Rare disease

Moyamoya disease in which pentazocine treatment caused cerebral infarction

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Summary

A 37-year-old man was admitted to hospital for treatment of perineum damage and haematoma in the scrotum. His consciousness deteriorated after two intramuscular injections of pentazocine 15 mg. Faint low signals in the left putamen to frontal island and frontal lobe and obtundation of the corticomedullary junction were apparent on head CT, which led to suspicion of cerebral infarction. MR angiography showed bilateral obstruction of the middle cerebral artery and moyamoya disease was diagnosed. Treatment with edaravone, argatroban and heparin was ineffective for opening the middle cerebral artery and serious after effects occurred. This case suggests that cerebrovascular accident should be suspected in a young patient with disturbance of consciousness but stable breathing and circulation, particularly if previous drug treatment has affected brain circulation. Moyamoya disease should be suspected based on medical or family history. In such a case, MR angiography is required for early diagnosis to facilitate treatment by re-establishment of blood circulation.

BACKGROUND

Non-arteriosclerosis-related disease should be considered as a cause of cerebral infarction in a young patient. Moyamoya disease is an important non-arteriosclerosis-related disease that is divided into ischaemia and bleeding types. Treatment for bleeding type moyamoya disease has not been established, whereas the efficacy of re-establishment of the blood circulation has been shown for the ischaemia type. Serious after effects can be avoided by early detection, early treatment, appropriate surgical management and guidance in subsequent everyday life. We experienced a case of moyamoya disease in which the patient had repeated transient cerebral ischaemic attacks caused by haemodynamic effects induced by pentazocine treatment. Broad cerebral infarction occurred and the patient had serious after effects. This is the first reported case of moyamoya disease with cerebral infarction caused by pentazocine.

CASE PRESENTATION

The patient was a 37-year-old man who was previously healthy and had no history of transient paralysis or loss of consciousness. He fell from an iron fence of 90 cm in height and received a blow on the perineum. Scrotum pain and swelling appeared gradually and he visited a urology practitioner early in the morning on the day after the accident. He was admitted to hospital for perineum damage and haematoma in the scrotum. An intramuscular injection of pentazocine 15 mg for sharp pain was given at 07:30. His consciousness level deteriorated at 09:30 and he became unresponsive. Head CT showed no abnormalities and the patient recovered without treatment after about 30 min. A second intramuscular injection of pentazocine 15 mg for increasing sharp pain was given at 10:30 and his consciousness level deteriorated again from about 11:30. Head CT still showed no abnormalities, but this time his

consciousness level did not recover and he was moved to our emergency and critical care centre at 20:30.

In family history, an uncle on the father's side had cerebral haemorrhage at 60 years old and two aunts on the father's side had cerebral haemorrhage at 62 and 66 years old. His consciousness level at arrival was Glasgow Coma Scale (GCS) E(1)V(1)M(4)=6. Vital signs were blood pressure 180/110 mm Hg, tachycardia pulse 120/min, respiratory rate 20 breaths/min, body temperature 38.9°C and saturation oxygen 99%. There was significant swelling of part of the scrotum and this region was dark brown. His pupils were dilated to 2.5 mm and showed a pupillary light reflex. The right upper and lower limbs had normal motion, but motion of the left lower limb was abnormal. The Babinski sign was positive on both sides. The deep tendon reflex was normal and there was no laterality. There were no important findings in blood and urinary tests.

INVESTIGATIONS

On head CT, a faint low signal was found in the left putamen to the frontal island and frontal lobe with obtundation of the corticomedullary junction (figure 1). Based on these findings, we suspected acute cerebral infarction. Head MRI gave broad high intensity signals on both sides of the middle cerebral artery (MCA) in diffusion-weighted imaging consistent with acute cerebral infarction (figure 2). Bilateral obstruction of the M1 segment of the carotid artery was suspected based on MR angiography (MRA) (figure 3).

OUTCOME AND FOLLOW-UP

The patient was not alert and he had paralysis of the left upper and lower limbs with bilateral positive Babinski signs. Bilateral blockage of the pyramidal tract was suspected and brainstem disorder was also assumed, but the cranial neuropathy was unclear. Moyamoya disease was

Figure 1 Head CT showing a low signal in the left putamen to the frontal island and frontal lobe and obnubilation of the corticomedullary junction.

diagnosed based on head CT and MRI findings suggesting acute cerebral infarction, the obstruction of the MCA on MRA, the age of the patient, the apparent absence of embolism and vasculitis, and the absence of risk factors for arteriosclerosis. We suspected that pentazocine administered for sharp pain led to a fall in blood pressure and caused cerebral infarction through a haemodynamic mechanism. Treatment was performed following the protocol for atheroma blood clot-related cerebral infarction. We started edaravone, argatroban and heparin and performed MRA every few days, but bilateral re-opening of the MCA did not occur. Bedside rehabilitation was initiated 1 week after the injury. Gastrostomy was performed after 6 weeks and the patient was moved to another hospital to continue rehabilitation after 8 weeks. His consciousness level at the time of discharge was restored to GCS E(4)V(2)M(6)=12 in comparison to GCS E(1)V(1)M(4)=6 at arrival. He was unable to speak properly at discharge, but he appeared to understand some words. He cried and spoke incomprehensibly. Limb movement was improved slightly, but quadriplegia of left predominance remained.

