Neuroendocrinology Letters Volume 43 No. 4 2022
ISSN: 0172-780X; ISSN-L: 0172-780X; Electronic/Online ISSN: 2354-4716
Web of Knowledge / Web of Science: Neuroendocrinol Lett
Pub Med / Medline: Neuro Endocrinol Lett

Acute ischemic stroke with hemichorea as a clinical manifestation

Jing Zhu[1], Ming Kong[2], Yan Pan[3], Bingfa Li[4]

1 Department of Neurology, Dongguan Songshan Lake Tungwah Hospital, DongGuan, 523808, China.
2 Department of Neurology, Dalian Jinzhou First People's Hospital, DaLian, 116100, China.
3 Department of Neurology, The Fifth Hospital of Xin Jiang Medical university, Urumqi, 831100, China.
4 Department of Orthopedics, Dongguan Songshan Lake Tungwah Hospital, DongGuan, 523808, China.

Correspondence to: Bingfa Li
Department of Orthopedics, Dongguan Songshan Lake Tungwah Hospital. No.1, Kefa 7th Road, Songshan Lake District, Dongguan, 523808,
Guangdong province, China
TEL: 0086-13688989120, E-MAIL: libingfaort@163.com

Submitted: 2022-08-08 Accepted: 2022-09-14 Published online: 2022-09-14

Key words: **case report; hemichorea; hypoperfusion; stroke; middle cerebral artery; stenosis**

Neuroendocrinol Lett 2022; **43**(4):227–232 **PMID:** 36528885 NEL430422C05

Abstract

Hemichorea can be the first clinical manifestation of an ischemic stroke, especially in the acute phase of a stroke, but hemichorea is extremely rare as a clinical manifestation of acute ischemic stroke and is easy to misdiagnose. Extending the therapeutic time window of intravenous thrombolysis and endovascular thrombectomy increases the likelihood of a bad clinical outcome. Herein we report a rare case of acute ischemic stroke with hemichorea as a clinical manifestation. A magnetic resonance angiography showed mild luminal stenosis of the anterior and middle cerebral arteries bilaterally and severe stenosis of the M1 segment of the right middle cerebral artery. A negative brain diffusion-weighted imaging-magnetic resonance examination may be related to a transient hypoperfusion of the subthalamic nucleus caused by severe stenosis of the right middle cerebral artery. In summary, the sudden onset of lateral limb choreiform movements cannot exclude the possibility of an acute ischemic stroke.

Abbreviations:

CT	- computed tomography
MRI	- magnetic resonance imaging
DWI	- diffusion-weighted imaging
MRA	- magnetic resonance angiography
CTP	- cerebral perfusion imaging:

INTRODUCTION

Hemichorea is an irregular, large, and random choreiform movement limited to one limb, most often the arm, leg, or face. Hemichorea is usually caused by damage to the basal ganglia or contact fibers in cortical motor areas and is a rare type of movement disorder after stroke (Salgado *et al.* 2017; Patel *et al.* 2019). Hemichorea is an uncommon clinical symptom of an acute ischemic stroke that is simple to misdiagnose. Extending the intravenous thrombolysis and endovascular thrombectomy therapeutic time window increases the risk of a poor clinical result. The pathogenesis of chorea is complex and can be observed in the acute phase of a predominantly thalamic infarction due to deafferentation or in the chronic phase of a stroke involving the contralateral basal ganglia, particularly the subthalamic and lentiform nuclei (Pandey, 2013).

CASE REPORT

Recently, symptomatic middle cerebral artery dissection (Chen & Xu, 2020; Strauss *et al.* 2019), ipsilateral cortical infarction (Wei & Zhang, 2021), and cortical ischemia lesions have been added to the list of stroke locations causing chorea (Cotroneo *et al.* 2020; Jacob & Gupta, 2016; Malhotra & Khunger, 2017; Strauss *et al.* 2019; Chung *et al.* 2004). Chorea is a hyperkinetic movement disorder characterized by excessive spontaneous movements that are irregularly timed, randomly distributed, and abrupt, and hemichorea is a hyperkinetic movement disorder affecting only one lateral half of the body (Wild & Tabrizi, 2007).

