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Ischemic Stroke and Intraventricular Hemorrhage in Moyamoya Syndrome Associated With Graves' Disease

A Case Report

Mufang Huang, MM, Siqiang Tang, MM,* Yongbiao Zou, MD,* Ge Yang, MD,† Yuyu Nan, MD,‡ Yanfang Li, MM,* and Chunhua Zhang, MD**

Introduction: Moyamoya syndrome is commonly associated with sickle cell anemia, neurofibromatosis type 1, cranial therapeutic irradiation, and Down syndrome. However, it is rare for Moyamoya syndrome associated with Graves' disease.

Case Report: Here we report a case of Moyamoya syndrome associated with Graves' disease in a 19-year-old girl with sudden weakness of the right arm, progressive caries, and alopecia for 4 years. Brain magnetic resonance imaging revealed acute intraventricular hemorrhage and cerebral infarction of left middle cerebral artery territory and narrowing of the proximal portion of bilateral anterior and middle cerebral arteries.

Conclusion: Acute cerebral infarction and intraventricular hemorrhage can occur simultaneously in Moyamoya syndrome associated with Graves' disease. Hydrocortisone, combined with prothiouracil medication, can correct thyroid dysfunction and improve neurological function. Caries may be the first symptom of Graves' disease.

Key Words: stroke, Moyamoya syndrome, Graves' disease

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Moyamoya syndrome is a progressive cerebrovascular disease characterized by stenosis or occlusion of the end of the internal carotid artery, proximal anterior cerebral artery, and proximal middle cerebral artery. Accompaniment of abnormal vasculature, also known as Moyamoya vessels, derive from near sites of steno-occlusion arteries.[1] Graves' disease is an autoimmune disorder in which autoantibodies to thyroid-stimulating hormone receptors cause high levels of thyroid hormone in blood, leading to hyperthyroidism. Moyamoya syndrome usually appears with some causative systemic disorders. These known diseases include sickle cell disorder, neurofibromatosis type 1, Down disorder, cranial therapeutic irradiation, and other rare disorders. However, Moyamoya syndrome associated with Graves' disease is rarely published, and its underlying mechanism is still unknown.

CASE PRESENTATION

A 19-year-old girl visited the emergency room with sudden weakness of the right limb for 1 day, and thyrotoxicosis, progressive caries and alopeca for 4 years (Fig. 1A). At the age of 15, the patient developed dental caries, which the doctor examined and found to be caused by thyrotoxicosis, and took methimazole regularly for 2 years. When she was 17 years old, she stopped methimazole by herself. From then on, she began to lose her hair and her periods were also irregular. However, the patient has no family history of hyperthyroidism, hypertension, diabetes, epilepsy, cerebral infarction, cerebral hemorrhage, and other medical histories. Examination at the time of admission

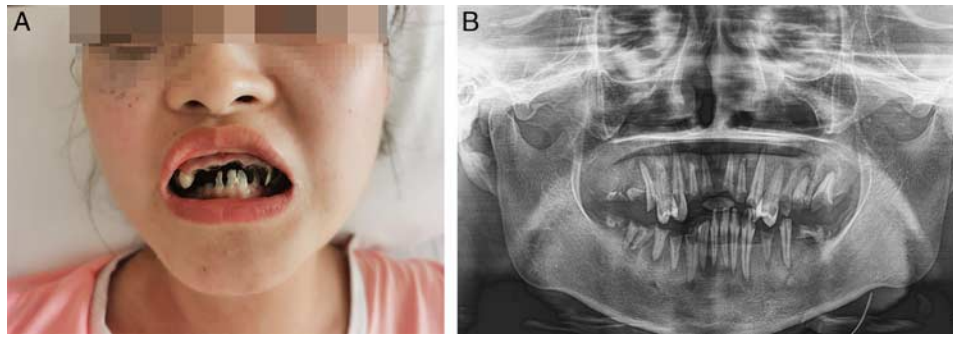

FIGURE 1. (A) The patient had severe dental caries and severe loss of upper and lower teeth, with multiple residual crowns and roots. (B) The panoramic image of oral cavity indicated multiple residual crowns and roots on both sides of mandible.

