

Recurrent cerebral venous sinus thrombosis in a patient with increased factor VIII activity, increased lipoprotein (a) level and leukocytosis: a case report

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Abstract

In this paper, we describe the case of recurrent cerebral venous sinus thrombosis in a patient with increased factor VIII activity, lipoprotein (a) level, and leukocytosis. In addition, we discuss the diagnosis of increased factor VIII activity in patients with cerebral venous thrombosis. With regard to therapy, studies need to be done to establish the duration of therapy with phenprocoumon and the possible use of new oral anticoagulant drugs (i.e., rivaroxaban and dabigatran) in first time and recurrent venous thrombosis.

Keywords

recurrent cerebral venous sinus thrombosis; increased factor VIII activity; increased lipoprotein (a) level; leukocytosis; oral anticoagulation

Introduction

Increased factor VIII activity is a common cause of hypercoagulability and can generate venous thrombosis [1]. Increased lipoprotein (a) level is also a risk factor for venous thrombosis [2]. In patients with essential thrombocytopenia, leukocytosis is a risk factor for venous thrombosis [3].

The morbidity of increased factor VIII activity in adult population is 11% [4]. The thrombosis risk conferred by increased factor VIII activity is similar to that of activated protein C resistance and deficiencies of coagulation-inhibiting proteins [1]. Increased factor VIII activity over 150% increases the thrombosis risk by five times.

Patient history

A 39-year-old man was admitted to our stroke unit department with right-sided tension headache, light sensitivity, and pain behind the right eye. The symptoms occurred 3 days before hospital admission, accompanied by nausea and vomiting. An ambulatory treatment with intravenous paracetamol administered by the family physician had no effect. The patient remembered that he was treated for severe headache 4 years ago in another hospital for approximately 1 week, but he had no hospital discharge letter and could not provide any informa-

tion about diagnosis and treatment. The anamnesis provided no other details. The clinical examination (i.e., general, neurological, and psychopathological) provided normal findings except for tachycardia (117/min.).

A standard laboratory blood test was done. The values of D-Dimer 0.69 mg/l (<0.23), alanine aminotransferase 92 U/l (10–50), glucose 132 mg/dl (60–120), C-reactive protein 0.8 mg/dl (0–0.5), leukocytes 12.9/nl (4.3–10) were increased, and of glomerular filtration rate 77.3 ml/min (>90) was decreased. All other investigated parameters (i.e., sodium, potassium, urea, magnesium, uric acid, gamma-glutamyl transferase, hemoglobin, hematocrit, international normalized ratio, creatinine, antithrombin III, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, mean corpuscular volume, activated partial thromboplastin time, thrombocytes, fibrinogen, erythrocytes, creatine kinase, calcium, lactate dehydrogenase, glutamic oxaloacetic transaminase, hemoglobin A1c, vitamin B12, and thyroid stimulating hormone) were normal.

CT head scan examinations, both native and angiography, showed signs of sinus saggitalis superior and right transverse sinus thrombosis. The angiography examination showed a normal contrast medium flow signal of left transverse sinus and a missing flow signal of sinus saggitalis superior and right transverse sinus. No signs

Published May, 2014.

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of cerebral arteries stenosis or occlusion were seen. Radiological examinations showed no signs of secondary hemorrhage. Following a lumbar puncture, a septic venous sinus thrombosis was ruled out. The patient was diagnosed with idiopathic cerebral venous sinus thrombosis.

To find out the cause of thrombosis several diagnostic tests for coagulation and vasculitis were done. All coagulation tests that were performed (i.e., factor II mutation, factor V mutation, activated protein C resistance, protein C activity, protein S activity, and lupus anticoagulant panel) did not offer any diagnostic clues. Vasculitis tests (i.e., IgG, IgA and IgM cardiolipin antibodies, IgG, IgA, IgM beta2-glycoprotein antibody, anti-nuclear antibody, and anti-neutrophil cytoplasmic antibody) were negative.

The patient received intravenous heparin therapy for 2 weeks. The heparin therapy was stopped before he was discharged from hospital and oral anticoagulation with phenprocoumon was started. The patient was supposed to receive ambulatory therapy with phenprocoumon for 6 months and then lifelong oral antiplatelet therapy with aspirin.

