelial cells, and is a potent agonist that induces platelet activation and aggregation.[5] Thrombin also induces endothelial release of tissue plasminogen activator.[6,7] Plasmin is then proteolitically formed from plasminogen. This results in an aggressive secondary fibrinolysis. Therefore, the clinical and laboratory manifestations of DIC result from generation of these two proteases, thrombin, and plasmin.

Excessive thrombin generation with secondary fibrinolysis may result in increased consumption of hemostatic components and bleeding. The overexpression of thrombin with relatively reduced expression of plasmin may result in large vessel thrombosis or microvascular fibrin deposition leading to organ dysfunction and ischemic necrosis.[8] It is important to recognize DIC in this stage to prevent from developing the second stage of this syndrome.

The most frequent laboratory abnormalities reported are: elevated fibrin degredation products (FDP); prolonged prothrombin time (PT), partial thromboplastin time (PTT), and thrombin time; and low fibrinogen. Despite the presence of a significant secondary fibrinolysis, screening assay for increased fibrinolysis, such as the dilute whole-blood clot lysis test or euglobulin clot lysis test, usually give normal results in patients with DIC. Furthermore, the clinician should be aware that there can be false-positive results if these screening tests are performed in patients with fibrinogen level <100 mg/dL.[9]

Because of the various clinical manifestations

Authors' affiliations: Department of Cardiac Anesthesiology, *Rajaee Heart Hospital, Iran University of Medical Sciences, **Army University of Medical Sciences, ***Baghiyatallah University of Medical Sciences, Tehran, Iran.
•**Corresponding author and reprints:** Hossein Naddafnia MD, Department of Cardiac Anesthesiology, Army University of Medical Sciences, Tehran, Iran. Tel: +98-213-995-5630,
Cell phone: +98-912-207-4302,
E-mail: h_nadafnia@yahoo.com.
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and heterogeneity of primary disorders associated with the development of DIC, presence of new coagulation test for the diagnosis of this syndrome is necessary.

The thromboelastograph (TEG) is a noninvasive diagnostic apparatus designed to monitor and analyze the coagulation state of a blood sample in order to assist in the assessment of patient's clinical homeostasis conditions. Coagulation evaluations are commonly used to assess clinical conditions such as postoperative hemorrhage and/or thrombosis during and following cardiovascular surgery, organ transplantation, trauma, and cardiology procedures.[10, 11] The overall coagulation profile can be qualitatively or quantitatively interpreted in terms of the hypo-, normal, or hypercoagulable state of the sample.[12]

The only device that recognizes stages 1 and 2 of DIC is TEG. In stage 1 hypercoagulable state and secondary fibrinolysis can be seen because of thrombin burst. In such cases, depending on the clinical situation, hypercoagulability maybe treated with anticoagulant drugs. In this situation an antifibrinolytic drug is contraindicated because fibrinolytic activations prevent microvascular fibrin deposit. In DIC stage 2 (hypocoagulable state), treatment is very difficult and patients have severe bleeding.[13]

Case Report

We present a 31-year-old nonobese woman with body weight of 70 kg and height of 160 cm (BMI = 27) who was diagnosed as having prosthetic valve staphylococcal endocarditis. The patient had undergone mitral valve replacement surgery in 1995 with carbomedix number 29. She did not have diabetes mellitus or any other diseases in her history. She was scheduled for renewed mitral valve replacement and extraction of vegetations.

She had fever, shivering, myalgia, petechia, splinter hemorrhages, and Janeway lesion. She had mitral regurgitation (2^+) and several vegetation on the prosthetic mitral valve. Ten days after operation, she developed petechia in distal limbs, arthralgia, myalgia, fever, leukocytosis, and thrombocytosis (platelet count = 636000/mm^3). Her blood pressure was 110/70 mmHg.

Laboratory data showed: blood urea nitrogen = 23 mg/dL, creatinine = 1.9 mg/dL, hemoglobin = 13 g/dL, white cell count =13700/mm^3, PT = 27 sec, PTT = 51 sec, and INR = 4.27.

Abdominal ultrasonogrphy demonstrated spleen abscess, which could be due to endocarditis.
The patient had tachypnea, fever, and obtundation. She was transferred to the operating room for partial splenectomy. We performed a TEG analysis, which demonstrated secondary fibrinolysis and perhaps mixed primary and secondary fibrinolysis (Figure 1). We started tranexamic acid in the intensive care unit (ICU) as an antifibrinolytic drug with a bolus dose of 12 mg/kg intravenously slowly in 100mL of normal saline and continued it with 6 mg/kg/hr for six hours postoperation after partial splenectomy. She received cloxacillin, ciprofloxacin, and imipenem after operation because of positive blood culture due to infection with gram-negative bacillus. She also received crystaloid solutions during the treatment. She had several episodes of metabolic acidosis, which was treated.

