Isolated Acquired FX Deficiency: A Case Report

Meltem AYLI*, Simten DAĞDAŞ*, Sevinç YILMAZ*

* Department of Hematology, Ankara Numune Hospital, Ankara, TURKEY

ABSTRACT

A female with no previous history of bleeding presented with active bleeding from multiple body sites, declining hemoglolobin levels, and markedly prolonged prothrombin times (PT), and activated partial thromboplastin times (APTT) with incomplete correction on PT mix assays. This patient showed a severe deficiency of factor X. FX levels and bleeding were refractory to multiple transfusions of fresh frozen plasma. Although plasmapheresis was started with concomitant intravenous immunoglobulin and steroid therapy, the patient died.

Key Words: FX deficiency, Acquired.

Turk J Haematol 2000;17(1):29-32.

Isolated FX deficiency is a hereditary or acquired condition. Acquired FX deficiency is generally observed in primary amyloidosis due to the irreversible binding of amyloid fibrils to FX[1,2]. Selective FX deficiency which causes reversible hemorrhagic diathesis has only been defined so far in some malignancies. The reported cases are as follows: 1 adrenocortical carcinoma case[3], 5 acute myelogenous leukemia cases[4], and 1 metastatic gastric adenocarcinoma case[5].

Selective and transient FX deficiency has been observed compared to FX deficiency accompanied by amyloidosis and malignancy. In the literature, only 11 cases have been reported. In the these cases, massive hematoma or ecchymosis, epistaxis, mucocutaneous hemorrhage, hemarthrosis, gross hematuria, and parapharyngeal or mediastinal hemorragia causing acute respiratory failure by obstructing the airway, and intrapulmonary hemorrhage have been detected. It should be noted, that in all these cases there is no history of hemorrhagic diathesis, hepatic and autoimmune diseases, and exposure to toxic substances[6-10].

There are some reports in the literature suggesting that acute viral infections or pneumonia are responsible as an etiological factor in transient acquired FX deficiency[11]. There is another case reported in which FX deficiency due to mycoplasma pneumonia normalised after treatment for pneumonia[12].

The pathogenesis of transient acquired FX deficiency has not yet been clearly explained. FX deficiency cannot be explained by a lack of production of FX because in these cases the level of the other coagulation factors (FII, FVII, FIX), also pro-

duced by the liver, are normal. In early reports, the existence of the inhibitor against FX were not mentioned[8,9], but, later on, two reports describe the existence of the inhibitor. It is shown by recent studies that the anti-FX antibodies cause FX deficiency. In these cases, sequential plasmapheresis, together with intravenous immunglobulin (IV Ig) and a steroid, has been found therapeutic[13].

CASE REPORT

A 58 year-old woman, complaining of gingival hemorrhaging for 4 weeks, in spite of no anamnesis of hemorrhagic diathesis, was admitted to our clinic in August 1998. The patient had not used any medication and was not exposed to toxic agents. The patient also informed us that she had no bleeding problems, either in the delivery of six children or in the 4 times she had had teeth extracted.

Upon physical examination, the skin and mucous membranes were pale, the oral cavity was not hygienic, and gingiva was hemorrhagic as oozing. She had extensive ecchymosis on her arms, legs, and the abdominal area.

In oscultation, the heart sounds were rhythmic, and tachycardic. S3 gallop was heard.

Organomegaly was not detected in the abdominal examination. Peripheral lymphadenopathy did not exist.

Laboratory findings are summarised in Table 1.

Serum protein electrophoresis and immunoelectrophoresis were normal. Proteinuria and microalbuminuria were not detected. Rectal and gingival biopsy for examining amyloidosis could not be performed because coagulation tests were never normalised. However, the laboratory findings did not support the existence of amyloidosis. The results of the coagulation test performed by combining the patient's plasma with normal plasma in a ratio of 1:1 are as follows: prothrombin time 33.6 sec. (N : 10-15sec), activated partial thromboplastin time 63.2 sec. (N : 25-45 sec.).