DISCUSSION

Moyamoya disease is associated with cerebrovascular accident in young patients. This disease is more common in Japan and East Asia compared to Europe and America with a clear ethnic difference. In reported cases, the onset age has two peaks: at around 5 years old and at 30–40 years old.^{1 2} Almost all paediatric cases develop cerebral ischaemia, whereas in adult cases about half have cerebral ischaemia and half develop cerebral haemorrhage. Moyamoya disease is caused by collateral circulation routes (moyamoya vessels) that develop to compensate for cerebral ischaemia with worsening of stricture of the circle of Willis starting from the carotid artery on both sides. The moyamoya vessels may expand into the main brain blood-stream and cause deterioration of brain circulatory reserve. As the brain blood flow deteriorates due to hyperpnoea, ischaemia can develop and bleeding is generated by the failure of moyamoya vessels. The side effects of pentazocine include decreases in the cardiac index³ and blood pressure.⁴ For this patient, because the episode that affected the brain circulation was only intramuscular injection of

Figure 2 Head MRI showing bilateral broad high intensity signals in the middle cerebral artery in diffusion-weighted imaging.

pentazocine and his consciousness level deteriorated twice in 30 min after administration of pentazocine twice, we concluded that pentazocine was the probable cause of the ischaemic attack. However, few articles have discussed the influence of pentazocine on blood circulation and we were unable to draw our conclusion with confidence.

Ischaemia of the cerebral hemisphere in moyamoya disease leads to symptoms of transient paralysis, perception disorders such as transient numbness, epileptic stroke and disturbance of consciousness. It is often accompanied by hyperventilation in children in whom moyamoya disease may occur during a musical instrument performance, exercise, heat, crying and excitement. For adults, bleeding caused by haemodynamic stress or rupture of a minute aneurysm may produce moyamoya vessels (table 1). Our case developed as a sudden disturbance of consciousness. The brain blood flow from the bilateral frontal lobe to the parietal lobe can deteriorate due to a pathological change in the first part of the circle of Willis. These lobes control consciousness and this may explain the disturbance of consciousness in our case. Cerebral ischaemia occurs with reduced brain blood flow and brain oxygen consumption,

Table 1 Symptoms of moyamoya disease¹⁵

	Children (0–9) N=431 (%)	Adults (30–39) N=235 (%)
Headache	8.6	58
Disturbance of consciousness	13	52
Convulsions	26	11
Mental symptoms	10	10.6
Exercise paralysis	78	35
Involuntary exercise	1.6	0.4
Sensory disorder	10	10
Speech disorder	19	14
Eyesight/field of vision abnormality	5.6	10.2

but blood flow to the cerebellum, medulla oblongata and base nucleus are comparatively unaffected,⁵ which results in maintenance of vital life signs such as breathing and circulation.

The cause of moyamoya disease is unclear. Family onset has been reported in about 15% of cases⁶ and asymptomatic moyamoya disease in blood relatives has been shown by MRA.⁷ In our case, the patient had three blood

Figure 3 MR angiography showing bilateral obstruction of the M1 segment of the carotid artery.

relatives with cerebral haemorrhage. This indicates that taking a clear family history is important when moyamoya disease is suspected. Cerebral blood vessel imaging is essential for diagnosis based on contraction or obstruction at the end of the carotid artery and in the anterior cerebral artery and proximal MCA in MRA. Bilateral abnormal blood vessels may also be observed in the cerebellum basal nucleus in MRA.^{8,9} Our case showed typical characteristics of moyamoya disease because obstruction was observed on both sides of the proximal part of the MCA in MRA.

Untreated cases of adult moyamoya disease have high rates of recurrence of cerebral blood vessel events. Convalescence is poor and re-establishment of blood flow is recommended^{10,11} for improvement of transient cerebral ischaemic attack, reduction of the risk of cerebral infarction, improvement of activities of daily living postoperatively and long-term brain function.¹² In Japan, a case with onset of cerebral infarction such as that caused by moyamoya disease is treated as an atheroma blood clot-related cerebral infarction, but evidence to support this approach is lacking. Cerebrovascular accident related to moyamoya results in major deterioration of function during convalescence^{10,11} and surgery should always be considered. However, this cannot be performed in most patients due to failure of early detection with resultant serious after effects.^{13,14}

The patient in our case had repeated transient cerebral ischaemic attacks and late diagnosis led to development of broad cerebral infarction and serious after effects. From our experience with this case, we suggest that cerebrovascular accident should be suspected in a young patient with disturbance of consciousness in whom breathing and circulation are stable, particularly if there is an episode in which a drug treatment affects the brain circulation before onset of disturbance of consciousness. In such a case, moyamoya disease should be suspected based on medical or family history. In our case, moyamoya disease was diagnosed using emergency MRA. For ischaemia-type moyamoya disease, early re-establishment of blood circulation is important to reduce serious after effects.

Reports on surgery for re-establishment of blood flow indicate stable outcomes and good convalescence. Many cases arrive at the emergency room with a slight ischaemic attack before a complete cerebrovascular accident occurs and it is important to make an appropriate diagnosis based on MRI and MRA at the stage of the slight ischaemic attack before performance of re-establishment surgery. Currently, there is no effective evidence-based treatment for cerebrovascular accident. We want to emphasise that 'the best method is to discover moyamoya disease at the stage of a slight ischemic attack and perform re-establishment surgery to prevent a cerebrovascular accident.'

Learning points

- ▶ Non-arteriosclerosis-related diseases such as moyamoya disease should be considered in young Asian patients with cerebral infarction after an episode that affects the brain circulation.
- ▶ Pentazocine, which decreases the cardiac index and blood pressure, may be a risk factor for onset of cerebral infarction in a patient with moyamoya disease.
- ▶ In a young patient with disturbance of consciousness in whom moyamoya disease is suspected by physical examination or based on medical or family history, MRI and MRA should be performed at an early stage to facilitate early diagnosis and treatment.

Competing interests None.

Patient consent Obtained.

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