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CASE REPORT

Deep vein thrombosis in a child with Down syndrome: A case report

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ABSTRACT

We report on the case of iliofemoral popliteal vein thrombosis in a child with Down syndrome who had surgery for a congenital heart defect. She was readmitted to our hospital because of gastroenteritis and generalized tonic-clonic seizures at age 14 months. On the second day of hospitalization, color Doppler ultrasonography revealed right iliofemoral and popliteal vein thrombosis. She was treated successfully with intravenous fluids and low-molecular-weight heparin. No predisposing factor other than dehydration could be found in the patient. We suggest that dehydration should be kept in mind as a cause of deep-vein thrombosis in patients with severe dehydration.

Key Words: Deep vein thrombosis, Down syndrome

ÖZET

Down sendromlu bir çocukta derin ven trombozu: Olgu sunumu

Burada iliofemoral ve popliteal trombozu olan, daha önce konjenital kalp defekti nedeniyle ameliyat edilmiş Down sendromlu bir olguyu sunuyoruz. Hasta 14 aylıkken gastroenterit, jeneralize tonik-klonik nöbetler nedeniyle başvurdu. Yatışının ikinci gününde renkli Doppler ultrasonografi ile sağ iliofemoral ve popliteal ven trombozu saptandı. Dehidratasyonu dışında predispozan faktör saptanamadı. Ağır dehidratasyonlu hastalarda derin ven trombozu etyolojisinde ağır dehidratasyonun akılda tutulması gerektiğini düşünüyoruz.

Anahtar Sözcükler: Derin ven trombozu, Down sendromu

INTRODUCTION

Thrombotic diseases are less frequent in children than in adults, but may result in severe morbidity and mortality. The incidence of venous thromboembolism is 5.3 per 10.000 hospital admissions or 0.7 per 10.000 children; the mortality rate is 2.2% [1].

The coagulation system is balanced to provide rapid activation to stop bleeding and appropriate inhibition to prevent unwanted clot extension. It is regulated by fibrinolysis and by three major anticoagulant pathways: the protein-C, antithrombin, and tissue-factor pathway inhibitor systems. Acquired or inherited abnormalities of coagulation proteins or hemostatic regulatory mechanisms, particularly when combined with dehydration or the presence of indwelling catheters, may pose a serious risk for thrombosis.

Thrombosis in a child warrants investigation of potential underlying prothrombotic conditions. These include abnormalities of the inherited anticoagulant factors including protein C, protein S, antithrombin, and factor V Leiden, as well as acquired disorders such as antiphospholipid antibodies and prothrombotic mutations [2]. Spontaneous thrombi in the iliofemoral, renal, or intracranial veins may also be observed in severely dehydrated children. Thus, children with severe gastroenteritis, diabetes mellitus, diabetes insipidus, and similar conditions are predisposed to thromboembolism.

CASE REPORT

A 14-month-old girl with Down syndrome (47XX + 21) and mental retardation was admitted to our emergency department with vomiting, diarrhea, fever, and generalized tonic-clonic seizures during the summer. She had undergone successful surgery for an atrioventricular septal defect when she was eight months old with no preoperative or postoperative complications. She also had no history of seizures.

Physical examination revealed a temperature of 38.8°C, pulse rate of 160/minute, respiratory rate of 60/minute, oxygen saturation of 95%, and blood pressure of 90/60 mm Hg, with features of severe dehydration, and II/VI degree systolic murmur on the 3^{rd}-4^{th} intercostal margins. Results of arterial examinations including the femoral arteries were normal. Deep-tendon and plantar reflexes were also normal. Initial hematologic tests disclosed that her complete blood count was within normal limits (hemoglobin 12.5 g/dL; hematocrit 37.9%; WBC count 9.5 x 10^9/L; and platelet count 381 x 10^9/L with 77% neutrophils, 14% lymphocytes, 6% monocytes, 2% eosinophils, and 1% basophils on peripheral smear). Laboratory data and clinical signs reflected significant hypernatremic dehydration and prerenal failure. The results of biochemical tests were as follows: glucose 102 mg/dL, blood urea nitrogen 40 mg/dl, creatinine 1.13 mg/dL, sodium 160 mEq/L, potassium 3.4 mEq/L, chloride 98 mg/dL, uric acid 10.2 mg/dL, calcium 10.2 mg/dL, and phosphorus 4 mg/dL. Arterial blood gas results indicated severe metabolic acidosis (pH: 6.91; pCO_2: 20 mm Hg; HCO_3: 4.0 mmol/L; and base excess: -27 mmol/L). Results of stool microscopy and culture were normal. The child was treated initially with bolus intravenous serum saline for severe dehydration and was treated with bicarbonate for metabolic acidosis. Hypernatremia was treated with 3500 mL/m^2/day proper concentration of serum saline. Seizures were controlled with diazepam and diphenylhydantoin. Results of a cranial computed tomography scan were normal. Her symptoms and laboratory data improved gradually; however, edema and erythema developed on the right leg on the second day of treatment. Arterial and venous color Doppler examination revealed a thrombus in the right iliofemoral and popliteal venous system, although the right femoral arterial system was intact. Results of an echocardiography were normal.

