CASE REPORT

Intermittent Akinetic Mutism after Bilateral Paramedian Thalamic Infarction Caused by Artery of Percheron Occlusion : A Case Report

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Abstract : Intermittent clinical course of akinetic mutism is very unusual. We describe a 74-year-old man who started to demonstrate episodes of altered mental state with stopped moving and talking, poor response to commands, and muscle stiffness in both upper limbs approximately 1.5 months after cardioembolic bilateral paramedian thalamic infarction. Their frequency gradually increased and poststroke nonconvulsive status epilepticus was suspected, but prolonged video-electroencephalography monitoring did not reveal any epileptiform abnormalities. The patient had no significant metabolic or infectious disorders. Thus, upon exclusion of other causes his condition was considered as intermittent akinetic mutism, which was indirectly confirmed by good response of symptoms to amantadine therapy and their recurrence upon termination of this treatment. J. Med. Invest. 71 : 306-309, August, 2024

Keywords **:** *Akinetic mutism, Bilateral paramedian thalamic infarction, Differential diagnosis, Intermittent clinical course, Treatment*

INTRODUCTION

Akinetic mutism may be caused by structural alteration of various brain regions, including anterior cingulate cortex, striatum, mesolimbic system, substantia nigra, and thalamus (1). Specifically, it may be related to bilateral paramedian thalamic infarction caused by occlusion of the distal basilar artery (BA) or artery of Percheron, a rare cerebrovascular variation with a single arterial trunk arising from the proximal posterior cerebral artery (PCA) to supply midbrain and both paramedian thalami (2-4). In such cases, akinetic mutism may be, correspondingly, a component of the top-of-the-basilar syndrome or bilateral paramedian thalamic syndrome being presented along with a variety of other symptoms, including prolonged disturbance of consciousness, somnolence, amnesia, subcortical dementia, paroxysmal sleep attacks, etc. The clinical course of akinetic mutism after cerebrovascular accident (CVA) is typically rather stable with a trend for incomplete regression of related neurological deficit within several weeks, whereas intermittent manifestations of related symptoms are very unusual. Herein we describe an elderly patient who started to experience episodes of altered mental state with stopped moving and talking, poor response to commands, and muscle stiffness in both upper limbs approximately 1.5 months after cardioembolic bilateral paramedian thalamic infarction, which upon exclusion of other causes were considered as intermittent akinetic mutism and demonstrated good response to amantadine therapy with subsequent recurrence upon termination of this treatment owed to related complication.

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CASE REPORT

A 74-year-old man was transferred by ambulance to our critical care center being in acute coma. At admission his Glasgow Coma Scale (GCS) score was 6 (eye opening, 1 ; verbal response, 1 ; motor response, 4), pupils had normal size, there was arterial hypertension (157/97 mmHg), and electrocardiogram demonstrated atrial fibrillation. His previous medical history was remarkable for meningitis (approximately 30 years ago), chronic hypertension, diabetes mellitus, dyslipidemia, and hyperuricemia. Emergency MRI revealed high signal intensity in paramedian regions of both thalami with extension on the anterior part of the left thalamus on diffusion-weighted (Fig. 1 A) and fluid-attenuated inversion recovery (FLAIR) images. MRA (Fig. 1 B) showed absence of the right vertebral artery (VA) and hypoplastic right P1 segment, while from P2 segment right PCA was well visualized due to fetal type of its origin. Of note, right VA was considered hypoplastic rather than occluded, since T2*-weighted MRI did not show any susceptibility signal from this vessel (Fig. 1 C), which, obviously, would not be a case in presence of its embolism, dissection, or atherosclerotic changes. Based on these clinical and radiological findings, the diagnosis of cardioembolic bilateral paramedian thalamic infarction was established. Since no other affected vascular territories of the brain were revealed on diffusion-weighted and FLAIR images, whereas entire BA and left PCA were well visualized on MRA, the occlusion of the artery of Percheron was suspected.

Because of prolonged unconsciousness and instability of vital functions, the patient was intubated and put on mechanical ventilation. Anticoagulant therapy with edoxaban (60 mg per day) was initiated. By next morning, his clinical condition improved significantly and GCS score was 9T (eye opening, 3 ; verbal response, intubated ; motor response, 6). He was extubated, and demonstrated gradual recovery thereafter. Although he remained disoriented and provided only slow responses, he was able to communicate and to stand up transferring from his bed to a wheelchair with minimal assistance. Neurologically, there was a vertical gaze palsy. Control MRA on the 15th day after CVA demonstrated restoration of the right P1 segment

with visualization of its perforating branch, which might be the artery of Percheron (Fig. 2). On the 21st day after CVA, he was transferred to rehabilitation facility, where his condition continued to improve. Specifically, he has started peroral food intake by himself.

