中文題目：毛毛樣血管病症候群與甲狀腺毒症：病例報告與文獻回顧

英文題目：Moyamoya Syndrome and Thyrotoxicosis: A Case Report and Literature Review

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Introduction:

Moyamoya disease describes a cerebrovascular disorder characterized by stenosis or occlusion of the internal carotid arteries and their proximal branches. The compensatory development of collateral vessels creates a moyamoya, meaning “puff and smoke,” appearance on angiography. Ever since its first observation in 1957, the condition can now be further divided into two categories. Those with typical moyamoya vasculopathy related to well recognized risks are categorized as having moyamoya syndrome (MMS), whereas patients without identifiable causes are considered to have moyamoya disease. Among various risk factors for MMS, a growing body of evidence has discovered its relationship with hyperthyroidism. Here, we report a rare case with concomitant thyroid storm and MMS, and make a systematic review to analyze the clinical features, pathogenesis and treatment of MMS associated with hyperthyroidism.

Case Description

A 22-year-old woman was diagnosed of Graves’ disease (GD) in 2010 but had irregular treatment. She used to work in night club and was on illicit drugs several months ago. She was brought to our emergency department on February 22nd, 2016 due to fever and progressive conscious disturbance for several days. She visited our emergency department twice in the past one week for watery diarrhea, abdominal pain, nausea and vomiting but all ended up with discharged against medical advice after her symptoms improved.

Upon arrival, she was disoriented with body temperature 36℃, pulse rate 182 beats/min, respiratory rate 26 /min and blood pressure 123/63 mmHg. Physical exams disclosed Grade III goiter with bruit and moist skin. Electrocardiogram showed extreme sinus tachycardia. Her complete blood count was unremarkable but biochemistry data yielded alanine aminotransferase 71 IU/L (14-40 IU/L), total bilirubin 1.52 mg/dL (0.3-1.2 mg/dL), direct bilirubin 0.38 mg/dL (0.1-0.5mg/dL), serum creatinine 0.87 mg/dL (0.4-1.2 mg/dL), serum sodium 156 mEq/L (136-141 mEq/L). Toxic screen panel and brain computed topography were arranged for evaluation of altered consciousness and results were insignificant. Thyroid echo revealed thyroid inferno and diffuse goiter. She was admitted for thyroid storm treatment. Propylthiouracil 100 mg, propranolol 20 mg and Lugol solution 5 drops were given orally every six hours in addition to intravenous hydrocortisone 100 mg

every 8 hours. Aggressive volume repletion and empiric antibiotics were also administrated. Final thyroid profile results showed TSH < 0.03 uIU/mL (0.25 ~4.0 uIU/mL), Free T4: 5.13 ng/dL (0.89 ~1.79 ng/dL), Total T3: 401.2 ng/dL (78 ~182 ng/dL), TSH Receptor Antibody: 88.45% (< 10%), Anti-microsomal Antibody: 981.60 IU/mL (1-16 IU/mL), compatible with Graves' disease.

Her vital signs gradually stabilized but conscious level remained impaired. Besides, slurred speech was noticed since the first day of her admission, which persisted in the following days. Brain magnetic resonance imaging (MRI) was arranged for further survey. To our surprise, segmental luminal narrowing involving left distal supra-clinoid internal carotid artery (ICA) to A1 of left anterior cerebral artery (ACA), M1 of left middle cerebral artery (MCA) and proximal A1 of right ACA were seen. The result raised the suspicion of autoimmune vasculitis or moyamoya vasculopathy. We checked autoimmune markers including Anti-nuclear antibody, Anti-dsDNA, Anti-Cardiolipin IgG/IgM, Anti β 2 glycoprotein IgG, p-ANCA, c-ANCA, C3, C4, rheumatic factor and lupus anti-coagulant but all were within normal limit. Meanwhile, angiography was also performed, which disclosed significant narrowing over left distal ICA, M1 and A1 segments, irregularity over right A1 and A2 segments with collateral circulation, compatible with MMS.

The patient recovered from thyroid storm and her slurred speech gradually resolved after adequate control of her thyroid function. She didn't receive bypass surgery and was discharged three weeks later. No neurologic symptoms ever happened again during follow up.

Discussion

Several diseases such as Down's syndrome, sickle cell disease, neurofibromatosis type 1 have been associated with MMS and hyperthyroidism remains a rare cause. Following the description of Graves' thyrotoxicosis and moyamoya disease by Kushima et al, the connection between these two seemingly unrelated diseases has gradually being explored. In our systemic review, total 104 cases were identified in 25 English literatures but only 63 cases had sufficient details for analysis.

We found that GD associated with MMS occurred more often in woman (53/63 patients [84%]) and in Asian ethnicity (56/63 [89%]). Mean age of MMS onset was 30 ± 14 years (Range 7 – 62 years) and could strike both children and adults with GD. The majority of patients had their GD diagnosed before (31/63 [49%]) or simultaneously with MMS (27/63 [43%]) but the reverse was also found. Although uncontrolled thyrotoxicosis is a strong precipitating factor for MMS, some patients are euthyroid (7/63 [11%]) during disease onset. There is no universal clinical presentation but motor deficit (42/63 [67%]) is the most common symptom followed by aphasia and headache. Three quarters of patients underwent bypass surgery for

MMS while the remaining only received treatment for GD. Both treatment modalities resulted in good outcome. Fatality is rare (2/63 [3%]) if timely treated.

How MMS develops in patients with GD remained controversial but several theories have been proposed. First, genetic susceptibility may play a role as Tokimura et al reported MMS and GD in two family members. One of the genetic loci for moyamoya disease on chromosome 8q23 is close to a gene locus of autoimmune thyroid disease spanning 8q23-q24, although the responsible gene still remained to be identified. Second, several studies also support the central role of autoimmunity because elevated thyroid antibodies were frequently seen not only in patients of MMS with GD but also in those having moyamoya disease without thyroid disease. Third, altered hemodynamics in brain circulation caused by thyrotoxicosis also contributes to the damages and ultimate obliterations of affected vessels. As for treatment options, there is still no consensus for optimal treatment owing to the rarity of this disease. The cornerstone is to treat hyperthyroidism promptly and avoid sudden surge of thyroid function. Bypass surgery is indicated for those with severe vascular compromise either clinically or angiographically. Prognosis is mostly benign if treated promptly and properly.

Conclusion

MMD associated with GD is a rare disease. Clinical alertness is necessary for prompt recognition. Exact mechanism remains elusive but probably encompasses genetic susceptibility, autoimmunity and altered hemodynamics in brain circulation. Ischemic symptom could be debilitating and sometimes fatal but with proper treatment, most patients obtain full recovery.