

Case Report

# Platelet dysfunction and gross bleeding associated with uremia

Ugur Goktas<sup>a</sup>, Nureddin Yuzkat<sup>a,\*</sup>, Yasemin Isik<sup>b</sup>, M.Bilal Çegin<sup>a</sup>, Onur Palabiyik<sup>c</sup>, Ismail Kati<sup>d</sup>

<sup>a</sup>Department of Anesthesiology, Faculty of Medicine, Yuzuncu Yil University, Van, Turkey

<sup>b</sup>Departments of Anesthesiology, Faculty of Medicine, İzmir Katip Çelebi University, İzmir, Turkey

<sup>c</sup>Department of Anesthesiology and Intensive Care, Sakarya Educations and Research Hospital, Sakarya, Turkey

<sup>d</sup>Departments of Anesthesiology, Faculty of Medicine, Gazi University, Ankara, Turkey

**Abstract.** Patients with chronic kidney disease (CKD) are prone to bleeding due to the platelet dysfunction caused by uremia. Therefore, the mortality and morbidity in patients with chronic kidney disease increase.

The 81-year-old female patient, in dialysis dependent CKD, had an emergency cholecystitis operation with uremia-induced platelet dysfunction has evolved. Patient with gross bleeding intraoperatively had a cardiac arrest during operation. After cardiopulmonary resuscitation cardiac impulses were started and patient was taken into intensive care unit. After the administration of estrogen and Factor VIII Inhibitor Bypass Activity treatment for the bleeding diathesis, bleeding has reduced and after 6 days from the operation patient was externed to his service.

The chronic kidney disease may lead to hemorrhagic diathesis and unexpected abundant bleeding by creating a platelet dysfunction. Such being the case, the utilization of desmopressin and Factor VIII concentrate during the treatment is an efficient treatment option.

Key words: Bleeding diathesis, gross bleeding, platelet dysfunction, uremia

## 1. Introduction

Hemostasis in a healthy person occurs through the multifaceted interaction among the structural integrity of the blood vessel walls, the platelets in blood circulation and the coagulation factors in the plasma. Disruption in any phase of hemostasis results in the prolonged bleeding and non-clotting of blood in humans. This condition is defined as hemorrhagic diathesis (1,2). Patients with chronic kidney disease (CKD) are prone to bleeding due to the platelet dysfunction caused by uremia. Therefore, the mortality and morbidity in patients with CKD increase (2-4). In this presentation, a case with hemorrhagic diathesis progressing at the stage of CKD and coursing with abundant bleeding was scrutinized.

This study was presented as an poster presentation in 45<sup>th</sup> National Congress of the Turkish Anesthesiology and Reanimation Congress, 26-30 October 2011, Antalya, Turkey.

\*Corresponding Author: Nureddin Yuzkat MD.

Yuzuncu Yil University, Faculty of Medicine, Dursun Odabaş Medical Center, Department of Anesthesiology and Reanimation, Zeve Campus, Van, Turkey.

Phone: +90 5052294728

Fax: 00904322122651

E-mail: nyuzkat@gmail.com

Received: 02.05.2014

Accepted: 05.02.2015

## 2. Case report

The 81-year-old female patient suffering from CKD for two months and from coronary artery disease for two years visited the emergency-department because of nausea-vomiting and stomachache. During the physical examination of the patient, there was tenderness in the epigastric region and the right upper quadrant. The blood pressure was 102/58 mmHg, and the heart rate was 82 BPM. A cholecystectomy operation due to cholecystitis was planned to be performed on the patient. Patient's hematologic laboratory values were normal, except hemoglobin: 9,4 (g/dL) K: 2.9 (mmol/L), was taken into dialyzing without heparin before surgery. All the biochemical parameters are given in Table 1.

An abundant bleeding of 1500 mL within 30 min. occurred in the patient in whom liver injury progressed intraoperatively. Blood request along with the fluid resuscitation was made. Hypotension had developed and afterwards dopamine infusion was started. She had a cardiac arrest intraoperatively at the 70<sup>th</sup> minute because of ongoing bleeding.

The response to CPR was received two minutes after it was applied. The blood pressure values were monitored up at 90/50 mmHg and above. Upon the persistence of the leakages, 5 mg of vitamin K (Libavit K ampoule, Liba, Turkey) was