From the *Shaoyang Central Hospital, Shaoyang; †Hunan Children's Hospital, Hunan; and ‡The First Affiliated Hospital of Zhejiang University, Zhejiang, China.
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Correspondence to: Mufang Huang, MM, Department of Neurology, Shaoyang Central Hospital, 36 Qianyuan Lane, Daxiang District, Shaoyang City, Hunan Province, 422000, China. E-mail: 774113025@qq.com.

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revealed a blood pressure of 158 mm Hg/72 mm Hg, heart rate of 142 beats per minute, sinus tachycardia on electrocardiogram, respiratory rate of 28. Physical examination showed obvious goiter and exophthalmos. Neurological examination observed her right limb paralysis with an initial score on the National Institutes of Health Stroke Scale (NIHSS) of 5.

Investigation

An initial head computed tomography (CT) scan was ordered for suspected stroke, which confirmed acute intraventricular hemorrhage and cerebral infarction of left middle cerebral artery territory (Figs. 2A–B). Diffusion-weighted imaging found a high signal on left middle cerebral artery territory (Fig. 2C), and apparent diffusion coefficient discovered low

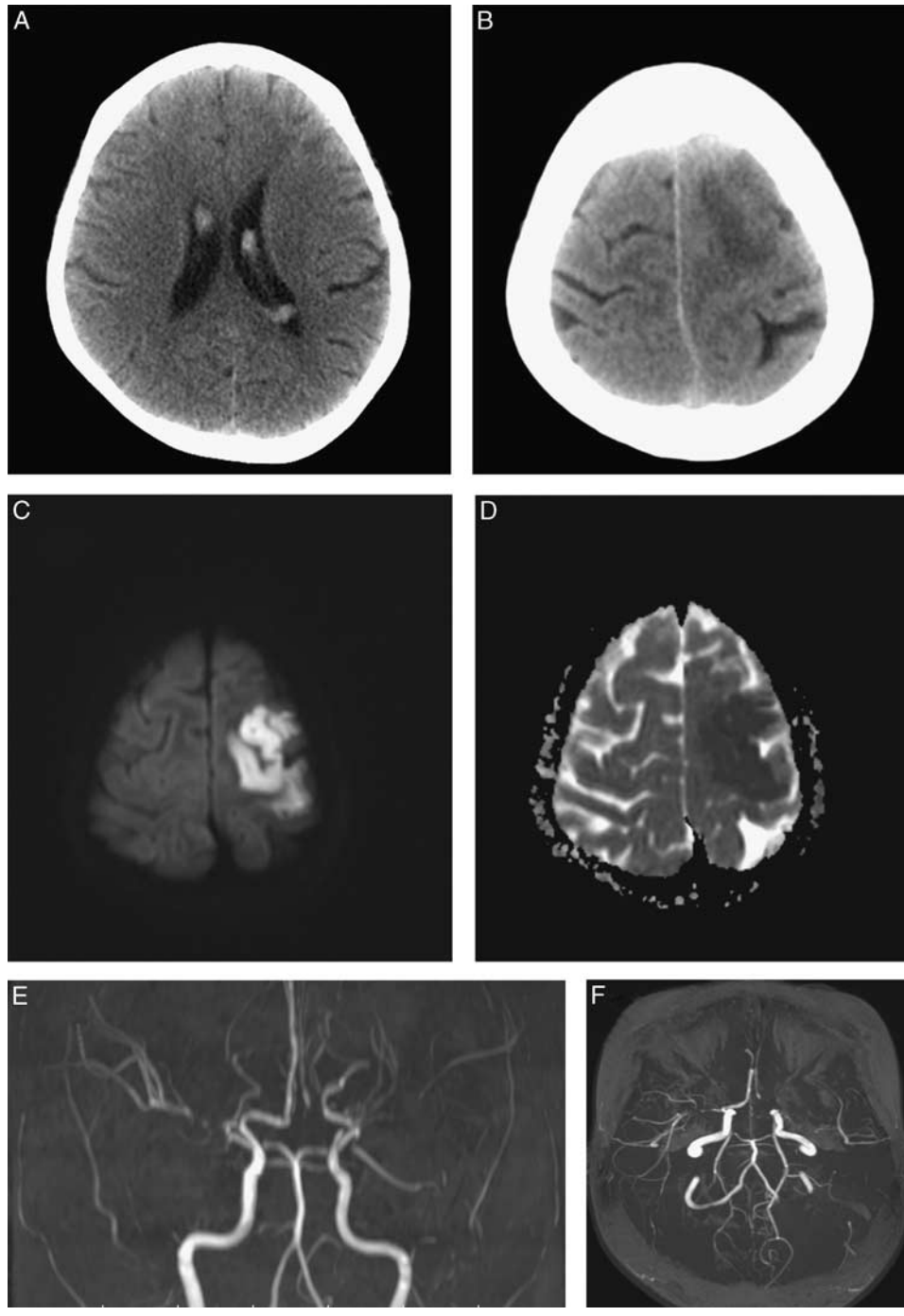

FIGURE 2. (A and B) Initial head computed tomography scan showed acute intraventricular hemorrhage and cerebral infarction of left middle cerebral artery territory. (C and D) Initial brain magnetic resonance imaging: diffusion-weighted imaging found high signal on left middle cerebral artery territory, and apparent diffusion coefficient discovered low signal on the same part. (E and F) Magnetic resonance angiography showed occlusion of bilateral proximal portion of the anterior and middle cerebral arteries, and these occluded vessels are surrounded by numerous small vessels.

