

## Case Report

# A rare case of pituitary dysfunction with Moyamoya disease

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### ABSTRACT

مرض مويامويا هو مرض انسداد وعائي مزمن ومتقدم مجهول السبب يصيب الفروع الشغائية داخل الجمجمة للشريان السباتي الداخلي. فشل هرمون النمو، وخلل في الغدة الدرقية، وانخفاض هرمون الكورتيزول هي عواقب لقصور الغدة النخامية. فتاة تبلغ من العمر 14 عامًا تعاني من قصر القامة تعاني من ضعف في الجانب الأيمن مرتبط بخلل في التلغظ. أظهر اختبار التحليل الهرموني وجود خلل في الغدة النخامية الأمامية أظهر انخفاضًا في حجم الغدة النخامية. أظهر تصوير الأوعية الدموية الدماغية مناطق متعددة من تضيق الشريان السباتي الداخلي الأيمن. أظهر تصوير الأوعية الدموية بالرنين المغناطيسي تضيقًا في المنطقة فوق السرج من الشريان السباتي الداخلي الشغائي. يعد خلل الغدة النخامية المرتبط بمرض مويامويا نادرًا ولكن يجب اعتباره تشخيصًا تفرقيًا لأي مريض يعاني من قصور الغدة النخامية. قد يرتبط خلل الغدة النخامية تحت المهاد نتيجة لإقفار الشريان السباتي بمرض مويامويا. ويحتاج هؤلاء المرضى إلى متابعة دقيقة وإجراء اختبارات هرمونية.

Moyamoya disease is an idiopathic chronic and progressive vaso-occlusive disease of the bilateral intracranial branches of the internal carotid artery. Growth hormone failure, thyroid dysfunction, and low cortisol hormones are consequences of hypopituitarism. A 14-year-old girl with short stature presented with right-sided weakness associated with dysarthria. Ahormonal assay test showed abnormality of the anterior pituitary hormones. Magnetic resonance imaging of the brain and pituitary gland showed a reduction in the size of the adenohypophysis. A cerebral vessel angiogram showed multiple areas of stenosis in the right internal carotid artery. Magnetic resonance angiography demonstrated stenosis at the suprasellar region of the bilateral internal carotid artery. Pituitary dysfunction associated with moyamoya disease is rare but must be considered as a differential diagnosis for any patient with hypopituitarism. Hypothalamopituitary dysfunction as result of carotid ischemia might be associated with moyamoya disease. Such patients require close follow-up and hormonal assay tests.

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Moyamoya disease is a rare idiopathic chronic and progressive vaso-occlusive disease of the bilateral intracranial branches of the internal carotid artery, especially the main arteries (the anterior, middle cerebral, and posterior communicating arteries) of the circle of Willis. Moyamoya syndrome is a vasculopathy associated with conditions like sickle-cell disease, neurofibromatosis type I, Down syndrome, and congenital cardiac anomalies.<sup>1-2</sup> Moyamoya has a bimodal two-peak distribution with the highest peak occurring at 5–9 years of age and the second peak occurring at 45–49 years.<sup>2-3</sup>

Hypopituitarism is the low production of one or more pituitary hormones like growth hormone, thyroid-stimulating hormone (TSH), and adrenocorticotropic hormone (ACTH). The link of between secondary dysfunction in pituitary hormones and moyamoya disease is not well understood. We report a case of a girl diagnosed with hypopituitarism associated with moyamoya disease.

**Case Report.** A 14-year-old girl presented with hemiparesis and complained of multiple episodes of right-sided weakness. This weakness started on 2009 at the age of 6 years and lasted for 30 min. It mainly occurred on the right side of the body and was followed

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by unilateral headache. It was not increased by the Valsalva maneuver or vomiting. Although she took paracetamol (500 mg) and ibuprofen (200 mg) for her headaches, the ailments did not improve. She also had short stature. She was diagnosed with hypothyroid, and the short stature was due to deficiency of growth

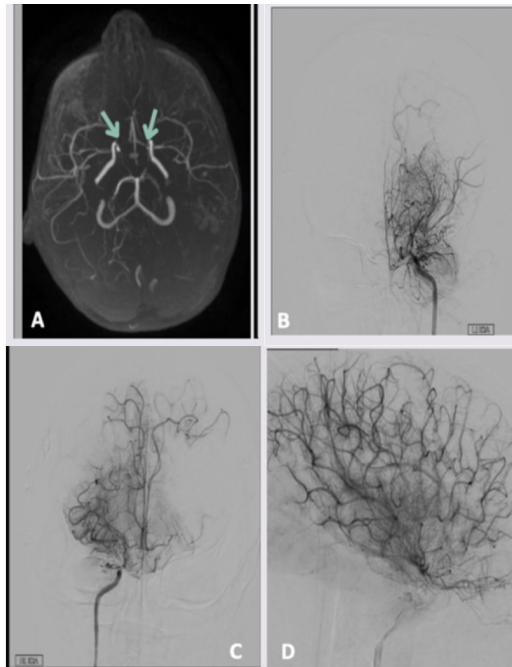
hormone. At this stage, she was seen by a neurologist and diagnosed with migraine.