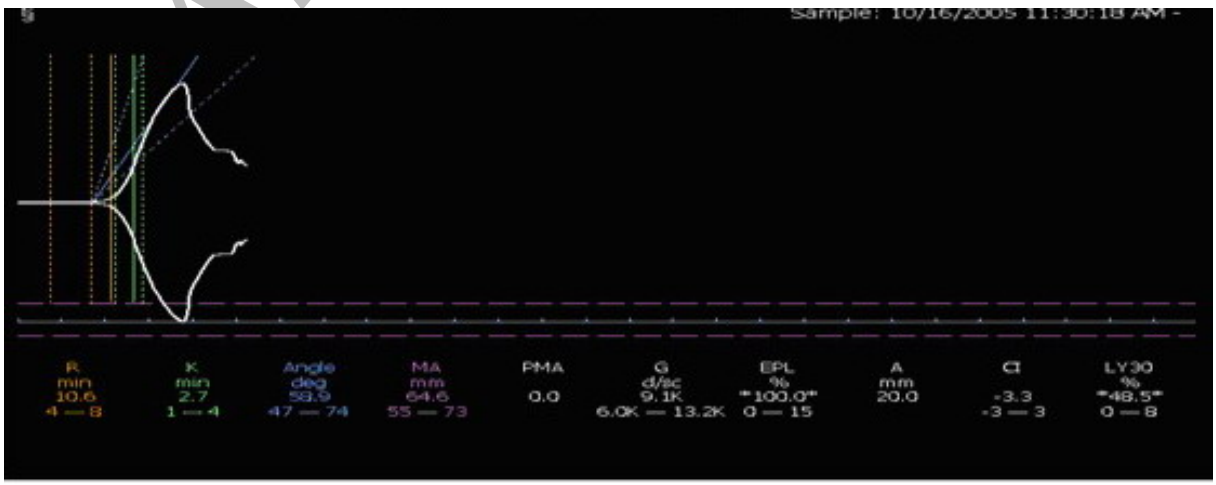

Figure 1. TEG profile in operative room.

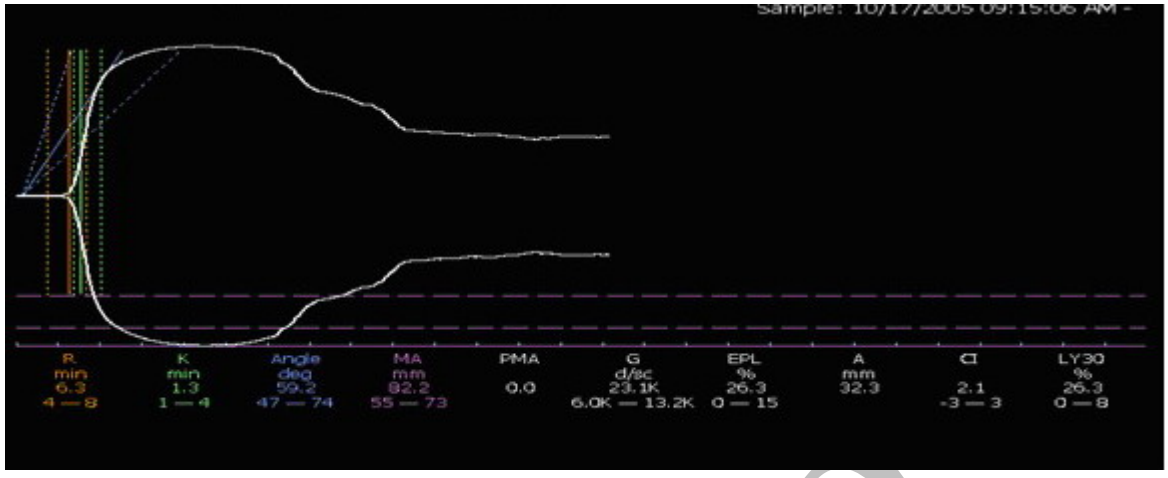

Figure 2. TEG profile after initiation of tranexamic acid.

She could not tolerate spontaneous ventilation and was dependent on the ventilator. Another TEG analysis demonstrated that fibrinolysis process had stopped but secondary fibrinolysis was showed in the TEG profile (Figure 2).

We prescribed 500 unit/hr heparin sulfate intravenously. Platelet count was 530,000/mm^3 and creatinine was 3.3 mg/dL. After heparin injection, creatinine level decreased to 0.8 mg/dL. After performing another TEG analysis that showed a hypercoagulable state without fibrinolysis, we increased the heparin dosage to 1000 units/h and prescribed aspirin (80 mg/day) (Figure 3).