signal on the same part (Fig. 2D). Magnetic resonance angiography showed occlusion of bilateral proximal portion of the anterior and middle cerebral arteries (Figs. 2E–F). We performed a lumbar puncture, and the presence of bloody cerebrospinal fluid further confirmed the ventricular hemorrhage. The panoramic image of oral cavity indicated multiple residual crowns and roots on both sides of mandible (Fig. 1B).

The thyroid enlarged diffusely both in thyroid ultrasonogram and magnetic resonance imaging (MRI). Thyroid scanning showed obvious increase of the function of uptaking radionuclides Te-99. Echocardiography indicated moderate mitral regurgitation and Sinus tachycardia, and there was no atrial fibrillation on 24-hour Holter monitoring. Contrast-enhanced ultrasonography of the right heart showed no obvious abnormality.

Treatment

Therapy was scheduled on day 1 of admission with hydrocortisone 100 mg intravenous drip Q12h, propylthiouracil 200 mg po Q8h (first dose doubling), propranolol 20 mg po Q8h, and nutrition support therapy. Two days after admission, the patient's right side weakness deteriorated further. Three days after admission, her neurological deficits did not worsen. After the treatment of hydrocortisone and propylthiouracil, the patient's symptoms remained stable and there was no further symptoms deterioration. After 11 days of treatment, re-examination of head CT indicated absorption of ventricular hemorrhage (Figs. 3A–B). Sixteen days after admission, the patient's NIHSS was 0 and the signal of infarction lesion on MRI was weakened (Figs. 3C–D). In thyroid function test, freeT3 was increased to 4.65 Pg/mL (reference: 1.71 to 3.71 Pg/mL). Free T4 was 1.37 ng/dL (reference: 0.70 to 1.48 ng/dL). Thyroid-stimulating hormone was decreased to 0 μIU/mL (reference: 0.35 to 4.94 μIU/mL).

