CASE REPORT

An unusual association between acute ischaemic stroke and cerebral venous thrombosis with thyrotoxic state

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SUMMARY

Arterial cerebral ischaemia has been described in different diseases of the thyroid. Likewise, cerebral venous thrombosis (CVT) has been reported in association with hyperthyroidism. However, the association of arterial and venous cerebral ischaemic events in patients with hyperthyroidism has not been previously described. We report the case of a patient with thyrotoxicosis who presented initially with an arterial ischaemic stroke complicated by a concomitant CVT, ultimately treated with decompressive craniectomy. Laboratory results revealed elevated factor VIII coagulant activity and a positive lupus anticoagulant IgG. In conclusion, CVT and arterial ischaemic events can happen concomitantly in patients with hyperthyroidism. Although there is insufficient evidence to prove that a hypercoagulability state in hyperthyroidism predisposes to cerebral ischaemia, the presence of antiphospholipid antibodies and other hypercoagulability studies should be performed in patients with thyrotoxicosis and ischaemic events.

BACKGROUND

Arterial cerebral ischaemia has been described in different diseases of the thyroid. Likewise, cerebral venous thrombosis (CVT) has been reported in association with hyperthyroidism. However, the association of arterial and venous cerebral ischaemic events in patients with hyperthyroidism has not been previously described.

Many abnormalities of blood coagulation are known in patients with thyroid dysfunction. Bleeding as well as thrombotic complications have been reported in patients with hyperthyroidism because it is known that thyroid dysfunction alters the coagulation-fibrinolytic system. Yet, the exact pathogenic mechanisms to explain this association have not been elucidated.

CASE PRESENTATION

In July 2010, a 21-year-old Caucasian woman presented to the emergency room with right arm weakness and expression aphasia that had progressed over the previous 7 days. She was healthy until 6 months prior to her presentation when she noticed nervousness, palpitations, weight loss, heat intolerance, tremulousness, insomnia and neck enlargement.

INVESTIGATIONS

A physical examination showed a large goitre, tremor of the extremities and tachycardia (HR=150 bpm). A neurological examination revealed a right homonymous haemianopia, left facial paresis, right upper limb paralysis and expression aphasia. A brain CT and MRI/MR angiography (MRA) showed a left frontal infarct and an occlusion of the left middle cerebral artery (figure 1A–C). Transthoracic echocardiography, cerebrospinal fluid analysis, carotid Doppler ultrasonography and Holter monitoring were all unremarkable. Hyperthyroidism was confirmed (thyroid stimulating hormone <0.05 µUI/mL; free thyroxin (FT4) =5.8 ng/dL) and treatment with methimazole and propranolol was initiated. Additional laboratory examinations were positive thyroid receptor and antithyroglobulin antibodies; normal electrolytes and renal function; and negative virus serology. Seven days after her admission, she experienced a sudden decrease in her level of consciousness and was taken to the intensive care unit (ICU). A brain CT and MRI/MRA showed thrombosis of the sagittal, left transverse and sigmoid sinuses (figure 1D–F). An additional workup was requested and showed increased factor VIII activity (>600%; reference range (RR) 60–150%) and positive antiphospholipid antibodies, but other examinations, including Leiden V factor, homocysteine levels, rheumatoid factor, cryoglobulins and antithrombin III, antinative DNA, antinucleus Hep-2 and antiextractable nuclear antigens antibodies were all normal.

DIFFERENTIAL DIAGNOSIS

Other causes of stroke in a young individual: cardioembolic, vasculitis and moya-moya disease.

TREATMENT

Despite anticoagulation therapy, she developed refractory intracranial hypertension and was treated with a bilateral frontal craniectomy. The patient spent 17 days in the ICU receiving iodine, methimazole, prednisone, propranolol and heparin.

OUTCOME AND FOLLOW-UP

The patient was discharged from the hospital on oral anticoagulants, presenting only expression aphasia without motor deficits.