After extubation, the patient developed cardiopulmonary arrest in the ICU because of massive bilateral empyema. She was resuscitated and the empyema was drained using a chest tube. She was scheduled for total splenectomy in the next day. We performed another TEG analysis, which showed normal profile (Figure 4).

She was extubated after operation in The ICU and after two days was discharged from the ICU, while her platelet count was 300,000/mm^3, PT was 17.4 sec, and PTT was 32 sec without any bleeding and other coagulopathy.

Discussion

DIC is a pathologic syndrome with variable expression. The main pathogenesis of DIC is the unregulated and excessive generation of thrombin that is a potent agonist inducing platelet activation and aggregation. Thrombin also induces the endothelial release of tissue plasminogen activators. DIC may be associated with hypercoagulability state, sepsis, and inflammation

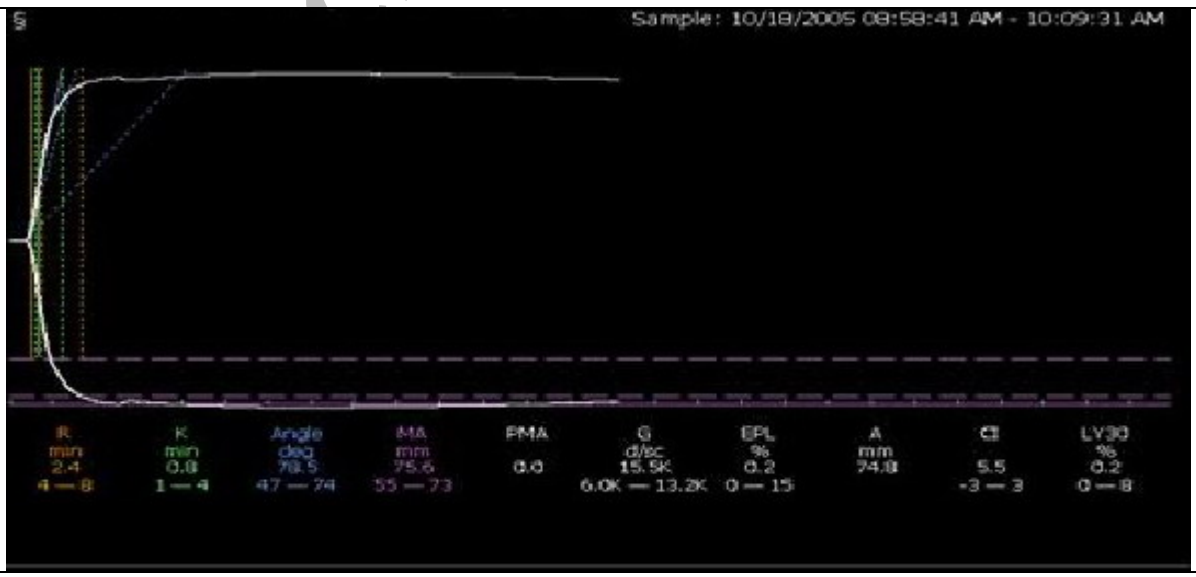

Figure 3. TEG profile before increasing the dosage of heparin and aspirin.