Supplementary diagnostic tests for coagulation were done 9 months after thrombosis. During these tests factor VIII activity was increased at 182% (50–175). Serum lipoprotein (a) level was increased at 42.6 mg/dl (0–30). The patient was advised to continue the oral antiplatelet therapy with aspirin, to ask his family physician for a therapy with low molecular weight heparin (e.g., enoxaparin, nadroparin) and to wear compression stockings during risk situations (e.g., restricted mobility, surgery, long trip), to reduce weight and to change his diet.

The patient was readmitted to our stroke unit department 10 months after first time thrombosis with the same symptoms (i.e., right-sided tension headache, light sensitivity, and pain behind the right eye). The symptoms occurred 1 day before hospital admission, accompanied by nausea and shivering, but no fever. An ambulatory treatment with intravenous paracetamol administered by the family physician had no effect. The family physician observed a temporary numbness of both arms and trunk. The clinical examination upon hospital admission (i.e., general, neurological, and psychopathological) provided normal findings except for tachycardia (117/min) and high blood pressure (189/85 mmHg).

A standard laboratory blood test was done. The values of D-Dimer 0.81 mg/l, alanine aminotransferase 73 U/l, and leukocytes 12.3/nl were increased, and of glomeru-

lar filtration rate 75.4 ml/min and mean corpuscular hemoglobin concentration 31 g/dl (32–36) were decreased. All other investigated standard laboratory blood test parameters were normal.

CT head scan examinations, both native and angiography, showed signs of new right internal jugular vein thrombosis, sinus sigmoideus thrombosis, and right transverse sinus thrombosis as well as recanalization of the old sinus saggitalis superior thrombosis. The angiography examination showed a missing flow signal of right internal jugular vein, sinus sigmoideus, and right transverse sinus as well as partial recanalization of sinus saggitalis superior. Radiological examinations showed no signs of intracerebral bleeding. The patient was diagnosed with recurrent cerebral venous sinus thrombosis.

The patient received intravenous heparin therapy for 2 weeks. The heparin therapy was stopped before he was discharged from hospital and oral anticoagulation with phenprocoumon was started again. The patient was prescribed lifelong ambulatory therapy with phenprocoumon.

Discussions

As proposed by others, diagnosis of increased factor VIII activity should be done 2 months after the thrombosis event, 1 month after ending the oral anticoagulation and should be repeated two or three times. Diagnosis can be done in women taking oral contraceptives. During the acute phase of the thrombosis event coagulation tests (i.e., factor II mutation, factor V mutation, activated protein C resistance, protein C activity, protein S activity, and lupus anticoagulant panel) and vasculitis tests (i.e., IgG, IgA and IgM cardiolipin antibodies, IgG, IgA, IgM beta2-glycoprotein antibody, anti-nuclear antibody, and anti-neutrophil cytoplasmic antibody) should be done. If they are negative, the activity of factor VIII should be determined 2 months after the thrombosis event. Values of factor VIII tested during the acute phase of the thrombosis event are diagnostically not reliable [5].

Treatment recommendations for venous thrombosis caused by increased factor VIII activity include weight loss and oral anticoagulation. There is a 1.3 times increased risk for venous thrombosis in overweight patients and 1.6 times in obese patients. As the increased body weight is a risk factor for venous thrombosis, encouraging patients to lose weight makes sense [6]. There are different recommendations for the duration of oral anticoagulation in first time thrombosis, from at least or more than 6 months [7] to 12–18 months [5]. In

recurrent thrombosis long-term oral anticoagulation therapy should be done, but recommendations do not clearly state the duration of therapy [4,5].

Conclusions

Increased factor VIII activity, alone or associated with increased lipoprotein (a) level and leukocytosis can generate venous thrombosis. The diagnosis of venous thrombosis caused by increased factor VIII activity is straightforward. With regard to therapy, studies need to be done to establish the duration of therapy with phenprocoumon and the possible use of new oral anticoagulant drugs (i.e., rivaroxaban and dabigatran) in the first time and recurrent venous thrombosis.

Conflicts of Interest

The author has no conflicts of interests that are directly relevant to the content of this manuscript.

Disclosure

No sources of funding were used to assist in the preparation of this manuscript.

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