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Progressive Ischemic Stroke due to Thyroid Storm-Associated Cerebral Venous Thrombosis

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Conflict of interest: None declared

Patient: Female, 49
Final Diagnosis: Cerebral venous thrombosis
Symptoms: Altered mental state • weakness in limbs
Medication: —
Clinical Procedure: —
Specialty: Endocrinology and Metabolic

Objective: Rare co-existance of disease or pathology

Background: Cerebral venous thrombosis (CVT) is a rare but fatal complication of hyperthyroidism that is induced by the hypercoagulable state of thyrotoxicosis. Although it is frequently difficult to diagnose CVT promptly, it is important to consider it in the differential diagnosis when a hyperthyroid patient presents with atypical neurologic symptoms.

Care Report: A 49-year-old Japanese female with unremarkable medical history came in with thyroid storm and multiple progressive ischemic stroke identified at another hospital. Treatment for thyroid storm with beta-blocker, glucocorticoid, and potassium iodide-iodine was started and MR venography was performed on hospital day 3 for further evaluation of her progressive ischemic stroke. The MRI showed CVT, and anticoagulation therapy, in addition to the anti-thyroid agents, was initiated. The patient's thyroid function was successfully stabilized by hospital day 10 and further progression of CVT was prevented.

Conclusions: Physicians should consider CVT when a patient presents with atypical course of stroke or with atypical MRI findings such as high intensity area in apparent diffusion coefficient (ADC) mapping. Not only is an early diagnosis and initiation of anticoagulation important, but identifying and treating the underlying disease is essential to avoid the progression of CVT.

MeSH Keywords: Early Diagnosis • Intracranial Thrombosis • Thrombophilia • Thyroid Crisis • Venous Thrombosis

Full-text PDF: http://www.amjcaserep.com/abstract/index/idArt/902297

Background

Cerebral venous thrombosis (CVT) is a rare but potentially fatal cerebrovascular complication of hyperthyroidism that is induced by the hypercoagulable state of thyrotoxicosis [1–6]. The clinical manifestation of CVT differs greatly between cases and this makes the diagnosis difficult for clinicians [7]. It is important to include CVT in the differential diagnosis and make further investigation when a hyperthyroid patient appears with atypical neurologic symptoms and findings on images [7,8]. To avoid the progression of thrombosis, it is necessary to make early diagnosis and initiate anticoagulation as well as provide treatment for the underlying disease. Here, we describe a unique patient who presented with hyperthyroid storm and progressive ischemic stroke caused by CVT.

Case Report

A 49-year-old Japanese female with an unremarkable medical history presented to an outside clinic with a one-month history of headaches, palpitations, diaphoresis, and weight loss. Her family history was not remarkable and the patient denied any history of tobacco smoking, heavy alcohol consumption, or substance abuse. Subsequent laboratory investigations revealed TSH of <0.01 mIU/L, free T3 of 7.82 pg/dL, and free T4 of 2.48 ng/dL (normal range: TSH 0.5–5 mIU/L; free T3 2–4.48 pg/mL; free T4 0.84–1.70 ng/dL). She was diagnosed with hyperthyroidism, and methimazole was initiated as an outpatient therapy.

Two days after the diagnosis, she started to have weakness in her left proximal upper extremity and left leg. Magnetic resonance imaging (MRI) of the brain showed cerebral infarction in the right pre- and post-central gyri. She was admitted to an outside hospital and started on intravenous argatroban. During the next six days, she developed weakness in her right leg as well. On day 7, a second MRI showed new infarctions in the left frontal lobe, posterior lobe, and right parietal lobe (Figure 1). On day 8, she was noted to have confusion, tachypnea, tachycardia, hyperthermia, and hypertension. Based on Burch and Wartofsky scoring system [9], the total score of her condition was 85 points and was highly suggestive of thyroid storm. She was transferred to our hospital for further evaluation and treatment.

On admission to our hospital, although she did not have apparent diffuse goiter or orbitopathy, she was diagnosed with Graves' disease based on thyrotropin receptor antibodies positivity [10] at 2.2 IU/L (normal range <2.0 IU/L). Thyroid function tests were as follows: TSH <0.005 mIU/L, free T3 8.10 pg/mL, free T4 4.41 ng/dL. She was started on glucocorticoid, beta-blocker, potassium iodide-iodine, and methimazole for thyroid storm. As the patient had no atrial fibrillation and MR angiography of the brain revealed no occlusion, MR venography of the brain was performed on hospital day 3 to clarify the etiology of her repeated infarction. The venography showed thrombosis in the left transverse sinus, sigmoid sinus, and internal jugular vein, confirming the diagnosis of cerebral venous sinus thrombosis; intravenous heparin infusion was started.

