

Original Article

Surgical treatment for a paraplegic patient induced by congenital factor X deficiency

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Received June 17, 2015; Accepted August 5, 2015; Epub August 15, 2015; Published August 30, 2015

Abstract: Congenital factor X (FX) deficiency is a rare disease which usually leads to coagulation disorders. We reported a case of paraplegic patient induced by traumatic spinal epidural hematoma which was associated with congenital FX deficiency. The treatments of this patient included elevating FX activity (FX: C) by adding fresh-frozen plasma (FFP) or prothrombin complex concentration (PCC) to improve his coagulation function, and doing operation to remove his spinal hematoma. Symptoms started to resolve after operation. Besides, we found one of his elder brother had the same disease as the patient himself via family follow-up. They can survive because their FX: C are relatively high enough to keep them away from fatal bleeding.

Keywords: Congenital factor X deficiency, spinal epidural hematoma

Introduction

Spinal epidural hematoma (SEH) is an uncommon disease firstly described in the 17th century [1]. Risk factors for SHE include using anticoagulant drugs, coagulopathy such as hemophilia A, B, spinal hemangiomas, trauma, vascular malformation, surgery or other percutaneous interventions to thoracolumbar areas [1-3]. Congenital factor X (FX) deficiency is a rare disease which has an incidence of 1:1,000,000 to 1:2,000,000 [4, 5]. FX is also named Stuart Prower factor because people recognized this factor in them [6, 7]. Surgery in patients with coagulation disorders was contraindication before people had found the first coagulation factor (Factor VIII) in 1936. The unmanageable bleeding is life-threatening for the patients.

Case report

A 48 year-old male was sent to our department (Peking University people's hospital, trauma system) for paralysis of the lower limbs after 1 week of his injury. He presented hypoesthesia of both his lateral feet, paresis of his both legs, urination and defecation function disturbance four days after his lumbar sprain. He was sent to local hospital and received MRI of thoracolumbar, which revealed space occupying lesion

of T10-L1 (**Figures 1-3**) considering epidural hematoma. Then he got catheterization and was sent to our department.

Physical examination showed vital signs were as normal, no subcutaneous hemorrhage. The flexion and extension activity of his lumbar were limited. There were tenderness and percussion pain besides the spinal processes of T10-L1. There was paresthesia of lateral sides of both feet. The motor power of both extension and flexion of digit 1 was grade 4/5. The feeling of perineum and crissum was reduced.

After tests of blood, his blood routine examination (including WBC, RBC, platelets and so on), liver function and renal function were normal. But his coagulation test showed that PT, APTT, INR prolonged (see the **Table 1**) which could be corrected by normal plasma. The tests of the activity of all coagulation factors of him, including factor II, V, VII, VIII, IX, X, XI, and XII showed the FX activity (FX: C) was only 2.4%. And the activities of other factors were normal.

With the advice of hematology department, the coagulation function of the patients' brother and sisters was tested. It showed the elder brother of the patient had almost the same results as the patient himself. His other three sisters' results were normal. Besides, the

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Figure 1. Preoperative lumbar MRI (sagittal plane, t2 imaging) showing a hematoma in the spinal canal at the T10-L1 level.



Figure 2. Preoperative lumbar MRI (sagittal plane, t1 imaging) showing a hematoma in the spinal canal at the T10-L1 level.

screening of the patient's autoantibodies, including IgA, IgG, IgM, lupus antibodies,