DISCUSSION

Moyamoya disease can be found in people of different ethnic groups and has a high prevalence among individuals of East Asian heritage, with the top 3 including Japanese, South Korea, China.[2] However, the mechanism of Asian susceptibility to Moyamoya disease is unclear, and there has been evidence that the prevalence of Moyamoya disease is much higher in Chinese than in Caucasians.[3] The incidence peaks occurred in 2 age groups: children aged about 5 and adults in their 40s. There are almost twice as many female patients as male patients.[4–6]

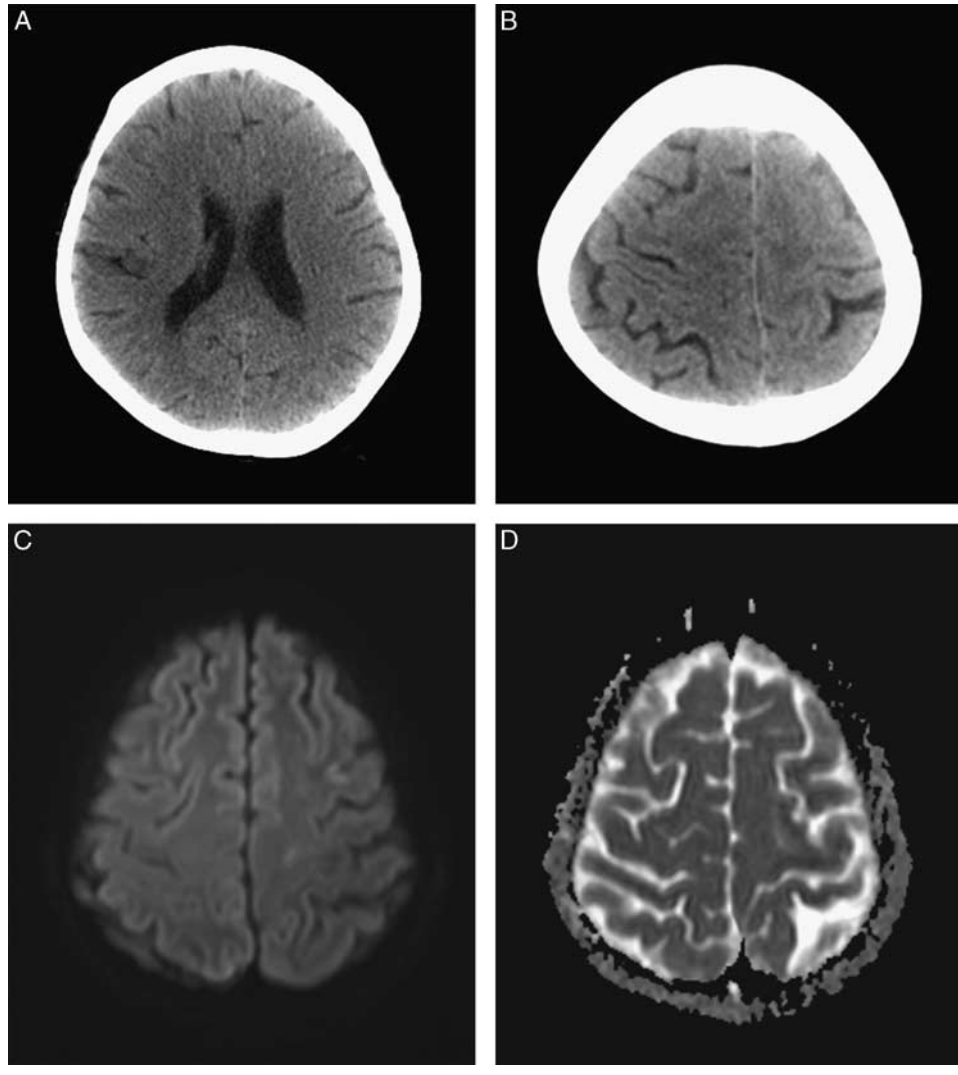

FIGURE 3. (A and B) After 11 days of treatment, re-examination of head computed tomography indicated absorption of ventricular hemorrhage and disappearance of infarction lesions. (C and D) After 16 days of treatment, re-examination of head magnetic resonance imaging indicated disappearance of infarction lesions.