Causes of hemichorea include tumors, systemic lupus erythematosus, non-ketotic hyperglycemia, Wilson's disease, and thyrotoxicosis, in addition to hemorrhagic or ischemic cerebrovascular disease (Patel *et al.* 2019; Qiu *et al.* 2018).

The presence of stroke-related abnormal hyperkinetic movements, such as chorea, has long been known, often as a result of infarction of deep brain structures like the subthalamic nucleus and other basal ganglia structures, with the suggested pathophysiology being a decreased activity of the "indirect pathway" in the classical basal ganglia circuitry scheme (Alexander *et al.* 1986). In some cases, chorea occurs as a result of sensory deafferentation caused by thalamic infarction (Carbayo *et al.* 2020).

Herein we report a rare case of an acute ischemic stroke with hemichorea as the clinical manifestation to improve clinicians' understanding of the disease and to avoid misdiagnosis and mistreatment.

CASE REPORT

A 73-year-old woman was admitted to our hospital on 16 August 2019 due to the acute onset of choreoathetosic movements of the left limbs for 1 day. The patient fell 7 h ago while walking up the stairs, without loss of consciousness or significant pain, and later developed involuntary movements of the left limb with a combination of chorea (irregular migrating contractions) and athetosis (twisting and writhing). The left forearm was internally rotated, the elbow and wrist were flexed and twisted rapidly (10-15 times) for about 1 min, and the toes and ankle of the left lower limb were turned rapidly with large involuntary movements, which disappeared during sleep. The patient had a history of hypertension (180/110 mmHg) for > 10 years and was regularly taking amlodipine besylate (5 mg /daily), which controlled the blood pressure at 160-180/90-110 mmHg. She had no history of diabetes mellitus, did not smoke cigarettes or consume alcohol, had no toxic exposure, and denied any family history of neurodegenerative diseases or genetic disorders.

The cranial Computed Tomography (CT) findings in the local hospital suggested multiple lacunar cerebral infarcts. The left limb involuntary movements persisted and worsened, with the frequency increasing to > 20 times per min, and the amplitude of the upper arm and lower limb increasing.

Physical examination

On arrival at the hospital, the patient was conscious, spoke fluently, the pupils were equal in size bilaterally, the light reflex was intact, and the muscle strength of the left and right limbs was grade IV and V, respectively. The muscle tone was normal, the tendon reflexes of all four limbs were symmetric (++), and pathologic signs were negative bilaterally. Involuntary movements of the left limb were also noted at 8-10 times per min.

On investigation

The low density lipoprotein cholesterol was 3.90 mmol/L, the high density lipoprotein cholesterol was 1.01 mmol/L, and the creatine kinase was 256.00 U/L. There were no significant abnormalities on routine laboratory testing, including the hemogram, serum electrolytes, blood glucose, thyroid function, urine and stool, and glycated hemoglobin. There were no significant electrocardiogram, chest X-ray, or electroencephalogram abnormalities. Cranial magnetic resonance imaging (MRI) showed multiple speckles on T1WI with low signals in the bilateral basal ganglia, paraventricular region, thalamus, and brainstem (Fig.1A, B), while the fluid-attenuated inversion recovery sequence had high signals (Fig/ 1C). Diffusion-weighted imaging (DWI) showed no high signals in the bilateral basal ganglia, parietal ventricles, thalamus, and brainstem (Fig.1D), and no low signals in the apparent diffusion coefficient at the corresponding sites (Fig.1E). Susceptibility-weighted imaging showed low signals in the bilateral cerebral hemispheres, basal ganglia region, thalamus, brainstem, and cerebellum (Fig.1F), suggesting the presence of intracranial microhemorrhage. Magnetic resonance angiography (MRA) showed luminal stenosis (mild) of the anterior and middle cerebral arteries bilaterally and severe stenosis of the right middle cerebral artery M1 segment (Fig. 2A).

Based on the findings, the patient was diagnosed of acute ischemic stroke, with hemichorea as a special clinical manifestation.