After infusing 6 units of fresh frozen plasma, the coagulation tests were performed and a PTT and PT were found as 86.4 sec. and 45.0 sec., respectively. While supporting the patient by infusing fresh frozen plasma and fresh whole blood, the patient started to complain of abdominal pain and distention on the 5th day. Ultrasonography results showed that a mass occupied the right quadrant of the abdomen. In a couple of days, abdominal distention progressed remarkably, so that the distention could be seen by the naked eye. By examining the CT, a retroperitoneal haematoma was found, which caused the displacement of the right kidney by occupying the right posterior pararenal area. At that time, the hemoglobin level decreased to 4.2 gr/dL from 10.5 gr/dL. Together with acute haemorrhage, acute renal failure occurred as a result of the rapid increase in urine and creatinine levels. It was planned to implement plasmapheresis and was started with 500 mg IV steroid. In addition, it was intended to apply IV immunoglobin, but the general condition of the patient became rapidly worse and the patient died.

DISCUSSION

Transient FX deficiency is a haemostasis defect causing a wide range of bleeding problems. This defect has not been clarified yet, although it was described in North Carolina University in 1956, and reported in 1959 for the first time.

It was suggested that the abnormal clearance of FX could play a role in physiopathology of this defect, but endogenously circulating inhibitors against FX have not been determined by the standard methods. However, the existence of circulating inhibitors was detected by Russel viper venom time (Ig G). FX inhibitors make viper venom time longer. Light chains of Ig G type antibody inhibate the activation of FX with TF/FVIIa, FIXa/FVIIIa, phospholipid complex or Russel viper venom by binding intact FX[8,9,13].

Although the existence of this acquired inhibitor has been demonstrated in recent literature, its etiology is not yet known. In the cases in which the existence of the inhibitor was demonstrated, any viral prodrome or upper respiratory disease has not been determined in contrast with the other coagulapathies.

Bleeding of various degrees of severity may occur in cases in which the patients have no hemorrhagic diathesis. In these cases, the severity

Table 1. Laboratory findings

Hemogram findings		Normal range
WBC	6.800 K/ML	4.600-10.200 K/ML
Neu	84.8%	37-80%
Lym	9.87%	10-50%
Mono	4.82%	0.0-12%
Eos	0.40%	0.0-7%
Rbc	2.16 M/µL	4.04-6.13 M/µL
Hgb	5.53 g/dL	12.2-18.1 g/dL
Hct	16.4%	37.7-53.7%
MCV	75.8 fl	80-95 fl
MCH	25.5%	27-31.2%
MCHC	33.7%	31.8-35.8%
RDW	24%	11.6-14.8%
PLT	385 K/µL	142-424 K/µL
Coagulation tests		
Prothrombin time	> 60 sec.	10-15
APTT	100 sec.	25-45
Fibrinogen	4.3 g/L	1.8-3.5
Factor II	78%	60-150%
Factor V	95.69%	70-140%
Factor VII	83.62%	70-150%
Factor VIII	150.03%	70-150%
Factor IX	91.6%	70-140%
Factor X	< 10%	70-120%
Protein C activity	82%	58-201%
Biochemical tests (Pathological)		
Glucose	144 mg/dL	75-115 mg/dL
Urea	38 mg/dL	11-37 mg/dL

of the bleeding is not correlated with FX deficiency. It is very difficult to treat hemorrhagic diathesis in these cases. Fresh frozen plasma, if it is used in conventional doses, reduces PT and normalises FX activity. However, in our case, active hemorrhagie could not be brought under control, and improvement in the results of coagulation tests performed by giving 15 u/kg/day, was not satisfactory.

Prothrombin complex concentrates (PCC) are given as replacements in cases of acquired deficiency. The improvement in PT and the increase in the FX level is observed by giving PCC. However, a case of multiple cerebral infarct, caused by higher coagulability due to PCC, was reported[6].

