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CASE REPORT

Choreoathetosis of the upper limb with contralateral substantia nigra lacunar infarction: A case report and literature review

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Abstract

Choreoathetosis of the upper limb as the first manifestation of contralateral substantia nigra (SN) lacunar infarction is extremely rare. We report a case of choreoathetosis of the right upper limb in a 60-year-old man with SN infarction. Emergency brain magnetic resonance imaging showed discrete lacunar infarction localized in the left SN. Magnetic resonance angiography showed atherosclerotic stenosis of the basilar artery and the left posterior cerebral artery. He was diagnosed with contralateral SN infarction and then treated with antiplatelet, loading-dose statins, and allopathic therapy to achieve a positive outcome. During the follow-up period, there was no recurrence of stroke, and his symptom of choreoathetosis resolved. More cases alike should be studied to achieve satisfactory outcomes through early diagnosis and appropriate treatments.

Keywords: Substantia nigra; Dance-like movements; Ischemic stroke

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1. Introduction

Substantia nigra (SN), a dopaminergic nucleus located in the midbrain, plays a key role in regulating motor movements. The previous studies have indicated that ischemia in distal brain regions may cause delayed neurodegenerative changes, such as hyperkinetic and hypokinetic syndromes (especially vascular parkinsonism)[1]. However, the previous literature has suggested an inconsistency in the incidence of cerebrovascular disease-related movement disorders due to the different perception of its scope. According to Alarcón *et al*., the incidence of post-stroke dyskinesia in 2004 was 3.7%[2]. Tater *et al.* have suggested that 1 –4% of all stroke patients may present with movement disorders[3]. In particular, there have been several reports of choreoathetosis associated with lacunar infarction involving the SN. In this article, we report an unusual case of the right upper limb choreoathetosis with primary SN infarction and review the relevant literature.

2. Case presentation

We report an interesting case of acute choreoathetosis as the presenting symptom of acute ischemic stroke in a 60-year-old man, which lasted for 5 days. It was characterized by involuntary, irregular, and continuous circular movement of the right upper limb, with the shoulder joint as the axis. The frequency and the duration were uncertain. According

to the patient, grasping the affected limb with his left hand prevented the attack. Although there was no disturbance of consciousness, slurred speech, clenched teeth, and salivation at the corners of his mouth, he experienced numbness. The aforementioned symptoms affected his daily life. The patient had no significant medical history. A physical examination on admission revealed that he had a temperature of 36.4°C, a heart rate of 80 beats/min, a respiratory rate of 18 breaths/min, and a blood pressure reading of 140/80 mmHg. Cardiopulmonary and abdominal examination showed no obvious abnormalities. Neurological examination indicated that he was fully conscious and oriented. Bilateral pupils, about 3 mm in diameter, were sensitive to light reflex. Except for the involuntary dance-like movements of the right upper limb, there were no positive signs.

A high-intensity lesion in the left SN was revealed by diffusion-weighted magnetic resonance imaging (MRI), as shown in Figure 1. Magnetic resonance angiography (MRA) showed basilar artery (BA) and posterior cerebral artery (PCA) stenoses, as shown in Figure 2. No atherosclerotic changes were observed via carotid ultrasound. Electrocardiogram was normal, and there was no potential cardiac source of embolism or right-to-left shunt detected by transthoracic and transesophageal echocardiography.