In 2016, the weakness initially occurred once a month and increased to 2–3 times a month. The patient was not able to walk or hold objects with her right hand. No paresthesia, numbness, or loss of vision was observed, and she had no history of a decreased level of consciousness. She then developed multiple episodes of seizure attacks that required admission for evaluation. Her perinatal and antenatal histories were unremarkable and were developmentally normal. The patient’s health records indicated consanguinity in the family. The family had no recorded history of migraine or any neurological disorder.

**Clinical findings.** We identified no dysmorphic features. The patient’s blood pressure was 98/55mmHg, and her pulse was 103 beats per minute (bpm). She was alert, cooperative, conscious, and not disoriented in regard to people, time, and place. Regarding growth parameters, her weight was 27.8 kg (-1 standard deviation (SD) below the 3rd percentile), her height was 137 cm (-3 SD of the 3rd percentile), and her head circumference was in the 2nd percentile.

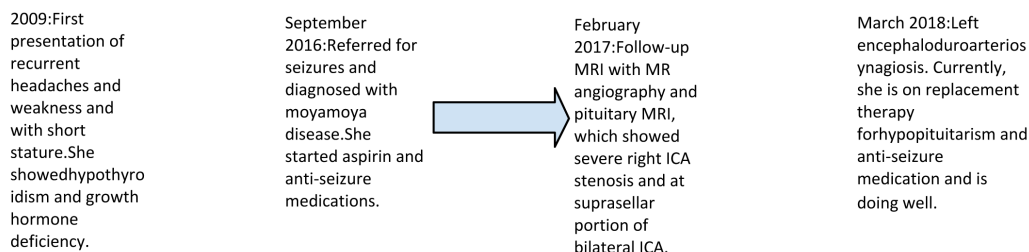
In the fundoscopic examination, her confrontation visual fields were normal, and there was no facial asymmetry. Her pupils were equally reactive to light and accommodation at 4 mm. Extra-ocular movements were intact. The tongue and uvula were well centralized.

A motor examination revealed hypertonia in the right upper and lower limbs. Her reflexes were +3 in the right upper and lower limbs. We observed no clonus in the plantar. The power in the right upper and lower limbs was +4 according to the Medical Research Council (MRC) grading. She had normal cerebellar and sensory examinations, her gait was spastic, and her skin and spine examinations were unremarkable.



**Figure 1** - Case 1A: An MR angiography scan of the brain demonstrating narrowing of the suprasellar portion of the internal carotid artery, which was bilaterally more on the left side, B, C, D: cerebral angiogram showing multiple areas of stenosis in the right internal carotid artery and significant collateral circulation from the posterior cerebral arteries and moyamoya vessels.

### Timeline of the sequences of the events



**Figure 2** - Timeline sequences of the events, diagnosis, and management.

**Table 1 -** Clinical results of hormonal assay.

Hormones	Result before intervention	Result after intervention (surgery and hormonal therapy)	Normal
Follicular stimulating hormone (FSH)	10.1 IU/L		1.5–12.4 IU/L
Luteinizing hormone (LH)	4.5 IU/L		1–11.4 IU/L
Thyroid-stimulating hormone (TSH)	7.8 mIU/L	0.4 mIU/L	0.27–4.2 mIU/L
Free T4	19.2 pmol/L		12–22 pmol/L
Adrenocorticotrophic hormone (ACTH)	0.9 pmol/L	3.8 pmol/L	1.6–13.9 pmol/L
Growth hormone level	10.14 pmol/L	21.6 pmol/L	18–44 pmol/L
Insulin growth factor 1	5.19 nmol/L	37.7 nmol/L	29.4–129.5 nmol/L

**Radiological features.** Magnetic resonance imaging (MRI) of the brain and pituitary gland showed a reduction in the size of the adenohypophysis. Her parasellar and parasellar spaces were intact. A cerebral angiogram of the blood vessels showed multiple areas of stenosis in the right internal carotid artery. The M1 and A1 segments showed significant collateral circulation from the posterior cerebral arteries and moyamoya vessels. These changes were consistent with moyamoya disease.

