Superior sagittal sinus thrombosis induced by thyrotoxicosis

Case report

CHENG-SHYUAN RAU, M.D., CHUN-CHUNG LUI, M.D., CHENG-LOONG LIANG, M.D., HAN-JUNG CHEN, M.D., PH.D., YEH-LIN KUO, M.D., AND WU-FU CHEN, M.D.

Departments of Neurosurgery and Neuroradiology, Chang Gung University, Kaohsiung Medical Center, Kaohsiung, Taiwan

There is a wide variety of disorders associated with thrombosis of the superior sagittal sinus (SSS), including infectious disease, noninfectious conditions such as vasculitis and hypercoagulable states, and complications arising from pregnancy or use of oral contraceptive medications. Despite these well-defined associations, approximately 25% of the cases remain idiopathic. In this article the authors describe a patient who was found to have SSS thrombosis while experiencing a thyrotoxic phase of Graves disease. The patient presented with intracerebral hemorrhage, subarachnoid hemorrhage, seizure, coma, a raised fibrinogen concentration, low protein C activity, and atrial fibrillations. Thrombolysis was successfully performed despite the coexistence of thrombosis and intracranial hemorrhage. Patients with thyrotoxicosis and a diffuse goiter may be predisposed to the development of SSS thrombosis, as a result of hypercoagulation and stasis of local venous blood flow. In the present case, a patient in whom thrombosis coexisted with intracranial hemorrhage was successfully treated using thrombolytic therapy.

KEY WORDS • sinus thrombosis • thyrotoxicosis • fibrinogen • protein C • thrombolysis

Superior sagittal sinus thrombosis is an uncommon cause of stroke. Initial symptoms include headache, vomiting, and somnolence, which are followed by either focal neurological deficits (often associated with focal seizure) or signs of increased intracranial pressure. The diagnosis is confirmed using computerized tomography scanning, MR imaging, or angiography.

A wide variety of disorders may be associated with thrombosis of the SSS, including infectious diseases, noninfectious conditions such as vasculitis, hypercoagulable states, and complications arising from pregnancy or use of oral contraceptive medications. Despite these well-defined associations, approximately 25% of cases of SSS thrombosis are still considered to be idiopathic.

Siegert, et al., have reported two cases in which there was a possible association between SSS thrombosis and the thyrotoxic phase of Graves disease. We present an additional case, noting that the occurrence of SSS thrombosis may be linked to the increased thrombotic risk associated with AF and hypercoagulability of blood during thyrotoxicosis. We describe a severely symptomatic patient who suffered from both SSS thrombosis and intracranial hemorrhage, and the successful treatment of this patient accomplished using direct urokinase infusion.

Case Report

History. This 60-year-old man with hyperthyroidism presented with a 2-day history of sudden-onset frontal headache and general weakness. He was transferred to our hospital and admitted because of a loss of consciousness and a generalized tonic–clonic seizure. Graves disease had been diagnosed 3 years before admission and treated by a

![Fig. 1. Computerized tomography scan of the brain revealing hemorrhage in the right parietal area (arrowhead) and the sulci (arrow).](image)
prescribed regimen of methimazole (10 mg every day) and propranolol (20 mg twice per day) to be taken while in a euthyroidic state. The patient had not been taking his prescribed medication during the 15 months before admission and had experienced thyrotoxic symptoms, including palpitation, sweating, and weight loss, during the 6-month period before hospitalization.

**Examination.** Physical examination revealed a comatose state, left hemiplegia, and generalized tonic–clonic seizure. In addition, a diffused Grade II to III goiter was noted. Laboratory investigations confirmed biochemical hyperthyroidism on the basis of the following values: thyroxin, 278.6 nmol/L (normal range 61.9–161.5 nmol/L); free thyroxin, higher than 77.3 pmol/L (normal range 0.9–2.8 nmol/L); and thyroid-stimulating hormone, 0.002 mU/L (normal range 0.35–5.5 mU/L). Hematological and coagulant parameters (including erythrocyte sedimentation rate, thrombocyte count, prothrombin time, activated and partial thromboplastin time, antithrombin III activity, protein S activity, complement component–4, and factor VIII coagulant activity) were all normal, with the exception of a high fibrinogen concentration (4.7 g/L, normal range 1.9–3.8 g/L) and low protein C activity (52%, normal range 75–107%). An electrocardiogram demonstrated that the patient suffered AF with a rapid ventricular response (heart rate 134 beats/minute).

Computerized tomography scans demonstrated intracranial hemorrhage in the right frontoparietal lobe and increased density of the right sigmoid sinus and sagittal sinus (Fig. 1).