However, on the 41st day after the initial CVA the patient was found unconscious. Although he was able to open his eyes spontaneously, his eyeballs remained fixed in central position and did not move. Emergency head CT did not demonstrate any new abnormalities. Approximately 7-8 hours thereafter, the patient regained consciousness and was able to comply with commands. Nevertheless, one week thereafter the similar episode happened again, while this time it was accompanied by twitch of both eyelids. Poststroke epilepsy was suspected and therapy with levetiracetam (1,000 mg per day) was initiated. Despite such treatment, similar conditions started to occur more and more often and finally began to appear 3-4 times per week and were not affected by gradual increase of the antiseizure medication (ASM) dose. Nonconvulsive status epilepticus (NCSE) was suspected, and on the 147th day after the initial CVA the patient was transferred back to our hospital for further clinical examination.

Upon arrival, he was active enough, was able to transfer from his bed to a wheelchair by himself, and did not recall any episode of his deterioration of consciousness. All ASM

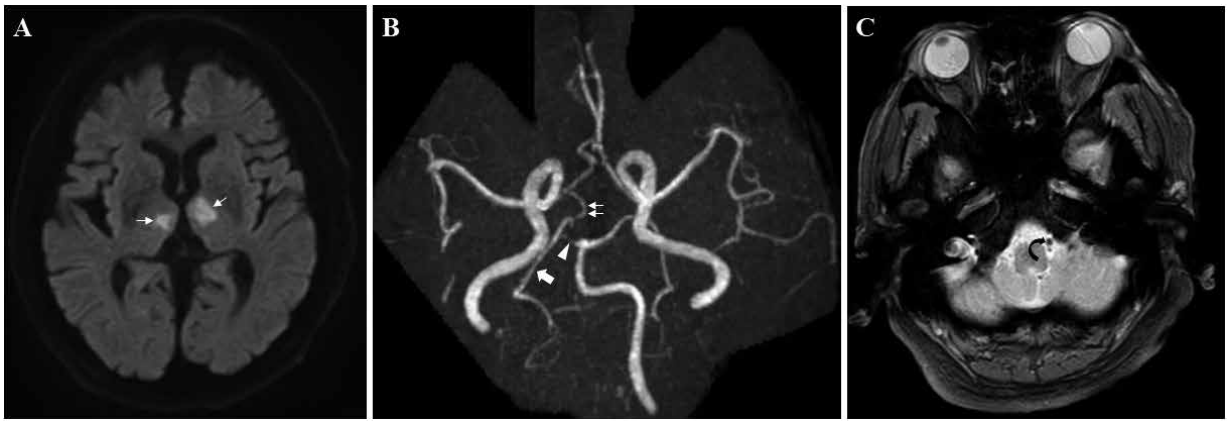

Fig 1.
Imaging findings in a 74-year-old man admitted in acute coma with arterial hypertension and atrial fibrillation. Diffusion-weighted imaging (A) revealed high signal intensity in paramedian regions of both thalami with extension on the anterior part of the left thalamus (*arrows*), whereas magnetic resonance angiography (B) showed absence of the right vertebral artery (VA) and hypoplastic right P1 segment (*arrowhead*), while from P2 segment right posterior cerebral artery (PCA ; *thick arrow*) is well visualized due to the fetal type of its origin through posterior communicating artery (*double arrows*). The entire basilar artery and left PCA are seen well. The diagnosis of cardioembolic bilateral paramedian thalamic infarction, presumably caused by the artery of Percheron occlusion, was established. Of note, right VA was considered hypoplastic rather than occluded, since T2*-weighted imaging (C) did not show any susceptibility signal from this vessel, in contrast to its left-side counterpart (*curved arrow*).

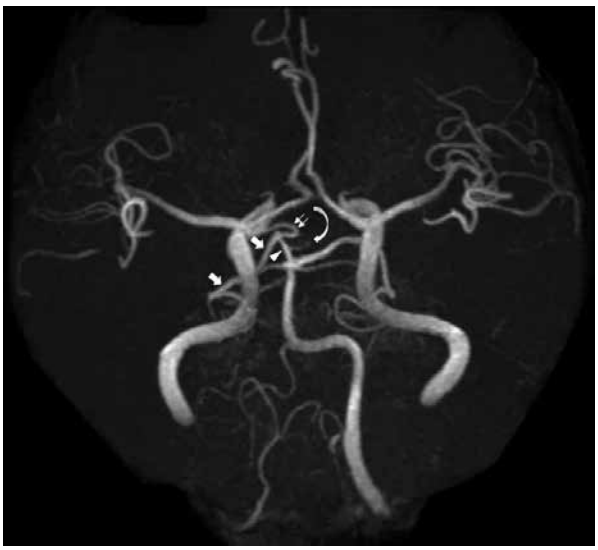

Fig 2.
Control magnetic resonance angiography on the 15th day after cerebrovascular accident at the time of clinical improvement demonstrated restoration of the right P1 segment (*arrowhead*) with visualization of its perforating branch (*curved arrow*), which might be the artery of Percheron. The entire right posterior cerebral artery (*thick arrows*) originating through posterior communicating artery (*double arrows*) is well preserved.