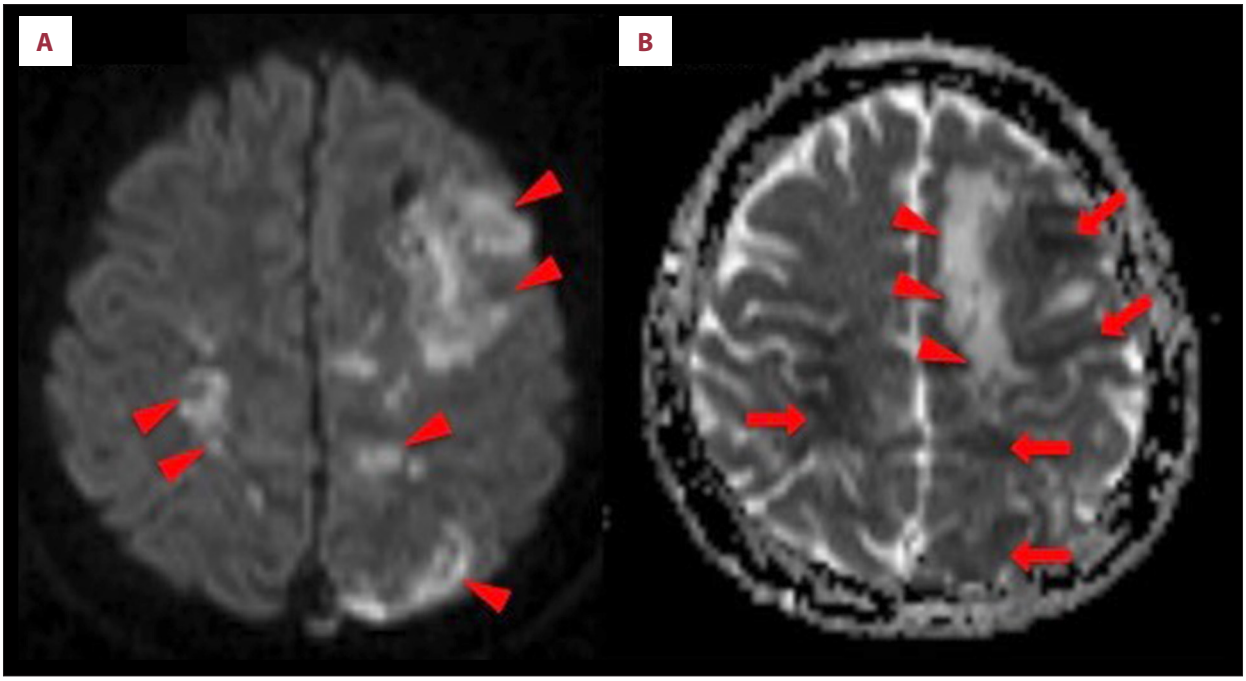

Figure 1. Magnetic resonance imaging on day 7. Hyperintensity areas (arrow heads) in diffusion weighted image (**A**). A hyperintensity area (arrow heads) mixed with hypointensity areas (arrows) in apparent diffusion coefficient map (**B**).

She underwent subsequent venous angiography and catheter thrombectomy with gradual clinical improvement. Her free T3 and free T4 slowly improved, normalizing by day 10, and was followed by the successful discontinuation of corticosteroid and beta-blocker. Her neurological condition was improving and she was transferred to a rehabilitation hospital on day 85.

Discussion

Here, we describe a rare case of hyperthyroid storm associated with progressive cerebral ischemia caused by CVT. Although cardioembolic stroke induced by thyrotoxic atrial fibrillation is well-recognized phenomenon, CVT has also been reported as a cerebrovascular complication of hyperthyroidism, due to the hypercoagulable state induced by thyrotoxicosis [1–6]. CVT is a very uncommon disease with an estimated incidence between 0.5% and 1% of all strokes in the general population and with a mortality rate of 5% to 30% [11]. Clinical manifestations of CVT vary between cases depending on the underlying disease and location of thrombosis, and this makes the timely diagnosis challenging [7]. It is important to consider CVT among the differential diagnoses of a patient with hyperthyroidism manifesting atypical neurologic symptoms and imaging findings such as bilateral progressive ischemic stroke, continuous headache, or seizure. Early diagnosis of CVT and rapid initiation of anticoagulation, along with treatment of the underlying disease, can effectively halt thrombosis progression.

