Journal of Cerebrovascular and Endovascular Neurosurgery
ISSN 2234-8565, EISSN 2287-3139, http://dx.doi.org/10.7461/jcen.2012.14.3.251

Case Report

The Role of Hyperthyroidism as the Predisposing Factor for Superior Sagittal Sinus Thrombosis

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Superior sagittal sinus thrombosis (SSST) is an uncommon cause of stroke, whose symptoms and clinical course are highly variable. It is frequently associated with a variety of hypercoagulable states. Coagulation abnormalities are commonly seen in patients with hyperthyroidism. To the best of our knowledge, there are few reports on the association between hyperthyroidism and cerebral venous thrombosis. We report on a 31-year-old male patient with a six-year history of hyperthyroidism who developed seizure and mental deterioration. Findings on brain computed tomography (CT) showed multiple hemorrhages in the subcortical area of both middle frontal gyrus and cerebral digital subtraction angiography (DSA) showed irregular intra-luminal filling defects of the superior sagittal sinus. These findings were consistent with hemorrhagic transformation of SSST. Findings on clinical laboratory tests were consistent with hyperthyroidism. In addition, our patient also showed high activity of factors IX and XI. The patient received treatment with oral anticoagulant and prophylthiouracil. His symptoms showed complete improvement. A follow-up cerebral angiography four weeks after treatment showed a recanalization of the SSS. In conclusion, findings of our case indicate that hypercoagulability may contribute to development of SSST in a patient with hyperthyroidism.

Keywords Cerebral venous thrombosis, Superior sagittal sinus, Hyperthyroidism, Hypercoagulability

J Cerebrovasc Endovasc Neurosurg. 2012 September;14(3):251~254
Received : 24 July 2012
Revised : 17 August 2012
Accepted : 6 September 2012

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INTRODUCTION

Cerebral venous and sinus thrombosis is a rare condition accounting for < 1% of all strokes.[7] Its annual incidence is estimated at three to four cases per one million members of the population, most often affecting young adults and children.[19] In adults, the peak incidence is in their third decade, and approximately 75% of adult patients are female.[5][7] Thrombotic risk factors or direct causes are identified in approximately 85% of patients with cerebral sinus thrombosis.[19]

Superior sagittal sinus thrombosis (SSST) is associated with a variety of hypercoagulable, states including Crohn's disease, diabetes insipidus, direct injury to the sinus, iatrogenic causes, malignancy, nephrotic syndrome, oral contraceptives, paroxysmal nocturnal hemoglobinuria, polycythemia, pregnancy, puerperium, systemic lupus erythematosus, and ulcerative colitis.[1][19] Coagulation abnormalities are commonly seen in patients with hyperthyroidism.[6][9][18] However, the association between hyperthyroidism and cerebral venous thrombosis is poorly understood. To investigate the possible association between these two clinical conditions, we report on a case of a

31-year-old male patient with a six-year history of hyperthyroidism who developed SSST.

CASE REPORT

A 31-year-old male patient was admitted to our institute with seizure, headache, and mental deterioration. During the recent six years, the patient had been prescribed methimazole for treatment of hyperthyroidism. However, three months before, the patient had arbitrarily stopped taking the medication. He did not undergo a regular follow-up and had poor compliance to the medication. One day before visiting our institution, the patient was admitted at a local hospital for transient weakness of both lower extremities. The patient underwent treatment for thyrotoxic periodic paralysis or thyroid crisis, but became progressively stuporous and experienced seizure attacks several times. Findings on immediate brain computerized tomography (CT) showed multiple hemorrhages in the subcortical area of both middle frontal gyrus (Fig. 1A, B).

After two hours, the patient was transferred to our institute and still exhibited a stuporous mentality with no motor weakness. A follow-up CT angiography was performed immediately after arrival at our institute. Findings on brain CT showed a slight increase of hemorrhage and CT angiography showed no abnormalities of the major cerebral artery system (Fig. 2A, B, C, D). During four hours, he presented with progressive neurological improvement. Laboratory results showed hyperthyroidism with the following values: 176.2 ng/dL of T3 (normal range, 80-200 ng/dL), 3.84 ng/dL of high free T4 (normal range, 0.89-1.76 ng/dL), and less than 0.01 μIU/mL of thyroid-stimulating hormone (normal range, 0.35-5.5 μIU/mL). Hematologic and coagulation parameters, including platelet count, prothrombin time, activated partial thromboplastin time, fibrinogen, anti-thrombin Ill, fibrin degradation products, D-dimer, lupus anticoagulant, protein C activity, and protein S activity were all normal. The patient also had a normal sinus rhythm on baseline electrocardiography.