Table 1. The patient's laboratory values

Parameter	Reference Value	Preoperative	Intraoperative	Postoperative 1st day
Glucose	70-110 mg/dL	67	60	76
Hemoglobin	12-16 g/dL	9.4	3.7	8.4
Thrombocyte	(150-300).10 <sup>3</sup>	220.10 <sup>3</sup>	112. 10 <sup>3</sup>	72.10 <sup>3</sup>
PT	10.1 – 14.9 sec	12.7	64.5	16.7
INR	0.8 – 1.2	1.0	8.6	1.47
aPTT	23 – 35 sec	25.6	300>	66.1
DDimer	< 500 ng/mL		5.5	7.49
Fibrinogen	202 – 430 mg/dL		219	169
Creatinine	0.5 - 1.5 mg/dL	2.6	3.5	2.9
Urea	8 – 23 mg/dL	44	52	60
Na+	136 – 146 mmol/L	138	144	136
K+	3.5 – 5.1 mmol/L	2.9	3.2	4.6
Ca <sup>++</sup>	8.8 – 10.6 mg/dL	8.9	6.2	8.3
AST	0 – 35 U/L	32	169	52
ALT	0 – 34 U/L	16	11	4
Total Bilirubin	0.3 – 1.2 (mg/dL)	0.2		2.2

administered to the patient and the operation was completed at the 105<sup>th</sup> min. Then the patient was taken to the Anesthesia ICU (Intensive Care Units). As the appropriate blood could not be provided for the patient during the intraoperative period, a massive amount of blood transfusion was performed in the intensive care unit (3 units of new full blood, 1 unit of TDP). The intraoperative and postoperative laboratory values are shown in Table 1. Since there was 800 mL of hemorrhagic drainage from the surgery region within the postoperative 30 min., the patient was taken into operation for the second time for bleeding control in the 45<sup>th</sup> minute. The bleeding in the form of an intraoperative leakage was observed. After performing bleeding control, the patient was once again taken into the intensive care unit.

It was considered that there could be a platelet dysfunction in the patient whose leaky bleeding continued despite the fact that the number of thrombocytes in peripheral smear was found normal. The Factor VIII Inhibitor Bypass Activity (Feiba Tim® 500 flakon) and an estrogen replacement therapy were planned to be administered to the patient (2). Feiba Tim® was administered twice to the patient, so bleeding reduced and 150mL drained at the 24-hour. The patient whose dopamine support was given up on the 3rd postoperative day underwent hemodialysis on the postoperative 2nd, 4th and 6th days. The case who had no more hemorrhage and whose hemoglobin value indicated no change was discharged from the intensive unit care on

the 6th day and was taken to the general surgery clinic.

### 3. Results and Discussion

Hemorrhagic diathesis due to platelet dysfunction and coagulation defect is a major problem. The hemorrhage that cannot be brought under control is the major reason for the perioperative period and the intensive care mortality (5). In spite of the fact that the number of platelet is normal, it is primarily thought that there are platelet dysfunctions in the patient in the presence of the bleeding of the primary hemostasis defect (5). Our case was taken to preoperative dialysis, and the patient's post-dialysis urgent examinations were analyzed and she was taken into operation under urgent circumstances. For this reason, no desmopressin (DDAVP) was applied. Separately, in the case whose clotting tests were normal, the bleeding time, as it was not a routinely- requested inspection, was not taken into account.

In the course of the operation, a total amount of 1500 ml of abundant bleeding occurred due to liver laceration in the patient progressing in a stable way. Since no hemorrhage was expected of the patient who developed a hemorrhagic shock and a cardiac arrest due to this, no pre-operative preparation for blood was made and no transfusion could be performed in the event of the unexpected hemorrhage. Besides, although the coagulation tests returned to normal after postoperative transfusion was performed, the patient's leakages continued and the bleeding

diminished after the administration of Factor VIII concentration.

The patients with CKD cannot compensate the normal stress of the surgery, since with these patients, the association of the conditions increasing morbidity, such as diabetes, hypertension, myocardial dysfunction, coronary artery disease, and peripheral artery disease, is common. In addition, the utilization of blood products in CKD makes the patient prone to potassium rise under such conditions as muscle trauma, hemolysis, metabolic acidosis, and hematoma resorption; to infections due their immunosuppressive quality; and to hemorrhage due to platelet dysfunction caused by uremia. Depending on these factors, the mortality and morbidity in patients with CKD increase (2-4).

In patients with uremia, a platelet dysfunction manifesting itself along with the decrease in platelet aggregation and adhesion is observed. This condition causes an increase in the incidence of coagulopathy. The clotting cascade functions are normal but the thrombocyte plug that occurs in the course of the primary hemostasis is insufficient. Taking the uremic patient to dialysis increases the hemostasis function (4,6,7). The desmopressin infusion to these patients could be useful. In the case presented here, there was no history of anticoagulant drug utilization. Furthermore, the patient had been taken to the pre-operative dialysis without heparin and the coagulation tests had proved normal. However, the fact that she had intraoperative bleeding and the persistence of the postoperative leakages were evaluated as bleeding diathesis due to uremia. At every stage of the platelet functions in renal failure, there may be a pathology in the occurrence of adhesion, aggregation, secretion or pro-coagulant activity (8).

