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WORD COUNT 1955
TIME SUBMITTED 09-AUG-2021 03:44PM
PAPER ID 75353512

Name of Journal: *World Journal of Clinical Cases*
Manuscript NO: 62054
Manuscript Type: CASE REPORT

Intraoperative thromboelastography-guided transfusion in a patient with Factor XI deficiency: a case report

TEG-guided perioperative transfusion for FXI deficiency

Wenjuan Guo, Weiyun Chen, Xuerong Yu, Le Shen, Yuguang Huang

Abstract

BACKGROUND

Factor XI (FXI) deficiency, also known as hemophilia C, is a rare bleeding disorder with unpredictable severity that correlates poorly with FXI coagulation activity. This often poses great challenges for perioperative hemostatic managements. Thromboelastography (TEG) is a viscoelastic hemostatic assay of the whole blood for overall coagulation status assessment. Here we present the successful application of intraoperative TEG monitoring in a FXI deficiency patient for an individualized blood transfusion strategy.

CASE SUMMARY

A 21-year-old male patient with FXI deficiency was scheduled to undergo reconstruction surgery for macrodactyly of the left foot under general anesthesia. To minimize the bleeding risk, he was to receive fresh frozen plasma (FFP) as an empirical prophylactic FXI replacement at the dose of 15-20 mL/kg of body weight (900-1200 mL) before surgery. Subsequent FFP transfusion should be adjusted per surgical need. TEG assessment was used at the beginning and towards the end of his surgery. Normalization of coagulation function was achieved with only 800 mL FFP infusion according to intraoperative TEG results, and blood loss was minimal. Patient had an uneventful postoperative course and was discharged on postoperative day 8.

CONCLUSION

TEG can be readily applied in the intraoperative period to individualize transfusion need in patients with rare inherited coagulopathy.

Key Words: factor xi deficiency; thromboelastography; transfusion; intraoperative; coagulopathy; case report

Guo W, Chen W, Yu X, Shen L, Huang Y. Intraoperative thromboelastography-guided transfusion in a patient with Factor XI deficiency: a case report. *World J Clin Cases* 2021; In press

Core Tip: Factor XI (FXI) deficiency is a rare bleeding disorder with unpredictable severity that correlates poorly with FXI coagulation activity, which poses great challenges for perioperative hemostatic managements. Thromboelastography (TEG) is a viscoelastic hemostatic assay of the whole blood for overall coagulation status assessment which is readily available and provides real-time monitoring. This case highlights the importance of using TEG in the intraoperative period to individualize transfusion in patients with rare inherited coagulopathy in hope to minimize transfusion-related risks.

INTRODUCTION

Hemophilia C or FXI deficiency is a rare autosomal coagulation disorder [1]. Patients may be asymptomatic until hemodynamically challenged following traumas or surgeries. In other cases, their coagulopathies are discovered as incidental laboratory findings for other medical conditions. This unpredictability of bleeding patterns often poses perioperative challenges for clinicians [2]. TEG is used to monitor and analyze the viscoelastic properties of blood clot formation and lysis. It has the advantages of working with patient's whole blood, providing real-time quantitative results on global hemostasis assessments [3]. Its adaptability for point-of-care (POC) testing makes this test particularly useful for intraoperative blood transfusion guidance. Here we present a case, in which the patient was diagnosed with FXI deficiency during preoperative workup for macrodactyly reconstructive surgery. POC-TEG monitoring was successfully used to help assessing the transfusion need.

CASE PRESENTATION

Chief complaints

A 21-year-old man was scheduled to have reconstruction surgery for macrodactyly of the left foot under general anesthesia.

History of present illness

The patient presented with significant enlargement of his left foot since birth, complicated by recurrent episodes of paronychia. He was scheduled to have reconstructive surgery at a local hospital. However, the surgery was deferred due to unexpected perioperative discovery of abnormal coagulation studies.

History of past illness

The patient denied previous history of easy bleeding or bruising.

Personal and family history

None.