Two days after the initial visit, the patient became nearly alert and fully oriented. Cerebral digital subtraction angiography (DSA) was performed in order to determine the causes of the non-traumatic cerebral hemorrhage. It showed multiple intra-luminal filling defects of the SSS (Fig. 3A, B). Cross-sectional echocardiography showed a normal left ventricular size and function with no evidence of intra-cardiac thrombus. Following the diagnosis of SSST, the patient received anticoagulation therapy with warfarin 5

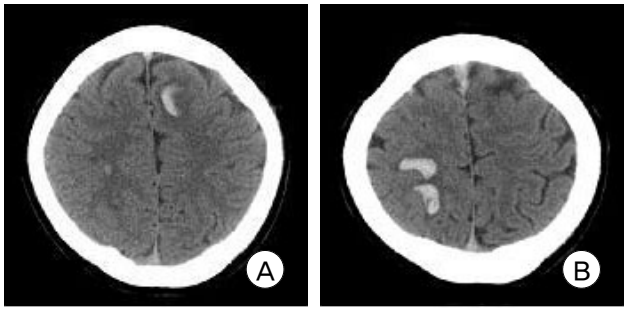

Fig. 1. On initial brain computerized tomography (CT) scans, there are multiple hemorrhages in the subcortical area of both middle frontal gyrus (A, B).

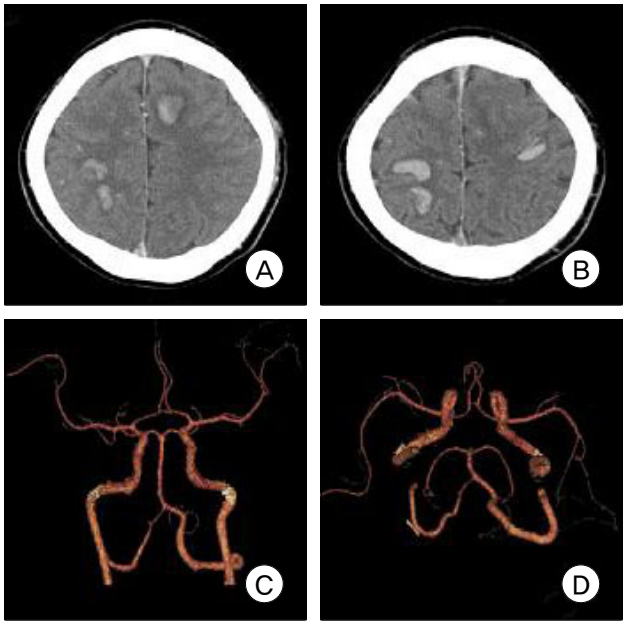

Fig. 2. On follow-up brain CT scans, there are new onset foci and a slight increase of hemorrhage (A, B). CT angiography does not show any remarkable findings of major cerebral vessels (C, D).

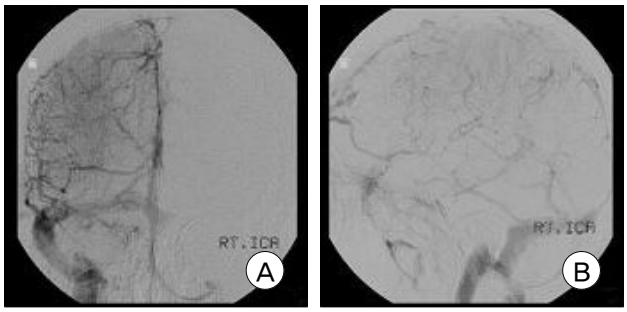

Fig. 3. Initial digital subtraction angiography (DSA) shows irregular intra-luminal filling defects of the superior sagittal sinus (A, B).