The basic screening tests intended to assess the tendency of hemorrhage in patients are the PT (prothrombin time), APTT (activated partial thromboplastin time), platelet count, and the bleeding time (BT) (3). The BT is a simple, cheap but a worthwhile test. It is the beneficial indicator of platelet adhesion and aggregation dysfunctions. Separately, the BT extends in cases like deficiency of vitamin C, vasculitic diseases, and in conditions where the hematocrit level is less than 25 % (7). Increasing the amount of hemoglobin partially improves the prolonged BT and hemostasis dysfunction. Nevertheless, the platelet dysfunction continues also after improving anemia (9).

Still surviving in the thrombosis pathogenesis, The Virchow's Triad comprises endothelial damage, stasis and hypercoagulability. The

chronic kidney patients may show potency to one or more elements of the Virchow Triad along with uremia and several environmental factors (10).

Our case was taken to pre-operative dialysis and her post-dialysis inspections were analyzed and she was taken into operation under urgent conditions. No DDAVP was performed for this reason. Additionally, in the case whose clotting tests were normal, the bleeding time, as it was not a routinely- requested inspection, was not taken into account.

In terms of the platelet dysfunction caused by uremia, performing DDAVP on the CKD patients undergoing dialysis prior to the surgical attempt may shorten the BT and the bleeding can be reduced during surgery even if the clotting tests are normal (6,7,11). Along with the treatment of the primary disease, intensive dialysis, 0.3 µg/kg of IV DDAVP and cryoprecipitate an hour before the surgical operation can be administered to the patients.

Conjugate estrogens can be applied as 0.6 mg/kg/day or for 5 days orally. The effects of the estrogen appear in 6 hours; however, the peak effect occurs in 5-7 days. It is required that the interaction between the blood vessels and platelet be enhanced by raising the hematocrit at least up to 30 %. To that end, platelet, erythrocyte and cryoprecipitate transfusions can be performed (8,9,12). Besides, it is suggested that the patients who had undergone dialysis with heparin should be awaited for at least 12 hours for the invasive surgical operation (13).

Consequently, the chronic kidney disease may lead to hemorrhagic diathesis and unexpected abundant bleeding by creating a platelet dysfunction. Such being the case, the utilization of desmopressin and Factor VIII concentrate during the treatment is an efficient treatment option.

## References

1. Aird WC. Vascular bed-specific thrombosis. *J Thromb Haemost* 2007; 5: 283-291.
2. Sadler JE. Von Willebrand factor, ADAMTS-13, and thrombotic thrombocytopenic purpura. *Blood* 2008; 112: 11-18.
3. Soykan LY. Kanamalı Hastaya Yaklaşım ve Transfüzyon. *Pediyatrik Aciller Sempozyumu*. İstanbul 2001; 131-144.
4. Reddy KR, Schiff ER. Complications in liver biopsy. In: Taylor G, editor. *Gastrointestinal emergencies*. 2 ed. Baltimore: Williams and Wilkins; 1997; 959-963.
5. Tekgündür E, Soysal T. Yoğun Bakımda Kanama Bozuklukları ve Tedavi. *Turkish Journal of Intensive Care Medicine* 2005; 3: 2.

6. Teke Z, Keskin A. Hematolojik Hastalıklarda Acil Cerrahi. Pamukkale Medical Journal 2008; 1: 73-81.
7. Ferhanoglu B, Başlar Z, Celkan T. Kanama ve Tromboza Eğilim Sempozyumu. No:36. In: Celkan T. Trombosit Fonksiyon Bozuklukları ve Vaskuler Nedenli Kanamalar 2003; 37-60.
8. Ferhanoglu B, Başlar Z, Celkan T. İç Hastalıklarında Aciller Sempozyumu. No: 29 Ferhanoglu B. Kanama Diatezli Hastaya Yaklaşım. 2002; 297-309.
9. Ar C. Edinsel Nedenli Koagülasyon Bozuklukları İÜ. Cerrahpaşa Tıp Fakültesi Sürekli Tıp Eğitimi Etkinlikleri 2003; 36: 87-92.
10. Kaptan K. Trombosit Fonksiyon Bozuklukları, Türk Hematoloji Derneği, Temel Hemostaz Tromboz Kursu.[http://www.thd.org.tr/thdData/userfiles/file/2007thtk\\_08.pdf](http://www.thd.org.tr/thdData/userfiles/file/2007thtk_08.pdf)
11. Tangün, Y, Koroglu, A. Kan Pıhtılaşması. <http://www.kanbilim.com/Trombofili.htm>. 2007.
12. Atamer T. Kanamaya Eğilimli Hastalarda Cerrahi Girişim Öncesi Hazırlıklar XXXVI. Ulusal Hematoloji Kongresi. Antalya 2010.
13. American Family Physician 2002; 66:1472.