**Treatment.** The patient was intubated and treated with phentoin, diazepam, methimazole, and propranolol. A cerebral angiogram demonstrated the filling defect in the SSS and the right transverse sinus (Fig. 2 left). Partial recanalization was achieved using local thrombolytic therapy with 900,000 IU of urokinase (Fig. 2 right). Subsequently, a follow-up MR venogram revealed flow through the SSS (Fig. 3).

**Posttreatment Course.** At the time of hospital discharge, the patient displayed excellent improvement. Follow-up assessment confirmed near-complete neurological recovery after 3 months.

**Discussion**

Thrombosis of the SSS associated with thyrotoxicosis is rare; it has previously been described only by Siegert, et al.17 To our knowledge, ours is only the third such case to be described in the literature. In the present case, SSS thrombosis developed during the thyrotoxic phase of Graves disease as a result of the patient’s failure to take medication during the 15 months before hospital admission. In general, the probability of venous thrombosis is promoted by three factors: hypercoagulability, stasis of the blood stream, and abnormality of the vessel wall. There are three differences between our case and the two cases reported by Siegert, et al. First, AF with a rapid ventricular response was noted during hospitalization, and hyperthyroidism was a causative factor. Atrial fibrillation is associated with uncoordinated, irregular atrial activity and may result in abnormalities of intracardiac blood flow that may contribute to a prothrombotic state.12,15 Second, in this

---

**Fig. 2.** Left: Right carotid artery angiogram, lateral view, revealing no opacification of the posterior half of the SSS (arrowheads). Right: Follow-up angiogram obtained after urokinase infusion demonstrating partial recanalization of the SSS (arrows) and an increased number of cortical veins (arrowhead).

**Fig. 3.** Follow-up MR venogram obtained 1 month after treatment demonstrating good opacification of the SSS (arrowhead).
patient the plasma level of fibrinogen was raised. The results of previous studies have demonstrated that an increased fibrinogen concentration is a risk factor for venous thrombosis.\(^1,13,14\) Fibrinogen is a major determinant of the viscosity of plasma and, therefore, of blood, and plays a major role in platelet aggregation, as well as acting as the substrate for fibrin formation. Thus, the presence of increased plasma fibrinogen in cases of SSS thrombosis lends further support to the possible thrombotic pathogenesis of this disorder. Furthermore, AF is related to an increase in plasma fibrinogen.\(^3,14\) Third, in this patient protein C activity was low. Protein C is an important inhibitor of plasma coagulation, and a deficiency in this protein may increase the risk for thromboembolic events. In fact, cerebral venous thrombosis associated with protein C deficiency has been reported by a number of researchers.\(^4,5\) Dehydration is a clinical risk factor associated with cerebral venous thrombosis.\(^6\) Thrombosis can result from changes in blood flow due to dehydration. In the present case, however, the patient was not in a dehydrated state on his arrival at the hospital. In addition, our patient presented with a larger goiter, which may cause stasis of venous blood flow. These hemodynamic factors may contribute to the multifactorial pathogenesis of SSS thrombosis.

Acute occlusion of the SSS (particularly the posterior half) and the dominant transverse and sigmoid sinuses can lead to significant cerebral edema, increased intracranial pressure, hydrocephalus, and venous congestion, resulting in hemorrhage and/or infarction. The treatment of SSS thrombosis is not uniform and the role of anticoagulant medications remains controversial because of the risk of provoking hemorrhagic cerebral infarctions, especially in patients with coexisting intracranial hemorrhage. Recent articles have shown that direct thrombolysis of dural venous sinus thrombosis should be considered for the rapidly deteriorating patient who has not responded to conventional medical therapy.\(^2,9,10,18,20\) Intracranial hemorrhage may not be an absolute contraindication for local urokinase therapy in the symptomatic patient with dural venous sinus thrombosis; a few cases have been reported in which thrombolysis was performed for thrombosis of the SSS in conjunction with cerebral hemorrhage.\(^9,10,16\) In our patient, in whom SSS thrombosis coexisted with intracranial hemorrhage, which was considered to be due to venous hypertension caused by occlusion, the condition was successfully treated using direct urokinase infusion.

**Conclusions**

The occurrence of SSS thrombosis during a thyrotoxic phase of Graves disease is extremely rare, with only two cases previously reported in the literature. The present case is the first in which the patient was documented as exhibiting a high plasma concentration of fibrinogen, low protein C activity, and AF—findings that need to be emphasized because of the important potential contribution to our understanding of the SSS and thrombosis.

Our findings support the theory that the pathogenesis of hypercoagulability and stasis of the venous blood flow may contribute to the development of SSS thrombosis in thyrotoxic patients.

---

### References


*Address reprint requests to: Wu-Fu Chen, M.D., Department of Neurosurgery, Chang Gung Memorial Hospital, Kaohsiung Medical Center, 123, Tapei Road, Niasung Hsiang, Koahsiung Hsien, Taiwan. email: wfchen@ms29.hinet.net.*