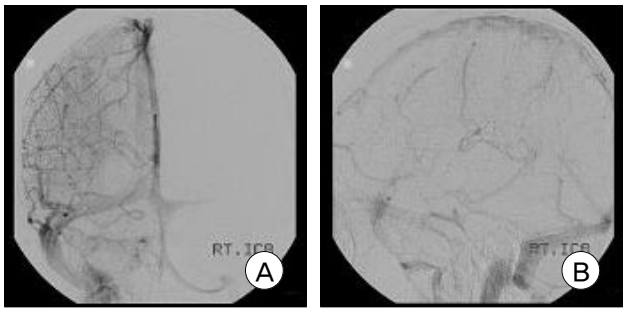

Fig. 4. A follow-up DSA shows a recanalization of the superior sagittal sinus (A, B).

mg QD and avoided systemic heparinization on account of the aggravating hemorrhage. In addition, hyperthyroidism was treated with prophylthiouracil. The patient's symptoms showed complete improvement. Four weeks after treatment, follow-up cerebral DSA showed a recanalization of the superior sagittal sinus (Fig. 4A, B), and laboratory findings indicated a normal free T4 level of 0.81 ng/dL. The patient had no recurrence of neurological symptoms and maintained a euthyroid state for the next nine months.

DISCUSSION

SSST is an uncommon cerebrovascular accident; due to a broad spectrum of symptoms and clinical courses, a diagnosis is still frequently overlooked or delayed.[7] The average delay from the onset of symptoms to the diagnosis is seven days.[8] In addition, approximately 15% of cases of SSST are considered to be idiopathic.[19] Although coagulation disturbances are reported in hyperthyroidism, an association between hyperthyroidism and cerebral venous thrombosis has not been well established. Schutta et al.[16] reported on a case of a 34-year-old male patient with hyperthyroidism and inherited plasminogen deficiency. This patient had thrombosis of the dural sinus and internal jugular vein. Siegert et al.[17] documented on two patients (a 24-year-old male and a 32-year-old female) with SSST during the thyrotoxic phase of Grave's disease. Dai et al.[4] demonstrated on a 39-year-old male patient with undiagnosed hyperthyroidism who developed SSST. The patient had a high free T4 level, hot thyroid uptake, and rapid atrial fibrillation. In our patient, along with previous reports, it can be hypothesized that hyperthyroidism is an independent risk factor for cerebral venous thrombosis.

Thrombotic events in thyrotoxic patients are in danger of systemic and cerebral arterial infarctions and have been directly attributed to atrial fibrillation, suggesting emboli as the causative agent.[2][11][13] In our case, however, normal sinus rhythm was observed on the electrocardiography. In addition, findings on echocardiography showed normal left ventricular size and function with no evidence of intra-cardiac thrombus. We also attempted to identify other predisposing factors for development of SSST. Development of SSST occurs due to multi-factorial causes, commonly including three factors: stasis of the blood stream, abnormalities of the vessel wall, and hypercoagulability. These three factors are involved in promoting venous thrombosis.[17] Large thyrotoxic goiters may cause stasis of venous blood flow from the cerebral circulation through local obstruction by itself or large blood flow of the thyroid gland.[3][10] However, our patient did not present with a goiter. And no other causes of vessel wall abnormality, such as vascular inflammation and direct injury to veins, were detected.

Therefore, we suppose that hypercoagulability was the main cause of SSST in our patient with hyperthyroidism. To date, numerous studies have indicated an association of coagulation disturbances with hyperthyroidism. Several authors have reported

that the intrinsic clotting system, particularly factor VIII, was markedly affected by hyperthyroidism.[6)9)15)18)] High adrenergic tone and hyper-metabolic state of hyperthyroidism resulted in factor VIII hyperactivity, thus increasing the likelihood of hypercoagulation.[6)14)18)] Although our patient exhibited a normal range of factor VIII activity (135%, normal range, 60 to 140 %), he showed high activity of factors IX and XI (> 160% for both). These results are consistent with hypercoagulation through activation of the intrinsic clotting pathway, factor XI in particular.[12)20)] In this regard, based on our case report, it is probable that activation of intrinsic clotting factors by hyperthyroidism might be the factor responsible for the occurrence of SSST. Abnormal activity of the clotting factor is recovered to normal after reaching the euthyroid state; therefore, anti-thyroid therapy constitutes an important part of the treatment.[6)9)15)18)]

CONCLUSION

We suggest that, because of the hypercoagulability, patients with hyperthyroidism may be predisposed to development of SSST. Consideration of the possibility of development of cerebral venous thrombosis in patients with hyperthyroidism who present with neurological symptoms is mandatory. Conversely, hyperthyroidism as the thrombotic factor in a patient with cerebral venous thrombosis who is not at risk of developing cerebrovascular events must also be considered.

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