The last report, which includes two cases of acquired idiopathic FX deficiency with severe life threatening bleeding, suggests that using a steroid and IV Ig, together with plasmapheresis is an efficient and life saving treatment [13]. Plasma is

used as a replacement during plasmapheresis, but the risk of viral and bacterial transmission and allergy or anaphylaxis should be considered, due to the use of high volume plasma in this process.

We believe, that in these cases, steroid and IV Ig treatment should be immediately started, even when the initial symptoms are mild, because these cases may progress rapidly and become fatal, as in our case. Plasmapheresis should be immediately applied if hemostasis cannot be brought under control, even when infusing fresh frozen plasma in conventional doses, together with the two agents mentioned above. In our case, the patient came to our clinic for mild gingival hemorrhage and was died within 18 days. We accepted the patient as an idiopathic, isolated acquired FX deficiency case because she had no history of bleeding and we could not find any primary pathology which caused the FX deficiency.

There has been no standard, accepted treatment for such cases. However, we believe, that the treatment should be started immediately with plasmapheresis, IV Ig, and IV corticosteroids. This treatment is also supported by the literature, even if the number of cases is limited.

REFERENCES

1. Furie B, Voo L, Mc Adam KPWJ, et al. Mechanism of Factor X Deficiency in Systemic Amyloidosis. New York J Med 1981;304:827-30.
2. Griepp PR, Kyle RA, Bowie EJW. Factor X Deficiency in Amyloidosis. A Critical Review. Am J Hematol 1981;11:443-50.
3. Stefanini M, Wiggishoff CC. Stuart Factor (Factor X) Deficiency Associated with Renal and Adrenal Cortical Insufficiency. Ann Intern Med 1966;64:1285-91.
4. Caimi MT, Redaelli R, Cattaneo D, et al. Acquired Selective Factor X Deficiency in Acute Nonlymphocytic Leukemia. Am J Hematol 1991;36:65-6.
5. Korte W, Flury R. Acquired Factor X Deficiency and Disseminated Intravascular Coagulation in a Case of Metastasising Carcinoma of the Stomach and its Course under Chemotherapy. Am J Med 1992;87: 583-5.
6. Henson K, Files JC, Morrison FS. Transient Acquired Factor X Deficiency: Report of the Use of Activated Clotting Concentrate to Control a Life Threatening Hemorrhage. Am J Med 1989;87:583-5.
7. Mulhare PE, Tracy PB, Golden EA, et al. A Case of Acquired Factor X Deficiency with in Vivo and in Vitro Evidence of Inhibitor Activity Directed Against Factor X. Coag. Transfus Med 1991;96:196-200.
8. Lunkiewicz MW, Bell WR. A Unique Circulating Inhibitor with Specificity for Coagulation Factor X. Am J Med 1992;93:343-6.
9. Rao LVM, Zivelin A, Hurbe I, et al. Antibody Induced Acute Factor X Deficiency: Clinical Manifestations and Properties of the Antibody Thromb. Haemost 1994;72:363-71.
10. Bayer WL, Borek D, Chondramohan M, et al. Acquired Idiopathic Factor X Deficiency. Blood 1982;60 (Suppl):207.
11. Currie MS, Stein AM, Rustagi PK, et al. Transient Acquired Factor X Deficiency Associated with Pneumonia. NY State J Med 1984;84:572-3.
12. Peuscher FW, Van Aken WG, Van Maurih JA, et al. Acquire, Transient Factor X (Stuart Factor) Deficiency in a Patient with Mycoplasma Pneumonial Infection. Scand. J Haemotol 1979;23:257-64.
13. Smith SV, Liles DK, White GC, et al. Successful Treatment of Transient Acquired Factor X Deficiency by Plasmapheresis with Concomitant Intravenous Immunoglobulin and Steroid Therapy. Am J Hematol 1998;57:245-52.

Address for Corrospondence:

Meltem AYLI, MD

Department of Hematology,

Ankara Numune Hospital, Ankara, TURKEY