It is very rare for a patient to have both hyperthyroidism and Moyamoya disease. In our case, some new information was provided. First, caries was the initial symptom in this case, and it progressed rapidly. Second, intraventricular hemorrhage and cerebral infarction occurred together in the recurrence of hyperthyroidism. Third, hydrocortisone combined with prothiouracil is effective in this patient. Fourth, after the treatment of hydrocortisone plus prothiouracil, the symptoms of the patient returned to normal, and the re-examination of CT and MRI indicated that the intraventricular hemorrhage was absorbed.

The coexistence of the Moyamoya syndrome and Graves' disease has been outlined in several studies.[7,8] The pathogenesis of Moyamoya disease and hyperthyroidism is still unclear. It is hypothesized that both genetic and immune factors play an important role in their pathogenesis.[9] Moyamoya disease and hyperthyroidism have an obvious familial tendency with female predominance.[10] Several papers mentioned the hyperthyroidism-associated Moyamoya syndrome and variants in *RNF213* gene.[11] Meanwhile, autoimmunity is hypothesized to contribute to common pathogenesis. Kitahara et al[9] reported autoantibodies of double-stranded deoxynucleotide and antinatural T-cell antibodies in patients with Moyamoya disease. T-cell dysfunction may be the pathophysiological mechanism of hyperthyroidism and Moyamoya disease.[12] Plasma exchange and glucocorticoid therapy can improve symptoms in patients with hyperthyroidism and Moyamoya disease during thyrotoxicosis.[13]

Until now, it remains unknown why ischemic stroke occurs during thyrotoxicosis in Moyamoya patients. Detailed evidence about this mechanism is inadequate. Circulatory system disorders, including tachycardia, hypertension, atrial fibrillation, are associated with cerebral thromboembolism. Also, free thyroxine levels were positively correlated with hyperhomocysteine, which could accelerate atherosclerosis.[14] In patients with hyperthyroidism, increased levels of coagulation factor VIII lead to hypercoagulability, which also contributes to ischemic stroke events in patients with Moyamoya disease.[15] Cerebral hemorrhage caused by Moyamoya disease is usually manifested as intraventricular hemorrhage, cerebral parenchymal hemorrhage and subarachnoid hemorrhage. As a branch of the internal carotid artery, the pressure of the anterior choroid artery is higher than that of the dilated smoky vessel, which leads to a higher risk of rupture and bleeding. Abnormal expansion or prolongation of the anterior choroid artery may be the main cause of ventricular hemorrhage in Moyamoya patients.[16]

Oral manifestations of thyrotoxicosis include increased susceptibility to dental caries, periodontal disease, maxillary or mandibular osteoporosis, accelerated tooth emergence, and burning mouth syndrome.[17] In our case, caries was the initial symptom. Therefore, it is important for dentists to be aware of thyroid disease Dentists may be the first to suspect serious thyroid disease and play an important role in detecting thyroid abnormalities. Dental treatment must be modified when treating patients with thyroid disease.

CONCLUSIONS

Acute cerebral infarction and acute ventricular hemorrhage may occur simultaneously in Graves' disease combined with Moyamoya disease. The specific pathogenesis is still lacking and needs to be clarified by more studies. The therapeutic effect of hydrocortisone combined with prothiouracil was significant. After treatment, CT and MRI re-examination showed that the infarct lesions weakened, which indicated that hydrocortisone combined with prothiouracil may improve neurological function in the acute stage. Dental caries can be the first manifestation of Graves' disease, and dentists should pay enough attention to monitoring thyroid function.

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