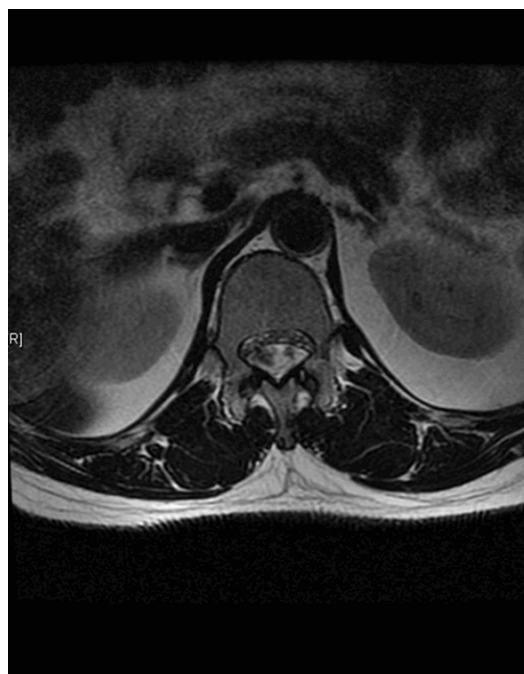


Figure 3. Preoperative lumbar MRI (axial plane, t2 imaging) showing a hematoma at the posterior surface of spinal cord.

M-protein, rheumatic factors were normal. Above all, the diagnoses of the patients were congenital FX deficiency, spinal epidural hematoma. It was necessary to do operation to remove the hematoma for the patient to decompress his spinal cord. However, doing operation in patients with coagulation function deficiency is challengeable.

Preoperative managements: The patient received 1000U (nearly 15 U/kg) prothrombin complex concentration (PCC) and then received testing of his coagulation function which showed PT and APTT had been corrected. Considering the risk of thrombus of using PCC, fresh-frozen plasma (FFP) 15 ml/(kg·d) was recommended. And the coagulation of the patient was normal in the help of FFP too.

On the operational day, his preoperative prescription included FFP 15 ml/kg, testing of FX: C which showed 70%, testing of coagulation function which showed normal, preparation of 400 ml RBC and another 800 ml plasma for his surgery. When we cut the skin of the patient's back, we found that his bleeding was more easily than other patients without coagulation disorders, even the test of his coagulation function showed normal. Thrombin, cellulose gel and gauze compression were used to control

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Table 1. The first test of the patient's coagulation function

	results	units	Reference range
PT	47.3	Hs	9.4-12.5
INR	4.17	H	0.9-1.2
APTT	72.5	Hs	25.4-38.4
Fibrinogen	302	mg/dL	200-400

Table 2. Some common reasons for acquired FX deficiency

Some common reasons for acquired FX deficiency
Liver disease
Vitamin K deficiency
Amyloidosis
Myeloma
Tumors
Infections
Drugs

the bleeding of the incision. After the partial laminectomy at T10-T12, an old puce hematoma was seen. Massive dark fluid drained when the hematoma was cut open and was evacuated at last.

Postoperatively, he received FFP 15 ml/(kg·d) or PCC 15 U/(kg·d) in the first week and coagulation function monitoring every day or alternate day. From the 8th day to the 14th day, after stitches were taken out, the patient received PCC 5-10 U/(kg·d). Successfully, on the second day after operation, his symptoms had much released. He could urinate automatically two days after surgery. And there were no any complications of his surgery. One month later, he told us that he had almost recovered unless paresthesia of his left foot sometimes.

Discussion

SEH is a relatively rare disease. It is blood collection in the epidural spaces that results in compression of spinal cord. Symptoms of SEH are broad. Neurological examination can be normal, or back pain, paresis or paraplegia [3, 8]. Most of SEH including the case we reported, is seen at posterior surface of the spinal cord because of the anatomical course of the venous plexus [9]. And we believe it's the congenital FX deficient that mainly leads to the patient's SEH.

FX plays a key role in keeping the balance of coagulation. FX is the first factor on the "com-

mon pathway" of coagulation cascades. It can be activated to FXa on the intrinsic pathway by FIXa and its cofactor FVIIIa. On the extrinsic pathway, it can be activated by FVIIa. And then, FXa with FVa, calcium ions and phospholipids complex will activate prothrombin to thrombin. Besides, FXa has interaction with FVII and FVIII. So FX deficiency can block both extrinsic and intrinsic coagulation pathway, and course different degrees bleeding events which depended on the level of FX: C.

Like the other vitamin dependent coagulation factors (factors II, VII, IX), FX is synthesized in the liver. The circulating concentration of FX is 10 µg/ml [10]. The human FX gene is located on autosome (13q34) [11]. And congenital FX deficiency is an autosomal recessive inherited disorder.