Physical examination

There was significant swelling of his left foot without erythema, rash, or discoloration. The bilateral lower extremity pulses were equal. The patient had a normal gait. Motor and sensations were intact.

Laboratory examinations

Preoperative laboratory workup showed increased activated plasma thromboplastin time (APTT) of 83.9s (reference: 23.3-32.5s), normal prothrombin time (PT) of 12s (reference: 10.4-12.6s) and internationalized normal ratio (INR) of 1.04 (reference 0.86-1.14). Further workup revealed the patient's FXI activity to be 3%. Mixing study (Table 1) showed patient's APTT could be corrected on mixing 1:1 with normal serum, indicating no FXI inhibitor.

Imaging examinations

None.

MULTIDISCIPLINARY EXPERT CONSULTATION

None.

FINAL DIAGNOSIS

Diagnosis of FXI deficiency was confirmed by a hematologist.

TREATMENT

Preoperative hematology consult suggested to empirically give fresh frozen plasma (FFP) as prophylactic FXI replacement at a dose of 15-20 mL/kg of body weight (patient weight 60kg, prophylactic dose 900-1200 mL FFP) before surgery. Subsequent FFP transfusion should be adjusted per surgical need. Oral tranexamic acid was suggested for a week postoperatively.

On day of surgery, patient received 400 mL FFP preoperatively. The first set of TEG (Figure 1A) right after FFP transfusion showed moderately increased activated clotting time (ACT), R time, K time, Max Amplitude (MA) and alpha angle. The operation was performed under general anesthesia and lasted about 4 h. Tourniquet was applied above the knee to minimize blood loss. Continuous nasal temperature monitoring was used to ensure of no intraoperative hypothermia. Patient received in total 2000 mL of Ringer lactated and 400 mL FFP intraoperatively. Urine output was 1400 mL, and blood loss was estimated to be about 300 mL. The second set of TEG (Figure 1B) towards the end of surgery showed improvements in all parameters.

OUTCOME AND FOLLOW-UP

Patient had an uneventful postoperative course (Figure 2). Oral tranexamic acid 0.5g three times per day was prescribed for a week. Surgical site drainage was 45 mL on postoperative day (POD) 1, then decreased to a minimal level. The drainage was removed on POD3. Patient received 400 mL FFP on POD 4 due to concerns of

prolonged APTT level (46.4s, reference: 23.3-32.5s) while surgical dressing remained dry and clean. He was discharged on POD 8.

DISCUSSION

Hemophilia C caused by a deficiency of FXI is a rare autosome inherited coagulopathy. FXI plays an important role not only in initiating clot formation but also in supporting its consolidation. Conventional coagulation tests like PT and APTT are less than satisfactory in the assessment of hemophilia C patients' clinical profiles and bleeding risks. These tests are limited for being end points assays that only test the speed of blood clot formation. However, they cannot reflect the process of further thrombin formation involved in clot consolidation and maintenance. Compared with hemophilia A and B, the clinical profile and bleeding management of hemophilia C is less clearly understood (Table 2). The relationship between bleeding phenotypes and baseline FXI level is poor, making perioperative bleeding risks hard to predict and manage [4].

TEG is a whole blood-based, viscoelastic hemostatic assay. It can be used as continuous assessment of the elastic properties of clot formation and lysis in both graphics and numbers. TEG measurements collected for analysis included reaction (R) time, coagulation (k) time, α angle, and maximum amplitude (MA), which are reflections of clotting factors, circulating inhibitory activity, fibrinogen and platelets level and function, etc [5]. TEG's short turnaround time makes it a promising measurement of global hemostasis in trauma or perioperative settings. It is considered to be better than conventional coagulation tests for monitoring coagulation profiles and predicting transfusion requirements [5]. It reduces the total amount of blood products transfused compared with an empiric transfusion policy or one guided by conventional coagulation tests [6]. Study results from trauma [7], liver transplant [8] and cardiac surgeries [9] have shown that the goal-directed allogeneic transfusion strategy is believed to provide better hemostatic competence. This is possibly due to more timely administration of blood products like plasma and platelet, which in turn, results in less blood loss [3], less blood transfused [10], lower cost and fewer potential adverse events [11]