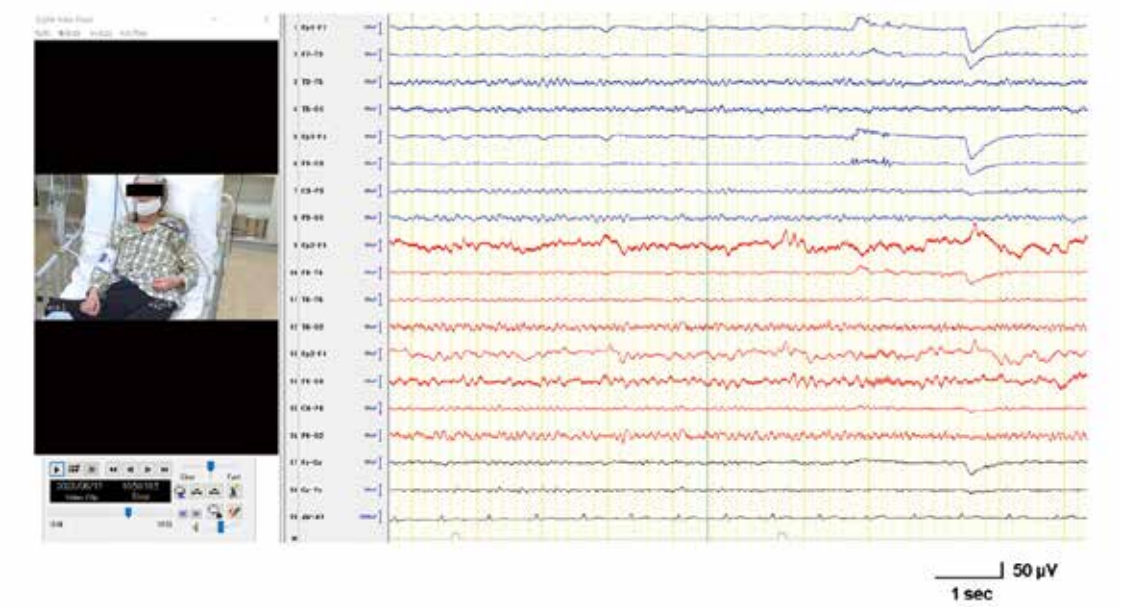

Fig 3.
Findings during video-electroencephalography monitoring (bipolar montage, time constant 0.1 s, high-pass filter 50 Hz) of the presented patient at the time of altered mental state reflected in stopped moving and talking, absence of response to commands, and appearance of muscle stiffness in both upper limbs. Background activity is quite normal and showing well organized rhythm of about 8-9 Hz with no significant asymmetry between sides or epileptiform abnormalities.

were discontinued and prolonged video-electroencephalography (EEG) monitoring was started, while it did not reveal any epileptiform abnormalities. On the 3rd day after re-admission, the patient suddenly stopped moving and talking, did not respond to commands, and showed muscle stiffness in both upper limbs. Still no abnormalities on EEG suggestive for NCSE were noted during this episode of altered mental state (Fig. 3). Blood and urine examination did not reveal significant metabolic disturbances and there were no obvious infectious disorders. Such patient's condition lasted for 4 consecutive days and was considered as manifestation of akinetic mutism caused by previous bilateral paramedian thalamic infarction. Because of parkinsonian symptoms (muscle stiffness, immobility), therapy with amantadine (100 mg per day) was initiated and resulted in prominent neurological improvement with restoration of speech and regained locomotion. The patient did not remember his condition during altered mental state. Soon thereafter, he was transferred back to the rehabilitation facility and never experienced such episodes of altered consciousness again as long as therapy with amantadine was continued. However, owed to related complication (ileus) this treatment was terminated, which resulted in recurrence of his symptoms.