The classification of FX deficiency includes acquired and congenital FX deficiency. The acquired one is more common than the congenital one. But both of them are rare. The usual reason is vitamin K deficiency. The patients of this type will also be lack of other VK-dependent factors. They may be diagnosed and cured easily by adding VK. Another common disease in clinics is FX deficiency following amyloidosis. It's reported nearly 14% incidence [12]. In this type, it may not be useful to add FFP or PCC for therapy because of rapid removal of FX from circulation in these patients [13]. And there are reports showing recombinant human factor VIIa may be helpful for these patients [14, 15]. Here we present some other common reasons for acquired FX deficiency in the **Table 2** [5].

Congenital FX deficiency can be divided into type one and type two. The former means the patients lack both the antigen of FX and FX: C. The other one means lacking of FX: C but the antigen of FX is normal [16]. There is another classification of congenital FX deficiency. It can be divided into three groups according to FX: C. For the severe group, the FX: C is less than 1%, which usually die from fatal bleeding in fetal period, neonatal period or childhood. For the moderate group, the FX: C is 1-5%. The case we reported belongs to this group. For the mild group, the FX: C is 5-10%. The optimum level of FX: C for hemostasis is 10% [17]. It's rare for people whose FX: C is more than 20% to suffer bleeding. Like hemophilia, the less the activity

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is, the severer bleeding will occur. The patient with congenital FX deficiency may suffer bleeding automatically or develop bleeding under mild injury from childhood. The signs and symptoms of FX deficiency differ from epistaxis to intracranial bleeding like the patient we cured.

Prolonged APTT and PT and low FX: C are the characteristics of FX deficiency. Besides, we indeed have to consider acquired FX deficiency for differential diagnosis. For the case we reported, examinations of all his coagulation factors, his autoantibodies and M-protein are necessary. All of them really indicate that his disease is congenital FX deficiency. Besides, evaluating the blood coagulation function of the patients' immediate families is useful. It helps us to diagnose the disease and to take care of the patient and his families, if his families have the same disease.

Replacement therapy is the most important way to treat congenital FX deficiency. But there is no pure FX available because of the rarity of FX deficiency. FFP and PCC are the most widely used drugs. FFP has all of coagulation factors. And it's cheaper than the later one. But FFP is collected from other human. The patient who has been receiving it for a long time may generate antibodies to FFP because of its antigenicity, which is fatal for the patient. PCC has a higher concentration of FX and it also contains factor II, VII, IX. It's really a strong material to enhance coagulation. But it has a higher incidence of thromboembolic episode and disseminated intravascular coagulation (DIC) too. So monitoring the coagulation function of patients is not only useful to evaluate the effects of treatments, but also helpful to find side effects timely. It may help to reduce the incidence of thrombus events. Karable *et al* recommended that heparin-added PCC can be used safely for effective prophylaxis [18].

Doing spinal canal surgery on patients with severe congenital FX deficiency is a challengeable job for orthopedics. As far as we know, only a small number of cases with congenital FX deficiency who need operations have been reported. After all, with the help of hematology department, we have succeeded in doing operation for this patient who was diagnosed as epidural hematoma. We concluded replacement therapy with FFP and PCC was very useful for these patients. And it's safe to use them with

the concentration we used unless he has anti-FX or other diseases like amyloidosis. But we should consider its side effects. Enough preparation with FFP or PPC and preoperative examination were necessary for this surgery. Besides, shortening the length of incision and operational time, adequate drainage and dressing with appropriate pressure were key points to prevent the wound complications.

Acknowledgements

This study was funded by Chinese National Ministry of Science and Technology 973 Project (No. 2014CB542201) and 863 project (No. SS2015AA020501), The ministry of education innovation team (IRT1201), the National Natural Science Fund (31371210, 31271284, 31171150), the Educational Ministry New Century Excellent Talents Support Project (No. BMU20110270).

Disclosure of conflict of interest

None.

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