The patient was initially treated with low-molecular-weight heparin (enoxaparin, 1 mg /kg x 2 doses). After the acute period, her anticoagulant treatment was changed to warfarin for the next three months adjusted by the

international normalized ratio (INR) between 2-3. A follow-up examination of the venous system using color Doppler on day 14 showed that the venous thrombosis was completely replaced by signs of recanalization on the iliofemoral vein. Owing to the thrombus in this child, we investigated probable risk factors. Her coagulation studies were as follows: prothrombin time 13.2 s, INR 1.1, activated thromboplastin time 21.6 s, fibrinogen 229 mg/dL, fibrin degradation proteins 10 mg/mL (reference value 0-5 mg/mL), and D-dimer 1.97 mg/mL (reference value 0-0.5 mg/mL). In searching for the etiology of the thrombosis, laboratory screening for thrombophilia revealed normal protein C, protein S and antithrombin III activity, factor VIII and factor XI concentrations, plasma prothrombin and lipoprotein (a) levels, and anticardiolipin antibodies. Results of tests for factor V Leiden, prothrombin G20210A, and methylenetetrahydrofolate reductase C677T mutations were all normal.

DISCUSSION

Venous thromboembolism develops as a result of multiple interactions between non-genetic and genetic risk factors. The most important non-genetic risk factors are age, surgery, trauma, oral contraception, pregnancy, obesity, and lack of physical activity. Common risk factors in children also include indwelling catheters, inherited prothrombotic conditions and severe dehydration. Inborn factors predisposing to thrombosis are usually present in the majority of patients [3].

Spontaneous thrombi in the iliofemoral veins, renal veins, or intracranial veins may be observed in children who are severely dehydrated. Thus, children with severe gastroenteritis, diabetes mellitus, diabetes insipidus, and similar conditions are predisposed to thromboembolism [4]. In addition, thrombotic complications may occur in patients with Down syndrome. The association of cerebral sinus thrombosis with trisomy 21 has been previously reported in a few cases [5-7]. Another study ascertained that possible causes of thromboses in those patients are due to several proteins encoded on chromosome 21, including superoxide dismutase 1, cystathionine β-synthase, and collagen type VI, which affects arterial physiology and may be involved in the narrowing process of the cerebral arteries [8]. A recent study has also reported the case of a cerebral venous thrombosis diagnosed in an adult with Down syndrome, moyamoya and Graves disease associated with antithyroid microsome antibodies and antiphospholipid antibodies [9]. These authors reported that the thrombosis could be due to antiphospholipid antibodies that are known to be related with an increased risk of venous and arterial thrombotic events. A venous thrombosis has also been demonstrated in the mesenteric and portal veins in an adult with Down syndrome [10]. In that case, the only risk factor for thrombosis detected was decreased protein S activity. Another child with Down syndrome and moyamoya disease who presented with recurrent strokes due to protein C deficiency was reported [11]. Our patient had Down syndrome and severe hypernatremic dehydration. We could not find any additional predisposing factors such as protein C and protein S deficiency, antiphospholipid antibodies or prothrombotic mutations. We believe that the thrombosis in our patient was due to severe dehydration.

Treatment of a thrombosis primarily involves using a rapidly acting anticoagulant such as heparin or low-molecular-weight heparin to prevent extension, and consequent anticoagulation with warfarin to prevent recurrence. Fibrinolytic therapy is used infrequently because of the risk of serious bleeding complications and is reserved for selected cases of arterial thrombosis to initiate rapid reperfusion of ischemic tissue, or it is used in patients with a large venous thrombosis and pulmonary emboli causing hemodynamic compromise. In our patient, because of the venous thrombus and her history of cardiac surgery, we started with enoxaparin followed by prophylactic warfarin treatment for three months.

In summary, we believe that the etiology of deep-vein thrombosis in our patient was due to dehydration. We suggest that children with mental retardation should be hydrated properly, especially during the summer or episodes of diarrhea, to prevent thrombotic complications.

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