Treatments

The patient was beyond the 4.5-hour time window for thrombolytic therapy at the time of admission. We started clopidogrel (300 mg) combined with aspirin (300 mg) antiplatelet therapy within 24 h of onset, and on day 2 clopidogrel (75 mg) combined with aspirin (100 mg) once daily for 21 days. In addition, haloperidol (2 mg twice/d) was administered to control involuntary movements and atorvastatin calcium (40 mg once/d) was added to intensify statin therapy immediately after admission. The blood pressure was maintained at 130-140/90-100 mmHg after admission, and amlodipine besylate was suspended to lower blood pressure. On the second day of admission, the frequency

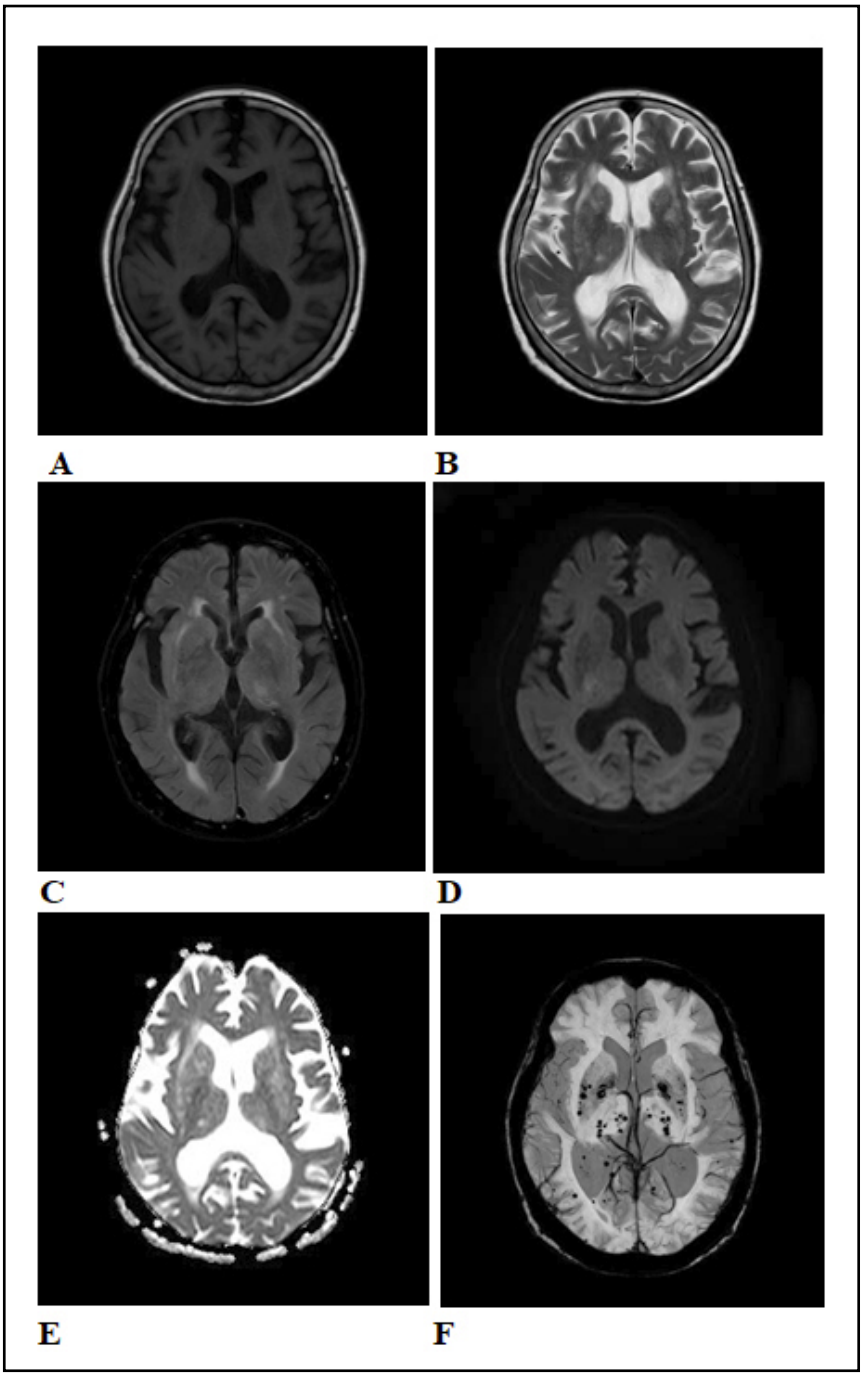

Fig. 1. A,B,C,D,E,F: magnetic resonance imaging showed no diffusion-limited signal in the diffusion-weighted imaging sequence.

of involuntary movements involving the left upper and lower extremities and toes decreased compared with the previous frequency (4-5 times per min). On day 3 of admission, digital subtraction angiography showed severe stenosis (70%) of the right middle cerebral artery M1 segment (approximately 2 mm in length; Fig. 2B). CT cerebral perfusion imaging (CTP) showed delayed perfusion in the supply area of the right middle cerebral artery (Fig. 2C).