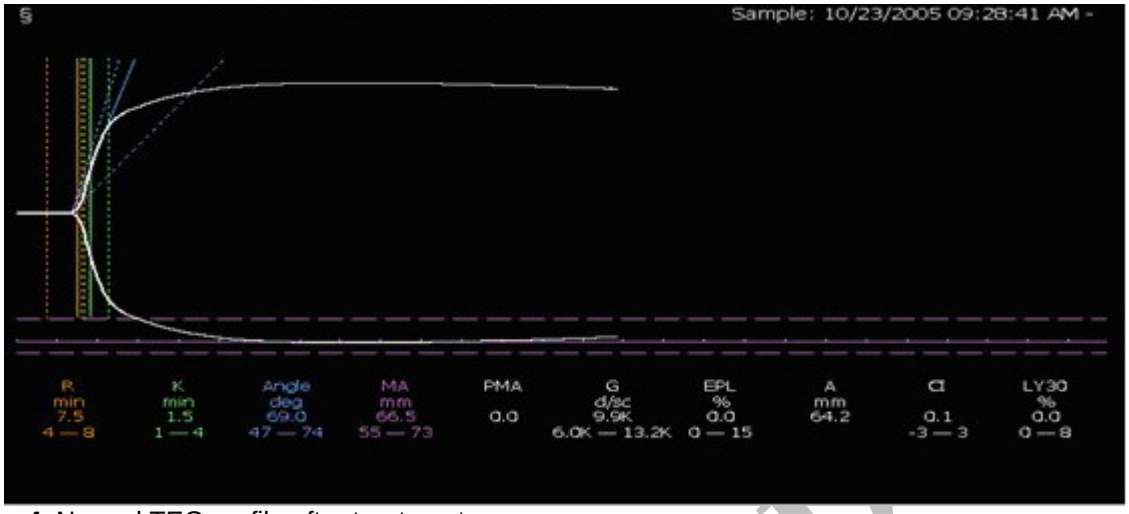

Figure 4. Normal TEG profile after treatment.

that are common in patients admitted to the ICU. The boundaries between the coagulation system and the inflammatory system are now less distinct than ever. It is known that activation of the contact system also activates the complement system.[13] Cytokines such as tumor necrosis factor activate both the inflammatory and coagulation systems and may serve as mediators of hypercoagulability.[13]

White blood cells contain a variety of powerful enzymes, some of which are strongly proteolytic and may enhance coagulation through their involvement with inflammation and infection.

The overexpression of thrombin with relatively reduced expression of plasmin may result in large vessel thrombosis or microvascular fibrin deposition leading to organ dysfunction and ischemic necrosis.[13]

Primary (early) fibrinolysis is a condition in which plasmin is produced without generation of thrombin. But in secondary fibrinolysis, plasmin is produced in the presence of thrombin and hypercoagulable state.

Thromboelastography can reflect the adequacy of whole blood coagulation within 20 to 30 minutes from the time that a small amount of whole blood (0.36 mL) is sampled from the patient. The principle and interpretation of TEG is well described in the literature.[14] The parameters of a TEG are interrelated and reflect activities of clotting factors and platelets, and their interaction.[15] Instead of monitoring an isolated portion of the coagulation cascade, as occurs with a standard laboratory coagulation profile, TEG monitors clot initiation and formation as well as its stability and strength. Therefore, it provides a better idea of the coagulability of whole blood.[16] The R (time to initial fibrin formation) on a TEG indicates clotting factor activity and correlates best with PT and activated PTT. The K (speed to reach clot strength), MA or Maximum Amplitude (dynamic properties of fibrin and platelet bonding, i.e., ultimate strength of the clot), and alpha angle (rapidity of fibrin build up and clot strengthening) indicate platelet and fibrinogen activity. The Lys30% and EPL (estimated percent of lysis) measure fibrinolytic activity and correspond to D-dimmer (cross-linked FDP).

The TEG monitors the thrombodynamic properties of blood as it is induced to clot under a low-shear environment resembling sluggish venous flow. The patterns of changes in sheer elasticity enable the determination of the kinetics of clot formation and growth as well as the strength and stability of the formed clot. The strength and stability of the clot to perform the work of hemostasis, while the kinetics determine the adequacy of quantitative factors for clot formation.[17] Therefore, thromboelastography measures all phases of hemostasis, from clot initiation to clot break down. It measures all states of patient's hemostasis as well; prothrombotic and/or hemorrhagic. This new assay also measures platelet function and platelet inhibition, which determines total platelet function and provides guidance in antiplatelet therapy and measures the effect of platelet-inhibiting drugs.[18]

Thromboelastography has improved our ability to distinguish surgical bleeding and bleeding due to specific deficits in coagulation. It has reduced the incidence of reoperation and has also reduced blood and fluid infusion volume.[19, 20, 21]

Despite the presence of a significant secondary fibrinolysis, other laboratory tests such as elevated FDP, prolonged PT and PTT, and screening assay for increased fibrinolysis such as dilute whole-blood clot lysis test or euglobulin clot lysis test are usually normal in patients with DIC.

The levels of D-dimmer are known to be elevated after major surgery and do not necessarily indicate a pathologic fibrinolytic process. Fibrinogen levels may be low due to either increased consumption or dilution. On the other hand, thromboelastography has been shown to be a more clinically reliable test of fibrinolysis compared with plasma concentration of D-dimmer.[22]

Our case had thrombocytosis. The TEG demonstrated the presence of secondary fibrinolysis and the a high percentage age of fibrinolysis (Lys30% = 48.5% and EPL = 100%) that cannot rule out primary fibrinolysis.

Primary fibrinolysis was stopped and tranexamic acid revealed secondary fibrinolysis.

Because primary and secondary fibrinolysis have distinct treatments and any mistake in the treatment can be fatal, thromboelastography in such situations can be the only measure to diagnose the stage 1 and stage 2 of DIC and can prevent the development of DIC stage 2.

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