Trauma as a risk factor for thrombosis in children: A report of three cases

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Thromboembolism is described as a multifactorial disorder including both congenital and acquired risk factors in children. Among these, trauma has been suggested as a possible risk factor for development of thrombosis.

In this study, we reviewed the data of 158 children with thrombosis. Trauma was the major risk factor for thrombosis in three children. Cerebral infarction and cerebral venous thrombosis were detected in two patients, and thrombosis of the inferior vena cava and left renal vein in the third. In addition, the factor V Leiden mutation was demonstrated in two trauma patients with thrombosis.

Thromboembolism in children is a multifactorial disorder in which both genetic and acquired risk factors play a role. In the first year of life, thrombosis usually occurs either in association with in-dwelling catheters or as renal vein thrombosis. In older children, catheterization remains one of the most frequent risk factors for development of thrombosis. Additionally, surgery, malignancy, infections, autoimmune disorders, homocystinuria and trauma have been described as the other contributory risk factors[1-4]. Although trauma has been shown to be one of the major risk factors for thrombosis in the adult population, only a few publications exist in children[5-8]. The factor V Leiden (FVL) mutation is the most widely recognized cause of hereditary thrombophilia[9-11].

In this study, we reviewed the data of 158 children with thrombosis with special emphasis on trauma and associated thrombophilic risk factors (protein C, protein S, antithrombin, factor VII, D-dimer antiphospholipid antibodies, homocysteine level, FVL mutation). Here, we describe three trauma patients with thrombosis, two of whom also had the FVL mutation as the underlying factor.

Case Reports

Case 1

A six-year-old boy presented with the complaints of paresis of lower extremities and enuresis, three weeks after he had fallen down from a tree about two meters in height. There was no family history of thrombosis. Physical examination was normal except for left hemiparesis. No fracture of the cranium was observed either on the plain films or cranial computerized tomography (CT). However, cranial CT and magnetic resonance imaging (MRI) were compatible with the infarction in the right centrum semiovale and edema in the right frontoparietal lobe. No hereditary thrombophilic factor was detected (Table I). Anticoagulation with unfractionated heparin was started. Within one week his clinical findings improved. He was then followed in the out patient clinic with cranial MRI, which demonstrated total resolution of the lesion within one year. Thirty months later, he was well with no sequelae, only receiving medication for hyperactivity attention deficit disorders.

Case 2

A 1.5-year-old boy presented with paresis in his right arm. His past history revealed a fall from his bed resulting in a loss of consiousness for about 12 hours. Paresis in his right arm later developed. He was the product of a consanguineous marriage. There was no family history of thrombosis. Cranial MRI revealed

the presence of thrombosis of dural sinus and deep cerebral veins, as well as hemorrhagic infarction in the bilateral thalamus, left caudate nucleus, and left occipital lobe, with collateral venous dilatations superior to these lesions. In addition to head trauma, homozygous FVL mutation and increased level of factor VIII were detected as the risk factors for thrombosis (Table I). Following anticoagulant therapy, he was completely recovered within 10 days. Two years after trauma, he was doing well without any sequelae.

Case 3

A one-year-old girl was referred to our hospital after a traffic accident. On admission, she had tachycardia (pulse rate:180/min) and tachypnea (breath rate: 52/min). She had bilateral large ecchymosis extending from the inguinal region to her buttocks. There was no family history of thrombophilia.

Laboratory data revealed hemoglobin level of 11.6 g/dl, hematocrit 35%, white blood cell count 21,500/mm^3, and platelets 290,000/mm^3. Urinalysis showed presence of microscopic hematuria. Plain radiography of pelvis was compatible with the fracture in her left iliac crest. In the abdominal ultrasonography (USG) enlargement of the left kidney was detected. Doppler USG demonstrated thrombosis of the left renal vein and inferior vena cava. Following admission, thrombolytic therapy was instituted with tissue plasminogen activator. About 12 hours later, thrombolytic therapy was stopped because of bleeding, and she was treated with unfractionated heparin. Blood biochemistry worsened over the next 24 hours with signs of prerenal/renal insufficiency. Heterozygosity for FVL mutation and positive D-dimer test were demonstrated (Table I). The left kidney atrophy developed within one month. On follow-up she was doing well with no clinical signs.

Clinical and laboratory data of these three children are summarized in Table I.

Discussion

Table I. Some Clinical and Laboratory Data of the Patients

	Patient 1	Patient 2	Patient 3
Age in years, gender	6y, M	1.5y, M	1y, F
Site of thrombosis	Cerebral infarction	Cerebral infarction, cerebral vein thrombosis	Left renal vein, IVC
PC (%)	124	84	146
PS (%)	105	144	89.4
AT (%)	123	29.2**	118
FVIII (%)	>200#	>200#	ND
D-dimer	negative	negative	positive
APA	negative	ND	negative
Homocysteine	ND	ND	8.9
FVL	absent	homozygous	heterozygous
Outcome	healthy	healthy	atrophy of the left kidney

* None of the cases possessed PT G20210A mutation.
** Antigen level of antithrombin was measured.
# Level of Factor VIII was high.

PC : Protein C.
AT : Antithrombin.
APA : Antiphospholipid antibodies.
IVC : Inferior vena cava.
PS : Protein S.
FVIII : Factor VIII.
FVL : Factor V Leiden mutation.
ND : not determined.

Previous studies have indicated that trauma may increase the risk of hypercoagulability due to stasis, vessel wall dysfunction and alteration in the clotting mechanism[5-7]. In addition, immobilization following head injury or long bone fractures may also contribute to the development of thrombosis[5-7]. Therefore, the trauma patient with multisystem injuries usually manifests an increased risk for thrombosis[5]. It has been shown that trauma was the causative agent in 10% of children with venous thrombosis[1]. In this study, we reviewed the records of 158 children with thrombosis under 17 years of age, and only three (1.9%) cases of thrombosis following trauma were documented. Homozygous FVL mutation was detected in one of two patients with cerebral thrombosis. Heterozygous FVL mutation was

found in the patient with thrombosis in the inferior vena cava and left renal vein following a traffic accident. Although the frequency of FVL mutation seemed to be significant in children with trauma who had thrombosis, the number of patients in this study is too small to draw a conclusion.

The activation of coagulation factors is well known in patients following head trauma[5]. In the present report, activation of the coagulation system might have played a role in the development of thrombosis in the two patients with head trauma. In our previous publication, FVL mutation increased the risk of thrombosis with additional factors, and was found in 32% of children with thrombosis[4]. FVL mutation is the most common abnormality, with a prevalence of 7% in Turkey[14]. Trauma associated with FVL mutation might have played a role in development of thrombosis in at least two patients in this report.

In conclusion, our data indicate that trauma associated with the FVL mutation in children may contribute to the development of thrombosis. We suggest screening for FVL mutation in children or adolescents with thrombosis following head trauma or multisystem injuries, especially in countries with a high frequency of FVL mutation. If necessary, antithrombotic prophylaxis should be started in this patient population.

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