A magnetic resonance (MR) angiography scan of the brain demonstrated narrowing of the suprasellar portion of the internal carotid artery, which was bilaterally more on the left side. Moreover, the middle cerebral arteries with multiple collaterals were bilaterally more pronounced on the left side, which was associated with a reduced flow signal and the left posterior cerebral artery. The MR cerebral venography of the brain using the prominent cortical veins in susceptibility-weighted imaging (SWI) showed an increase in deoxyhemoglobin and hypoperfusion. The image was consistent with moyamoya disease stage 2. We obtained an electroencephalogram for her recurrent seizures, which appeared intermittently in the left hemisphere with no potential epileptogenic discharges.

**Laboratory findings.** Table 1 shows the results of the hormonal assay test. Her TSH level was 7.8 mIU/L. An ACTH stimulation test showed a low level of 0.9 pmol/L (1.6–13.9 pmol/L), and her growth hormone level was 10.14 pmol/L (18–44 pmol/L). Her level of insulin growth factor 1 was 5.19 nmol/L (29.4–129.5 nmol/L).

The patient received a referral for neurosurgery and underwent rightencephaloduroarteriosynangiosis. Later, she came to the clinic for follow up at the age of 16 years, and her hormonal assay parameters had normalized. After one treatment with levothyroxine (75 µg), her TSH level decreased to 0.4 mIU/L (0.27–4.2 mIU/L). She had also started taking growth hormone at 1.5 units subcutaneously daily, and her growth hormone level

was 21.6 pmol/L (18–44 pmol/L). After she started hydrocortisone at 5 mg twice daily, her ACTH level improved to 3.8 pmol/L (1.6–13.9 pmol/L).

**Discussion.** Our patient was short stature with hypothyroidism and received a diagnosis of hypopituitarism based on clinical and laboratory findings. There is insufficient understanding of the link between secondary pituitary dysfunction and moyamoya disease according to the literature. A proposed mechanism involves the vascular supply of the hypothalamic-pituitary regions arising from the anterior cerebral arteries and the internal carotid arteries (superior hypophyseal and meningo-hypophyseal arteries). These arterial branches undergo stenosis or occlusion in moyamoya disease. Progression of chronic cerebrovascular insufficiency may result in pituitary dysfunction.<sup>4</sup> A thorough search of the literature revealed that this is the first case report of moyamoya disease associated with pituitary dysfunction in Saudi Arabia.

Pande et al. reported a 22-year-old female who presented with secondary amenorrhea and showed abrupt loss of three consecutive menstrual cycles. Her TSH, thyroxine, and post-Synacthen cortisol levels were normal, and she presented with high prolactin levels. Contrast-enhanced MRI revealed partially empty sella syndrome with enhanced linear and curvilinear structures in the suprasellar cistern, which was similar to findings in our patient.<sup>2</sup>

Our patient showed narrowing of the suprasellar portion of the internal carotid artery. MacKenzie et al. also reported this in a 7-year-old boy with moyamoya disease, who had growth hormone failure and short stature.<sup>5</sup> Gungor et al.<sup>6</sup> reported dysfunction of the pituitary gland secondary to involvement of the sellar-suprasellar internal carotid artery in a 71-year-old elderly male. The patient had symptoms of hypopituitarism, hyperprolactinemia, and visual-field defect. The

findings revealed sellar-suprasellar aneurysm causing compression on the hypothalamo-pituitary axis.<sup>6</sup>

A hypothesis that could explain the link between conditions is pituitary insufficiency secondary to chronic stenosis or narrowing of the internal carotid artery leading to hypoperfusion in part of the hypothalamic region. This might explain the disturbance of the hypothalamopituitary axis in moyamoya disease.<sup>7</sup> Further progression of the disease may lead to the development of multiple pituitary-hormone insufficiencies.<sup>8</sup>

In conclusion, pituitary dysfunction associated with moyamoya disease is rare but must be considered during differential diagnosis for any patient with hypopituitarism. Ischemia of the internal carotid artery causes hypoperfusion in the hypothalamus, which might explain the disturbance of the hypothalamopituitary axis in moyamoya disease. The progression of the disease may lead to the development of multiple pituitary-hormone insufficiencies. Thus, such patients need close follow-up with hormonal assay tests.

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