CASE REPORT

Cerebral Venous Thrombosis in a Patient with Sarcoidosis

Aikaterini Selvi1, Maria Diakou1, Sotirios Giannopoulos1, Anastasia K. Zikou2, Maria I. Argyropoulou1 and Athanassios P. Kyritsis1

Abstract

Cerebral venous thrombosis (CVT) may present with a variety of symptoms and findings consisting of either only persistent headache, or slowly progressive stroke over several days, or even coma. CVT may develop in relation to hypercoagulable states. However, even after extensive investigation, a predisposing factor could not be identified in some cases. We report a case of CVT associated with heterozygous V Leiden mutation and sarcoidosis. Since most factor V gene heterozygous individuals do not exhibit clinical thrombotic events, the venous thrombosis of our patient suggests convergence of an inherited predisposition (heterozygous factor V Leiden mutation) with an acquired thrombogenic stimulus (sarcoidosis). Early diagnosis and treatment with anticoagulation is pivotal for a favorable outcome.

Key words: cerebral venous thrombosis, sarcoidosis, Factor V Leiden mutation

(Int Med 48: 723-725, 2009)
(DOI: 10.2169/internalmedicine.48.1809)

Introduction

Cerebral venous thrombosis (CVT) is an uncommon condition with strikingly diverse manifestations that range from isolated headache to coma and may mimic a variety of other neurological conditions. More than 100 cases of CVT have been recorded in the medical literature (1). However, even with extensive investigation, a predisposing factor could not be identified in 20%-25% of cases (2). CVT may develop in relation to hypercoagulable states. Inherited pre-thrombotic conditions, such as factor V Leiden homozygous mutations, protein C and S and antithrombin III deficiencies, account for approximately 10%-15% of cases (3). There have been sparse reports in the literature linking sarcoidosis to venous thrombosis (4, 5). We report a case of CVT associated with heterozygous V Leiden mutation and sarcoidosis.

Case Report

A 38-year-old Caucasian male was brought to the Emergency Department (ED) with a four-day history of headache, confusion and disorientation. His past medical history was significant for deep venous thrombosis of both lower extremities several years earlier and pulmonary sarcoidosis diagnosed with lymph node biopsy but currently he was not receiving any treatment. General physical examination was unremarkable and his vital signs showed only moderate tachycardia (heart rate of 110/min). Neurological examination revealed decreased mental status with the patient able to follow only one-step commands, and mild tetraparesis with bilateral Babinski signs.

A short time after his ED admission he had one episode of generalized tonic-clonic seizures lasting few minutes. The brain CT scan revealed bilateral fronto-parietal hemorrhagic infarcts (Fig. 1A, circular arrows), and the brain CT venography demonstrated thrombosis of the superior sagittal sinus (Fig. 1B, arrow). The chest x-ray showed bilateral hilar adenopathy consistent with the previous diagnosis of lung sarcoidosis. Serum laboratory findings showed PT 15.9/13 sec, aPTT 37.9/28 sec, fibrinogen 269 mg/dL, D-dimers >2,000 ng/mL and slightly elevated serum angiotensin-converting enzyme level of 56.7 UI/L (4-52 UI/L). Anti-beta 2 GPI antibody, lipoprotein (a) and homocystein were not measured. Anticardiolipin antibodies, lupus anticoagulant, ANA and HIV antibodies were negative. Protein S was 68% (60-120%), protein C was 92% (70-140%) and antithrombin III was 98% (85-125%) but the resistance to activated protein C...
was increased and the genetic test for the coagulation factor revealed a heterozygous mutation in factor V (Factor V-Leiden 1,691 G>A). The patient was admitted to the neurology ward and was started on continuous heparin infusion for the CVT (a bolus of 5,000 units followed by 1,000 units/hour to keep aPTT 1.5-2.0 times the control aPTT), and valproic acid for his seizures. His hospital stay was complicated by an episode of status epilepticus which responded to administration of diazepam and leveciracetam. Three days later he was switched to warfarin to maintain INR between 2 and 3 and heparin was gradually discontinued. The patient showed continuous improvement and 15 days later he was discharged from the hospital with minimal disability consisting of slight left sided spasticity without hemiparesis.

Discussion

CVT has been associated with many congenital and acquired hypercoagulable states (6). The diagnosis of CVT is frequently overlooked, especially when the only symptom at presentation is headache (7). Most homozygous V Leiden gene individuals will experience at least one thrombotic event in their life (8). By contrast, heterozygous individuals do not have clinical thrombotic events, suggesting that clinical thrombosis in such individuals may result from the coexistence of the inherited factor V Leiden gene mutation with an acquired thrombogenic stimulus (9, 10).

Although sarcoidosis has not been directly linked to CVT it may be associated with venous thrombosis (4, 12). The management of CVT involves anticoagulation even when hemorrhagic infarcts are present, since venous hemorrhages result from venous hypertension, and by arresting the thrombotic process venous hypertension and the tendency to bleed are reduced (6). However, heparin should be quickly switched to warfarin to avoid further thrombosis due to heparin-induced thrombocytopenia in some patients, or use of low-molecular weight heparin instead of classic heparin (11).

To our knowledge there are no other reports that correlate CVT with sarcoidosis, but there are two reported cases of deep venous thrombosis related to sarcoidosis (5, 12). Widespread and recurrent thrombophlebitis has also been attributed to sarcoidosis (4). Abnormalities of tissue pre-coagulation and fibrinolysis have been described in sarcoidosis, such as enhanced tissue factor pathway activity, increased tissue thromboplastin activity, diminished plasminogen activator activity and increased thrombin activatable fibrinolysis inhibitor (13). These tissue alterations may favor thrombus formation in susceptible individuals. Increased d-dimer levels in the blood of sarcoidosis patients also support the concept of coagulation activation and an increase in deposition of fibrin in tissues (14).

In conclusion, we describe a case of CVT in a patient with sarcoidosis and heterozygous factor V Leiden mutation. Although the exact mechanism of thrombus formation in sarcoidosis is unclear, our case suggests that sarcoidosis was the acquired thrombogenic stimulus that along with the inherited heterozygous V Leiden mutation resulted in CVT.

References


© 2009 The Japanese Society of Internal Medicine
http://www.naika.or.jp/imindex.html