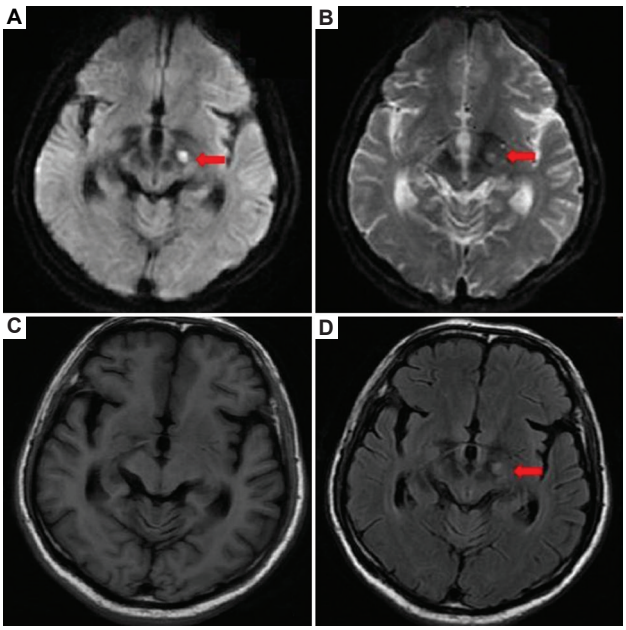

Figure 1. Magnetic resonance imaging indicating a discrete lacunar infarction in the left substantia nigra (SN). (A) Diffusion-weighted imaging (DWI) showing a new infarct in the SN of the left cerebrum. (B) An image of DWI sequence (b0), which is similar to a fast-scan T2WI sequence. (C) No abnormal signals in T1-weighted image. (D) T2-weighted image/fluid-attenuated inversion-recovery (FLAIR) showing a high-signal lesion located in the left SN.

Laboratory examinations showed no abnormalities besides hemoglobin A1c and glucose levels. The levels of C-reactive protein, erythrocyte sedimentation rate, liver and renal function, blood lipid, electrolytes, homocysteine, coagulation indices, including antithrombin III, prothrombin time, activated partial thromboplastin time, and D-dimer, were all within normal limits. Antinuclear antibody, anti-dsDNA antibody, anti-Smith (Sm) antibody, anti-SS-A/B antibody, proteinase 3 antineutrophil cytoplasmic antibody (PR3-ANCA), myeloperoxidase antineutrophil cytoplasmic antibody (MPO-ANCA), as well as beta-2-glycoprotein I, human immunodeficiency virus (HIV), and syphilis antibodies were all negative. The laboratory results are shown in Table 1. The patient was diagnosed with contralateral SN infarction and was started on antiplatelet therapy with aspirin 100 mg and clopidogrel 75 mg orally once daily for 21 days, followed by long-term maintenance of aspirin 100 mg. He was also given oral atorvastatin calcium tablets 20 mg once daily to the lower lipid levels and stabilize atherosclerotic plaques. The patient took oral metformin 500 mg twice/day and gliclazide 30 mg once a day for Type 2 diabetes. To control the involuntary movements of his right upper limb, he was given thiopride 50 mg thrice daily, and the dose was gradually increased to 100 mg; when his symptom was significantly alleviated, the dosage of thiopride was tapered until discontinuation. There were significant improvements in choreoathetosis and no recurrent strokes over a 6-month follow-up period post-discharge.

3. Discussion

Acute stroke is a common and prevalent clinical condition, which is characterized by sudden focal neurological deficit. Its clinical presentations vary depending on the site of involvement. The most common symptoms are facial weakness involving the mouth, slurred speech, paralysis, and sensory impairment, followed by dizziness, headache, choking after drinking, dysphagia, ataxia, and even loss of consciousness in severe cases. Movement disorders may be caused by small vessel disease in the middle or posterior cerebral artery territory supplying the basal ganglia[4,5].

Choreoathetosis of the right upper limb refers to the simultaneous occurrence of dance-like movements and athetosis, in which the latter is characterized by slow, twitchy, and peristaltic involuntary movements of the distal extremities, which may assume a variety of abnormal postures. However, the symptom usually resolves spontaneously over time. Despite specific anatomical and imaging evidence supporting its diagnosis, choreoathetosis, as a broad disease spectrum, is an uncommon manifestation of acute stroke. To better