Interventional surgical treatment was clearly indicated, but the patient was mildly symptomatic, and multiple stenoses and overly tortuous vessels were noted in the cerebral vessels on digital subtraction angiography, thus conservative treatment was selected. At the time of hospital discharge, involuntary movements of the left limb occurred occasionally, 1-2 times per day, thus haloperidol was reduced to 1 mg twice per day.

Follow-up evaluation

The patient was discharged from the hospital on 1 September 2019. At the follow-up evaluation 1 month after discharge, the left upper and lower extremity chorea symptoms had resolved. On 5 December 2019, the patient revisited the outpatient clinic. She was conscious and fluent without involuntary movement

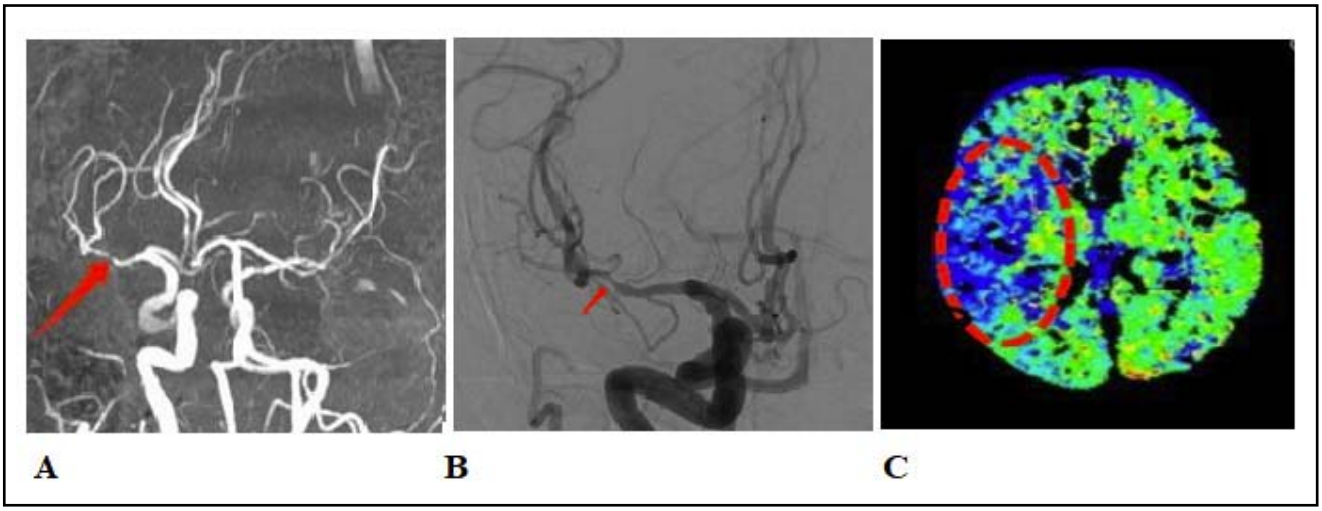

Fig. 2. A,B: Magnetic resonance angiography and digital subtraction angiography showed severe lumen stenosis in the M1 segment of the terminal right internal carotid artery (red arrows). C: Cerebral perfusion imaging under Computed tomography revealed a large ischemic penumbra surrounding the infarct (red, dotted circles).

of the limbs. The muscle strength of the four limbs was grade IV, and the muscle tension of the four limbs was normal. The tendon reflexes of the four limbs were symmetric without obvious abnormalities in the depth and superficial sensation and bilateral pathologic signs (-). The continued medications were as follows: aspirin, 100 mg once daily; atorvastatin calcium, 20 mg once daily; and levamlodipine, 5 mg once daily.