DISCUSSION

The diagnosis of the artery of Percheron occlusion is generally based on typical MRI findings on diffusion-weighted and FLAIR images and specific neurological deficit (2-4). In our patient, the area of high signal intensity on MRI at admission extended not only on paramedian regions of both thalami but on the anterior part of the left thalamus as well, while without midbrain involvement. This variant of bilateral paramedian thalamic infarction is considered the least prevalent (2, 4), while some studies does not confirm it (3). In such cases, differential diagnosis should always include the distal BA occlusion, but the latter usually also affects vascular territories supplied by PCA, as well as superior cerebellar and pontine arteries (2, 4), which was not evident in our patient. In addition, MRA demonstrated hypoplastic right P1 segment with the fetal type of the right PCA origin, and well visualized the entire BA and left PCA. Of note, direct visualization of the artery of Percheron with MRA, CT angiography, or digital subtraction angiography, is considered inconsistent (2, 4). However, in the presented case, MRA at the time of clinical improvement on the 15th day after CVA demonstrated restoration of the right P1 segment with visualization of its perforating branch, which might be the artery of Percheron. Obviously, perfusion CT examination may be helpful for diagnosis of any CVA (2), but it was not done in the presented case. Our patient was admitted in coma with GCS score of 6, which is rather common in cases of the artery of Percheron occlusion (2-4). For instance, in the series of Chiang *et al*. (4), 9 out of 10 such patients were presented with altered mental status (while the authors did not provide more details of their condition). Our patient also demonstrated vertical gaze palsy, which is rather typical in cases of the artery of Percheron occlusion (2-4).

Akinetic mutism is a serious consequence of bilateral paramedian thalamic infarction. It is usually noticed upon improvement of the patient's consciousness level, and may significantly complicate rehabilitation and return to social activities, occasionally leaving affected individual bedridden. Although such clinical condition may be caused by alterations of various brain structures, it is believed that the primary mechanism of its pathogenesis is related to dysfunction of the frontal-subcortical circuitry, for which thalamus is playing one of the central roles (1). It was particularly proved by Katsuki *et al*. (5), who used ^{123}I-IMP-SPECT and DTI-based tractography in a patent with akinetic mutism caused by the artery of Percheron occlusion and revealed decreased blood flow in medial frontal lobes on both sides and interruption of the white matter tracts from thalami to the frontal cortex.

Intermittent clinical course of akinetic mutism is very unusual. It was mainly described in cases of recurrent chronic hydrocephalus accompanying episodes of shunt malfunction,

which was linked to compression of the dopaminergic projection system in the paraventricular regions by repeated extensions of the cerebral ventricles (6, 7). On the other hand, Burruss and Chacko (8) reported episodically remitting akinetic mutism in severely disabled patient, who underwent clipping of ruptured BA aneurysm and demonstrated recovery of alertness and affect after epileptic seizures, but no reliable explanation of his condition could be given. Similarly, in our patient the pathophysiological mechanism of intermittent akinetic mutism accompanied by parkinsonian symptoms, which appeared on the medium-term follow-up after bilateral paramedian thalamic infarction remained obscured, while it can be related to subtle changes of the cerebral perfusion or metabolism. Although it was suggested that akinetic mutism can be occasionally induced by levetiracetam (9), it should be noted that by the time of last episode of altered mental state in our patient all ASM were discontinued.

Intermittent akinetic mutism should be clearly distinguished from other clinical conditions. While its differentiation with NCSE by means of prolonged video-EEG monitoring is rather straightforward, as has been re-confirmed in the presented case, exclusion of akinetic "catatonic disorder due to another medical condition" (10) may be much more difficult due to overlapping symptomatology (11-13). Moreover, recurrent catatonia in Parkinson disease has been reported (14), and it might alternatively explain the condition of our patient. Of note, he did not recall any episode of his altered mental state and it is considered more typical for akinetic mutism in difference to catatonia, which is usually remembered by the affected individual (11). However, neither lorazepam challenge test suggested for differential diagnosis of catatonia (13), nor DTI-based tractography, which may reveal different patterns of the white matter tracts alterations (5, 15) were applied in our case.

Although differentiation of akinetic mutism and akinetic catatonia may be quite difficult, either of these conditions may be effectively treated by NMDA receptor antagonists, such as amantadine, which may similarly relieve a dopaminergic dysfunction of the frontal-subcortical circuitry (in cases of akinetic mutism) or wider cortico-striato-thalamo-cortical circuits (involved in pathophysiology of catatonia) (13). In our patient such therapy provided good effect, which lasted until termination of treatment owed to related complication. Considering wide clinical experience with amantadine in management of Parkinson disease, good safety profile of this drug, and coverage of its use in patients with such consequences of CVA as diminished motivation, impaired spontaneity, and hypomotility by medical insurance (at least in Japan), the aforesaid therapy may be considered a reasonable option in cases of akinetic mutism caused by bilateral paramedian thalamic infarction.

CONCLUSIONS

Akinetic mutism after bilateral paramedian thalamic infarction caused by the artery of Percheron occlusion may occasionally demonstrate intermittent clinical course, which requires differentiation with NCSE and akinetic catatonia. As was demonstrated in our patient, treatment with amantadine in such cases may be quite effective, and this therapeutic option should be given full consideration.

CONFLICT OF INTEREST DISCLOSURE

The authors have no personal or institutional interests in drugs, materials, or devices described in this paper.

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