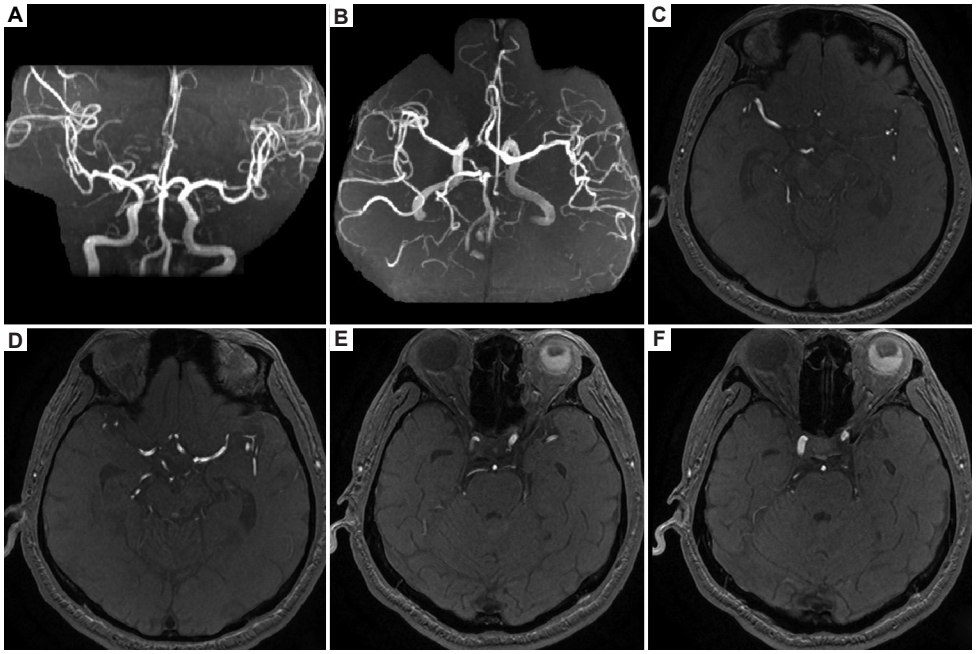

Figure 2. Cerebrovascular imaging of the patient. (A and B) Magnetic resonance angiography revealing atherosclerotic stenosis of the basilar artery and the left posterior cerebral artery (PCA). (C–F) Four images showing the cross-sectional images of BCA and PCA, with observable left PCA stenosis.

understand these conditions, we searched PubMed for reports using several keywords, such as "SN," "ischemic stroke," "dyskinesia," "movement disorders," "motor deficit," and so on. Table 2 is a summary of several patients with SN infarction presenting with movement disorders[6-14]. Nine patients were reviewed (excluding the present patient), including six male and three female patients, age ranging from 18 to 83. All patients exhibited symptoms similar to Parkinson's disease. Six patients presented with static tremor, four with bradykinesia, and three with rigidity. Besides these symptoms, other symptoms such as apathy, speech disorder, and panic gait also occurred. With regard to their previous medical history, there were six cases of hypertension, one case of diabetes, one case of hyperlipidemia, one case of myocardial infarction with atrial fibrillation, one case of cerebral infarction, and one case of subarachnoid hemorrhage.

However, the patient reported in this paper presented with choreoathetosis in contrast to the Parkinson's-like symptoms. This case caught out attention since there have not been any similar reports in the literature we reviewed. In this case, functional imaging examination was not performed to verify the motor dysfunction of the patient. However, the acute onset, rapid progress, and existence of risk factors for cerebrovascular disease suggested the different causes of choreoathetosis. Therefore, there is sufficient evidence to prove that the patient's clinical manifestation was in fact caused by the lacunar infarction located in the SN.

The pathogenesis of hyperactivity disorders may be related to elevated monoamine activity and/or relative cholinergic deficiency, or even the dysfunction in the cerebellum-thalamic or striatum-thalamic pathway[8]. The nucleus basalis is a group of grey matter nuclei under the cerebral cortex, consisting of the caudate nucleus, the shell nucleus, the pallidum, the subthalamic nucleus, and the SN[15]. It regulates motor function mainly through the cortico-basal ganglia-thalamo-cortical loop. In this loop, the neostriatum receives afferent fibers from the sensorimotor cortex of the brain, and its efferent fibers reach the basal ganglia output structures (globus pallidus internus [GPi]/substantia nigra reticularis [SNr]) through direct and indirect pathways. The direct pathway refers to the excitatory projection of glutaminergic nerve fibers from the cerebral cortex to the striatum, which, in turn, sends inhibitory projections of gamma-aminobutyric acid (GABA) nerve fibers to the GPi and SNr complexes. The GABA nerve fibers emanating from the latter can emit inhibitory projection to the ventrolateral thalamic nucleus[16]. When infarcts occur in the SN, the projection function of both the thalamus and the thalamic cortex is enhanced because of the reduced GPi-SNr complex activity. The motor impulses that generate in the cortex cannot be terminated, and it cannot receive impulses from the cerebellar-red nucleus-striatal pathway, thus leading to the development of choreoathetosis. From the perspective of neurotransmitters, the excitatory and inhibitory effects of neurotransmitters on neurons are in a coordinated

Table 1. Results of laboratory investigations.