DISCUSSION

The patient had an acute onset seizure-like, stereotyped, and repetitive clinical presentation, which needs to be differentiated from epilepsy. Acute ischemic stroke with chorea-like movements as the first clinical manifestation is not common, especially in the acute phase of a stroke, and it is often easy to misdiagnose and miss the optimal time for thrombolysis and endovascular treatment (Chung *et al.* 2004; Cardoso *et al.* 2006). This case is unique as an acute ischemic stroke with a negative cranial MRI and clear evidence of hypoperfusion due to occlusion or stenosis of the responsible artery, with chorea-like movements as the first clinical manifestation. The responsible vessel was the right middle cerebral artery and the staging was atherosclerotic. The etiology may have been related to a severe stenosis of the right middle cerebral artery leading to transient hypoperfusion of the basal thalamic nucleus.

Chorea is a symptom marked by involuntary movements that occur as a result of a continuous stream of random muscular contractions (Cardoso *et al.* 2006). Infections, autoimmune diseases, drug-induced disorders, metabolic diseases, neurologic diseases, and stroke can all cause new-onset chorea (Cardoso *et al.* 2006). Stroke is the leading cause of sporadic chorea, and hemichorea is the most prevalent involuntary movement disorder associated with the condition (Ueta *et al.* 2021).

Focal brain lesions can lead to different types of movement disorders, including hemichorea, dystonia, tremor, myoclonus, and hypokinetic syndrome, of which stroke is the most common cause. In addition to stroke, tumors, trauma, hypoxia, vascular malformations, and multiple sclerosis can also lead to movement disorders (Jiang *et al.* 2021; Defebvre & Krystkowiak, 2016). The precursory symptoms of cerebral infarction due to stenosis of the middle cerebral artery can manifest as persistent hemichorea (Ge *et al.* 2019); however, dyskinesia as a clinical manifestation of acute ischemic stroke is relatively rare and can be transient or persistent. Therefore, it is very easy to misdiagnose and thus delay the timing of intravenous thrombolysis and endovascular thrombectomy treatment. Currently, scholars have found that lateralized chorea is the most common movement disorder after ischemic stroke, usually secondary to infarcts in the basal ganglia, thalamus, and cortex, especially infarcts in the deep brain structures, including the basal thalamic nucleus, nucleus accumbens, and other basal ganglia structures.

We report a case of acute ischemic stroke presenting for the first time with hemichorea. Recently, hemichorea has been reported as the only clinical manifestation of early stroke onset in cases suggesting an underlying dysfunction of the pathway connecting cortical motor areas to the basal ganglia (Gasca-Salas & Lang, 2015; Carbayo *et al.* 2020).

Hemichorea was first described by Whittier in 1949 when he studied the rhesus monkey thalamic nucleus basalis, which showed that damage to 20% of the area induced choreic movements in the contralateral limb (Patel *et al.* 2019). At present, the pathophysiologic mechanism of hemichorea remains to be fully elucidated. Hemichorea may be related to mutual

antagonism of neurons between the cortex, thalamus, and basal ganglia (Qiu *et al.* 2018; Jiang *et al.* 2018). The main pathway is the cortico-striato-medial pallidum-thalamo-cortical loop, which increases the activity of the lateral pallidum neurons by blocking the transmission of γ-aminobutyric acid from the striatum to the lateral pallidum, thereby inhibiting the basal nucleus of the thalamus and leading to loss of control of the medial pallidum neurons, causing increased movements. Involvement of the lesion in the cortex, the thalamic floor nucleus, and either part of the pathway may result in involuntary movements (Jiang *et al.* 2018; Defebvre & Krystkowiak, 2016; Ge *et al.* 2019).

Cortical stroke has a better prognosis than thalamic nucleus basalis lesions, which could be related to temporary hypoperfusion between the borders of the vessels in distinct arterial supplies rather than disruption of basal ganglia circuits (Defebvre & Krystkowiak, 2016). Strokes in the region of the middle cerebral artery are prevalent, although post-stroke movement problems are unusual. Although the basal thalamic nucleus is the most common site for hemodynamic changes, the striatum, thalamus, pallidum, frontal, and parietal lobes can also be involved, with diffusion-limited signal shadows seen on cranial DWI sequences (Hui *et al.* 2015).