in the TEG-guided transfusion group compared to the conventional group. One study also suggested that TEG-guided transfusion can substantially affect patient outcomes, including length of hospital stays, odds of reoperation, and short-term mortality [9]. For inherited coagulopathies like hemophilia A and B, a combination of standard coagulation laboratory tests and TEG tests result in better understanding of the hemostasis in an individual patient, giving insights into their long-term hemostatic management [12], as well as in more pressing situations like traumas or surgeries. In latter cases, studies from hemophilia A and B patients suggested that TEG could be successfully used in the perioperative settings to evaluate the efficacy of various hemostatic agents like factor VIII concentrate, cryoprecipitate, and prothrombin complex concentrates [3]. TEG has the potential to assess the role FXI plays in global hemostasis. However, its application in perioperative hemophilia C patients' transfusion management has not been extensively studied.

Normally, FXI deficiency patients will require a careful, individualized and multidisciplinary preprocedural planning. It starts from a meticulous assessment of patient's bleeding history and pattern. This is followed by thorough laboratory tests including basic coagulation function like PT, APTT, FXI level and mixing study. Moreover, the nature of the procedure scheduled should also be taken into consideration. Operations on sites with higher fibrinolytic activities like the pharynx and the urinary tracts put the patients at higher risks for bleeding [13]. The use of antifibrinolytic medication may help improving overall hemostasis [14]. For major procedures in individuals with severe FXI deficiency or significant bleeding phenotype, prophylactic replenishment using factor XI concentrates or FFP is recommended in the preoperative period [1]. Factor XI concentrate has been associated with a higher thrombotic risk compared with FFP [15]. Some suggested a "wait and watch" attitude towards factor replacement, only giving FXI concentrate when excessive bleeding occurs. Prophylactic FFP replacement is the most commonly available option in our institute. However, this comes with risk of volume overload. Because FXI levels do not correlate well with bleeding phenotypes, replacement therapy remains somewhat

empirical. Therapeutic plasma exchange (TPE) may lower the risk of circulatory volume overload [16]. Yet, this is a complicated procedure and other transfusion related adverse effects and the added costs should not be overlooked.

The patient we present here has no history of spontaneous bleeding, or any surgery done in the past. This made the perioperative bleeding risks hard to predict, and prophylactic transfusion management hard to plan. The consulting hematologists suggested a loading dose of 15-20 mL/Kg of body weight FFP to bring FXI level to satisfactory (FXI:C, 30–45%), inevitably resulting in large volumes of FFP needed. This is when TEG monitoring comes in handy. TEG-guided prophylactic FFP replacement may allow for more parsimonious use of replacement therapy in patients with severe FXI deficiency undergoing surgery. It can reduce the risks of volume overload, transfusion related acute lung injury, transmission of infectious diseases, thrombosis, allergic reactions and development of inhibitors to FXI [13]. In the case we present, our patient was to empirically receive a loading dose of 900-1200 mL FFP according to preoperative hematology consultation. In reality, based on the results from intraoperative TEG monitoring, our patient received 800 mL FFP in total before and during the whole procedure with minimal blood loss and an uneventful postoperative recovery. This experience is limited for being one case report. However, we believe with improved technology and accessibility of TEG, anesthesiologists and other medical care workers will be able to provide transfusion therapy tailored to each individual FXI deficiency patient's need.

CONCLUSION

FXI deficiency is an underrecognized disorder with a wide range of clinical presentations and poor correlation with coagulation studies. It poses great challenges for perioperative management. FXI concentrates, FFP, TPE and antifibrinolytic therapies are the mainstream treatment for FXI patients with surgical needs. POC-TEG could be readily applied in the perioperative period to individualize transfusion on a case-by-case basis, giving insights to the appropriate blood products administered in hope of

minimizing transfusion and the associated risks. Further large-scale study is needed to assess the potentials of using TEG for perioperative transfusion guidance in FXI patients.

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