Parameter	Result (Reference range)
CRP	<0.50 mg/L (0 – 10)
WBC	9.17×10^9/L (3.5 – 9.5)
RBC	4.62×10^{12}/L (4.3 – 5.8)
HGB	138 g/L (130 – 175)
PLT	236×10^9/L (125 – 350)
ESR	3.8 mm/h (0 – 15)
PT	9.6 s (9 – 14.5)
APTT	28.8 s (22.5 – 40.5)
TT	17.00 s (14 – 21)
D-dimer	0.320 mg/L (0 – 0.5)
INR	0.82 (0.8 – 1.5)
ALT	13.0 U/L (9 – 50)
AST	13.0 U/L (15 – 40)
GLU	12.28 mmol/L (3.8 – 6.1)
HbA1c	9.3% (4.2 – 6.2)
UA	134.0 μmol/L (135 – 425)
CREA	71.0 μmol/L (59 – 104)
CHOL	5.59 mmol/L (2.8 – 6.0)
TG	0.46 mmol/L (0.56 – 1.71)
HDL-C	1.73 mmol/L (1.2 – 1.68)
LDL-C	3.41 mmol/L (2.07 – 3.1)
Hcy	6.15 μmol/L (5 – 14)
HBsAg	Negative
HCVcAg	Negative
A-HCV	0.010 AU/mL (0 – 5)
HIV combi PT	0.010 AU/mL (0 – 1)
TP-CLIA	0.240 mIU/mL (0 – 10)
ANA	Negative (<1:100)
Anti-SSA	4.0 AU/mL (0 – 120)
Anti-SSB	23.0 AU/mL (0 – 120)
Anti-Sm	42.0 AU/mL (0 – 120)
Anti-dsDNA	70.0 AU/mL (0 – 120)
RF	1.2 IU/mL (<20)
ASO	18.0 IU/mL (<200)
Anti-PR3	3.0 AU/mL (<120)
Anti-MPO	3.0 AU/mL (<120)
Anti-GBM	1.0 AU/mL (<120)
AKA	Negative
Anti-CCP	1.1 AU/mL (< 120)

A-HCV: Hepatitis C antibody; AKA: Antikeratin antibody; ALT: Alanine transaminase; ANA: Antinuclear antibody; anti-CCP: Anti-citrullinated protein antibody; anti-MPO: Anti-myeloperoxidase antibody; anti-PR3: Anti-proteinase-3 antibody; APTT: Activated partial thromboplastin time; ASO: Antistreptolysin O; AST: Aspartate transaminase; CHOL: Cholesterol; CREA: Creatinine; CRP: C-reactive protein; anti-dsDNA: Anti-double stranded DNA antibody; ESR: Erythrocyte sedimentation rate; anti-GBM, anti-glomerular basement membrane antibody; GLU, glucose; HbA1c, hemoglobin A1c; HBsAg: Hepatitis B surface antigen; HCVcAg: Hepatitis C virus core antigen; Hcy: Homocysteine; HDL-C: High-density lipoprotein cholesterol; HGB: Hemoglobin; HIV: Human immunodeficiency virus; INR: International normalized ratio; LDL-C: Low-density lipoprotein cholesterol; PLT: Platelet; PT: Prothrombin time; RBC: Red blood cell; RF: Rheumatoid factor; anti-Sm: Anti-Smith antibody; anti-SSA: Anti-Sjögren's syndrome antigen A antibody; anti-SSB: Anti-Sjögren's syndrome antigen B antibody; TG: Triglyceride; TP-CLIA: Chemiluminescence immunoassay for *Treponema pallidum*; TT: Thrombin time; UA: Uric acid; WBC: White blood cell