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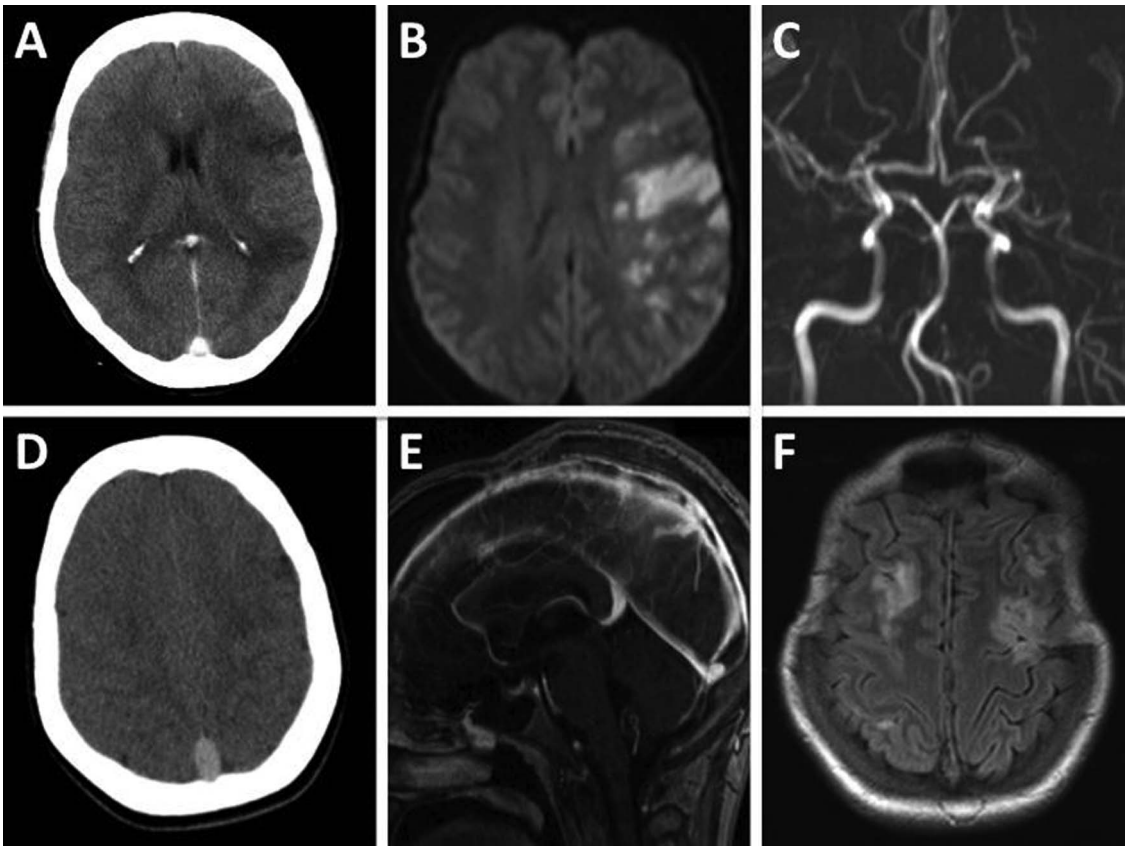

Figure 1 Non-contrast head CT showing frontal and parietal hypodensities. (A) Diffusion-weighted imaging showing areas of restricted diffusion on left middle cerebral artery (MCA) territory. (B) MRI showing an occlusion of the left MCA. (C) Non-contrast head CT with sagittal sinus hyperdensity, suggestive of venous thrombosis. (D) Venous MR angiography showing a superior sagittal sinus, thrombosis with a partial recanalisation (E) and fluid attenuated inversion recovery sequence demonstrating bilateral frontal hyperintensities suggestive of venous infarction and a bifrontal craniectomy (F).

DISCUSSION

Hyperthyroidism is a well-known risk factor for ischaemic stroke in young patients.[1] The most frequent mechanism described is cardioembolic stroke due to atrial fibrillation. However, many other abnormalities of blood coagulation have been described in patients with thyroid dysfunction. Bleeding as well as thrombotic complications have been reported in patients with hyperthyroidism because it is known that thyroid dysfunction alters the coagulation-fibrinolytic system.[2–4] The first clinical association was made in 1913, when Kaliebe described a venous cerebral thrombosis in a thyrotoxic patient.[5] Since then, the incidence of vascular cerebral disease has been estimated at 1:250 000 cases/year, with mortality ranging between 5% and 30%.[2] The procoagulant influences in the thyrotoxic state are haemodynamic factors, dehydration and venous stasis caused by the goitre.

However, because a number of thyroid dysfunctions have an autoimmune pathogenesis, we can expect that other autoimmune disorders involving the coagulation system, such as antiphospholipid syndrome (APS), may be concomitantly described in such patients.[2 3] Thyrotoxicosis alone has been described as a risk factor for ischaemic and CVT in some reported cases, but the concomitant association of arterial and venous thrombosis is an extremely rare situation that can be explained by the presence of APS.[3] There are indications that genetic predisposition can explain the presence of APS in patients with autoimmune thyroid disorders, and it has been suggested that some anticardiolipin antibodies may act as thyrotropin receptor-stimulating antibodies. The hypercoagulable state observed in APS is primarily mediated by the interference of antiphospholipid antibodies in the function of the phospholipid-binding protein β2-glycoprotein I (β2-GPI) thus inhibiting contact activation of the intrinsic coagulation pathway. Crossreactivity between β2-GPI and thyrotropin receptor epitopes has been hypothesised as a pathogenic mechanism explaining the association between these two autoimmune conditions.[2 3] This case represents a rare but noteworthy condition where a hypercoagulability state, represented by thyrotoxicosis, APS and a coagulation test disorder should be suspected, particularly when it occurs in a younger individual.

Learning points

- Hyperthyroidism is an autoimmune thyroid disorder that may appear associated with other autoimmune disorders.
- Cardiovascular effects of hyperthyroidism are well known, but often associated with the presence of arrhythmia.
- Thrombotic complications have been reported in patients with hyperthyroidism because it is known that thyroid dysfunction alters the coagulation-fibrinolytic system.
- Fast diagnosis and approach should be performed when an atypical presentation occurs in a young patient.
- A multidisciplinary team, including endocrinologists, neurologists, neurosurgeons, haematologists, rheumatologists, despite nurses and physiotherapists is needed to support this type of patient.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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