Our patient had involuntary motions, but no diffusion-limited signal on DWI sequences, which could be attributed to blockage or stenosis of the middle or anterior cerebral arteries, thus causing hypoperfusion hemodynamic alterations. This outcome is in agreement with relevant international reports. In 2015, Anthony, a canadian scholar, reported recurrent hemichorea movements due to middle cerebral artery stenosis secondary to transient ischemic attacks (Gasca-Salas & Lang, 2015). In the same year, Kodera, a Japanese scholar, also published a case of involuntary movements of the right limb with hypoperfusion caused by middle cerebral artery stenosis (Kodera *et al.* 2015).

The pathogenesis of all these cases was related to middle cerebral artery stenosis or occlusion, which when combined with our case, suggests that both intra- and extra-cranial large artery stenosis or occlusion can be the cause of involuntary movements with evidence of limited hypoperfusion in the symptomatic phase (Hui *et al.* 2015).

In contrast, this case was unique in that no ischemic lesion was evident on imaging, but there was clear evidence of hypoperfusion due to occlusion or stenosis of the responsible artery. Similar reports without definite new lesions causing hemichorea movements are rare. Hemichorea movements due to ischemic stroke are usually self-limiting, with most patients resolving or improving spontaneously within weeks-to-months (Patel *et al.* 2019; Qiu *et al.* 2018; Jiang *et al.* 2018). In the early stages of the disease, hemichorea movements may be injurious to the patient and have a diverse pathogenesis, making treatment challenging.

Early treatment is pharmacologic, and the main drugs commonly used include dopamine receptor antagonists, which reduce input from cortical sensory areas to motor areas by blocking dopamine receptors, such as antipsychotics like haloperidol, which are effective in most patients but carry the risk of causing delayed dyskinesia or Parkinson's syndrome (Qiu *et al.* 2018; Jiang *et al.* 2018; Defebvre & Krystkowiak, 2016; Ge *et al.* 2019; Gasca-Salas & Lang, 2015; Carbayo *et al.* 2020). Therefore, dopamine-depleting agents are preferred in most patients because dopamine-depleting agents do not cause delayed dyskinesia by inhibiting presynaptic dopamine release and blocking postsynaptic dopamine receptors, especially when combined with dopamine receptor antagonists. The representative drugs of this class are tetrabenazine and butenazide (Patel *et al.* 2019; Qiu *et al.* 2018). For medical-refractory hemichorea after an ischemic stroke, pallidum destruction or deep brain stimulation may also be an option (Qiu *et al.* 2018). In our patient, haloperidol was administered to control the symptoms of hemichorea, which improved at discharge and resolve after 1 month.

We believe that the good prognosis of this patient was due to early recognition and timely intervention while maximizing reversal of neuronal damage and reducing stroke disability. We suggest that we should consider the possibility of acute ischemic stroke in patients encountering sudden involuntary limb movements in clinical practice. CT perfusion imaging in this patient showed significant hypoperfusion of the right middle cerebral artery supply area. Therefore, the etiology was thought to be atherosclerosis causing vascular stenosis, neurotransmitter imbalance in the basal ganglia motor circuit, and insufficient blood perfusion, thus inducing cellular dysfunction leading to increased movement.

Overall, hemichorea can be the first clinical manifestation of ischemic stroke, especially in the acute phase of a stroke, and is often misdiagnosed or missed, thus missing the best time for thrombolysis and endovascular treatment is missed. Early recognition and timely intervention to maximize the reversal of neuronal damage can reduce the disability following stroke.

ACKOWLEDGMENTS

None.

Funding

None.

DISCLOSURE

Conflicts of interests

We have no conflicts of interest.

Ethics approval and consent to participate

The research was conducted ethically in accordance with the World Medical Association Declaration

of Helsinki, and was approved by the ethics committee of our hospital. Written informed consent to participate in the study has been obtained from the patient.

Consent to publish

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

Availability of data and material

The data analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

All the authors have participated in the clinical data collection and clinical diagnosis, JZ did the literature review and analysis, and wrote the 1st draft of the manuscript. MK, YP and BL did the literature review and analysis, critical review and revised the manuscript draft. All the authors have approved the final draft for submission.

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