and unified state. The motor function downstream of the basal ganglia circuit is regulated through two transmitters, dopamine (DA) and acetylcholine (Ach), which control the output of excitatory and inhibitory signals[17]. It is known that early ischemic stimulation of neurons increases the synthesis of neurotransmitters, while nerve terminal synapses practically lose their effect on the storage and reuptake of neurotransmitters, resulting in the release of large amounts of neurotransmitters into the synaptic gap. In a physiological state, the synthesis, release, degradation, and reuptake of DA are a dynamic equilibrium process, which depends on the adenosine triphosphate (ATP) energy supply. When cerebral ischemia occurs, neuronal energy metabolism is impaired, leading to decreased Na^+-K^+-ATPase activity. The automatic depolarization of neurons triggers a spontaneous release of DA from nerve terminal vesicles; a large amount of DA is thus released into the intercellular space. In addition, normal synaptic release is dependent on intracellular calcium ion (Ca^{2+}) levels. Since ischemia causes Ca^{2+} influx, it prompts the release of DA. The transmitters released into the synaptic gap are metabolized by two pathways: Reuptake and monoamine oxidase (MAO). During ischemia, there is reduced MAO activity, decreased degradation of DA, and inhibition of reuptake, resulting in increased DA and excitability. This is consistent with the research results of Brannan *et al.*[18]. In addition, acute cerebral ischemia/reperfusion experiments have demonstrated a significant reduction in hippocampal Ach levels during acute cerebral ischemia[19]. Nigrostriatal lesions can also impair the function of the striato-nigral-striatal loop, which may result in an imbalance between DA and Ach. The function of dopaminergic neurons becomes relatively hyperactive, whereas Ach levels are reduced due to decreased choline acetyltransferase activity. With the aggravation of ischemia, the neuronal damage is aggravated, and the synthesis and release of DA are inhibited. Therefore, movement disorders caused by stroke usually resolves spontaneously over time[20]. The above mechanisms play a joint role in the occurrence of the disease.

Although the diagnosis of this patient was apparent, this kind of infarction associated with choreoathetosis is extremely rare and varies greatly among individuals. It is difficult for clinicians to make this diagnosis through medical history, symptoms, signs, and ancillary examination results. The previous literature has indicated that there is an ongoing debate on the pathogenesis of choreoathetosis and whether or not it is an epileptic syndrome. In this case, the patient did not undergo electroencephalogram (EEG) examination or any experimental treatment with antiepileptic drugs. To summarize the clinical features of this type of disease, more case studies are needed.

Table 2. Previous reports of substantia nigra infarction.

Literature	Sex	Age	Clinical symptoms/manifestations	Medical history
Robles[6]	Female	68	Bilateral lower limb resting tremor	Hypertension and dyslipidemia
Ohta and Obara[7]	Male	61	Bradykinesia, cogwheel rigidity, and resting tremor of the left hand	Hypertension
Hunter *et al.*[8]	Male	62	Right-sided parkinsonism characterized by rigidity and flexion	Hypertension
Kim and You[9]	Female	71	Akinetic mutism and decreased speech, movement, and emotional reactions	Hypertension, diabetes, and old cerebral infarction
Orta Daniel and Ulises[10]	Female	45	Bradykinesia, hypomimia, hypophonia, dysarthria, hypokinesia, rigidity in the neck and all four limbs, resting tremor in the left arm, and festinating gait	Systemic lupus erythematosus
Gonzalez-Alegre[11]	Male	18	Parkinsonian tremor in the contralateral foot	Subarachnoid Hemorrhage
Akyol, Akyildiz , and Tataroglu[12]	Male	80	Bradykinesia, resting tremor of the left hand, and tremor of the lower limbs in an upright position, particularly in the left leg	–
Caparros-Lefebvre *et al.*[13]	Male	70	Biballism or paraballism	Hypertension
McKee *et al.*[14]	Male	83	Visual hallucinations, disordered sleep, and mild cognitive impairment	Myocardial infarction with atrial fibrillation

4. Conclusion

We present a case of choreoathetosis as the first manifestation of an ischemic lesion involving the contralateral SN. In our reported case, it is of concern that the localization of lesion shown by MRI, DWI, and MRA is associated with the sudden specific clinical symptom. This enlightening case suggests that clinicians should consider the possibility of ischemic stroke in the contralateral nigrostriatal pathway in patients presenting with sudden and rapidly progressive dance-like movements.

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Conflict of interest

The authors declare they have no competing interests.

Author contributions

Conceptualization: Yanqiang Wang
Investigation: Mengxin Li and Xiaojun Zhang
Supervision: Yanqiang Wang
Writing – original draft: Mengxin Li and Yanqiang Wang
Writing – review & editing: Mengxin Li and Yanqiang Wang

Ethics approval and consent to participate

Written consent was obtained from the patient. The Medical Ethics Committee of the Affiliated Hospital of Weifang Medical University approved the study. The approval number is wyfy-2022-ky-182.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Availability of data

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

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