Although hyperthyroidism is not a widely acknowledged risk factor for venous thrombosis, a possible association between thyrotoxicosis and venous thrombosis has been reported previously [1–6]. A case of thyroid storm complicated with disseminated intravascular coagulation (DIC) was also reported [12]. CVT with thyrotoxicosis was described as early as 1927 by Doyle [1]; and previous studies suggest that thyrotoxicosis increases plasma levels of tissue factor, Factor VIII, Factor IX, von Willebrand Factor, fibrinogen, d-dimer, and plasminogen activator inhibitor-1 [5,6].

In addition to arterial ischemia, physicians should also consider CVT when a hyperthyroid patient presents with stroke; the venous pathophysiology of which is different from its arterial counterpart. Arterial infarction leads to cell membrane damage, causing cytotoxic brain injury and edema. In contrast, venous sinus thrombosis and the associated impairment of venous drainage can cause an increase in venous and capillary pressure. The increased intravenous pressure contributes to an increase in intravascular pressure and a lowering of cerebral perfusion pressure resulting in both vasogenic and cytotoxic edema [8]. Due to this edema, clinical manifestations of CVT may differ widely depending on the underlying disease and location of thrombosis. In general, CVT-associated symptoms are grouped into three categories: isolated intracranial hypertension syndrome, focal syndrome, and encephalopathy [7]. These multiple manifestations, which overlap with other common diseases including primary headache, intracranial hemorrhage, and arterial infarction, make it difficult for physicians to consider CVT in their differential diagnosis. As such, recognition of these imaging findings may play an important role in the rapid diagnosis of CVT.

Imaging characteristics differ between arterial stroke and CVT. On MRI, cell membrane damage induced by hypoxic changes from arterial infarction manifests as hyperintensity in diffusion-weighted imaging (DWI) and hypointensity in the acute phase of apparent diffusion coefficient (ADC) mapping images, which may evolve into hyperintensity after 10 days [13]. In contrast, the increase in capillary pressure from CVT induces vasogenic edema, which manifests as hyperintensity in ADC mapping, and hypo-, iso-, or hyperintensity in DWI. Later, when increased venous pressure results in arterial malperfusion, arterial infarction will occur, typically manifesting as hyperintensity mixed with hypointensity in ADC mapping [8]. Edematous changes and early phase hyperintensity in ADC mapping is characteristic in CVT and can assist in identifying an otherwise challenging diagnosis, with subsequent MR venography or CT venography performed for definitive diagnosis. In our case, we retrospectively reviewed the ADC mapping MRI performed on day 7 at the previous hospital, a few days after new muscle weakness developed. It demonstrated new hyperintensity lesions, which did not exist in the first MRI (Figure 1). This was suggestive of venous sinus thrombosis rather than arterial stroke, and in retrospect, an evaluation of the venous sinus may have been advised at this point.

Delays in diagnosis of CVT are common and may lead to significant morbidity. The median delay from onset of symptoms to hospital admission, as well as from symptom onset to diagnosis, were reportedly four and seven days, respectively [7]. Thrombosis progresses rapidly if left untreated, and we should consider CVT when patients with hyperthyroidism have atypical imaging studies and neurologic findings. To prevent progression of CVT, swift treatment with adequate anticoagulation is critical. Although anticoagulation during the acute phase of arterial stroke is usually not recommended due to hemorrhagic risk; however, it is strongly recommended, even in the acute phase, for venous sinus thrombosis [14]. In addition to anticoagulation therapy, it is necessary to identify and treat the underlying cause of thrombosis. As Factor VIII activity usually returns to normal after a few weeks of anti-thyroid therapy, correction of the hyperthyroid state was an important part of the treatment strategy for CVT in our case [5,15]. An extensive search in all-language literature that identified all the case reports of CVT published from April 2005 up to December 2010 found only 26 cases [3]. In addition, there were 12 cases that

reported on the relationship between hyperthyroidism and CVT [16–27]. Although it is not common, physicians should be aware of hyperthyroidism as a potential cause of CVT. In order to prevent further deterioration of established thrombosis, it is essential not only to make rapid diagnosis of CVT and initiate anticoagulation but also to treat the underlying disease such as hyperthyroidism.

Conclusions

We reported here on a case of CVT associated with hypercoagulability of hyperthyroidism. Clinicians should consider venous sinus thrombosis when they encounter a stroke in a hyperthyroid patient and thyroid function tests should be checked for a cause of thrombosis. The hyperintensity or mixed intensity in ADC map can be helpful for the diagnosis of CVT.

Conflict of interest

The authors state that they have no conflict of interest (COI).

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