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CASE REPORT

Lack of motivation: Akinetic mutism after subarachnoid haemorrhage

M.W. Herklots[1], A. Oldenbeuving[2], G.N. Beute[3], G. Roks[1], G.G. Schoonman[1]

Departments of [1]Neurology, [2]Intensive Care Medicine and [3]Neurosurgery, St. Elisabeth Hospital, Tilburg, the Netherlands

Correspondence

M.W. Herklots - m.herklots@elisabeth.nl

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Abstract

Akinetic mutism is a rare neurological condition characterised by the lack of verbal and motor output in the presence of preserved alertness. It has been described in a number of neurological conditions including trauma, malignancy and cerebral ischaemia. We present three patients with ruptured aneurysms of the anterior circulation and akinetic mutism. After treatment of the aneurysm, the patients lay immobile, mute and were unresponsive to commands or questions. However, these patients were awake and their eyes followed the movements of persons around their bed. MRI showed bilateral ischaemia of the medial frontal lobes. Our case series highlights the risk of akinetic mutism in patients with ruptured aneurysms of the anterior circulation. It is important to recognise akinetic mutism in a patient and not to mistake it for a minimal consciousness state.

Introduction

Akinetic mutism was introduced by Karl Kleist (1922) to denote a syndrome characterised by profound apathy and a lack of verbal and motor output, in the presence of preserved alertness. Patients display no emotions, lay immobile, mute and are unresponsive to commands and questions. They do not initiate eating or drinking. Even during a painful stimulus, they remain indifferent. Patients seem awake and visually track objects.[1] Akinetic mutism is generally associated with bilateral lesions of the medial frontal lobes (cingulate gyrus), although bilateral lesions of the thalamus/basal ganglia and the upper brainstem have also been described.[2,3] Incomplete or partial forms of akinetic mutism are called abulia. Abulia is part of a spectrum of motivational impairment with akinetic mutism as the most extreme state.

One of the causes of akinetic mutism is delayed cerebral ischaemia after a subarachnoid haemorrhage (SAH). The incidence of SAH, caused by a ruptured cerebral aneurysm, is estimated to be between 5 and 10 per 100,000 per year.[4,5] One of the major threats after an aneurysmal SAH is delayed cerebral ischaemia, caused by cerebral vasospasm. Cerebral infarction on CT scans is seen in about 25 to 35% of patients surviving the initial haemorrhage, mostly between days 4 and 10 after the SAH. In 77% of the patients the area of cerebral infarction corresponded with the aneurysm location. Delayed cerebral ischaemia is associated with worse functional outcome and higher mortality rate.[6]

Cases

Case 1: Anterior communicating artery aneurysm

A 28-year-old woman with an unremarkable medical history presented with a Hunt and Hess grade 3 and Fisher grade 3 SAH *(figure 1A)*. Initial CT angiography (CTA) showed a small anterior communicating artery aneurysm. Cerebral angiography demonstrated a 4 mm aneurysm, which could not be coiled *(figure 1B)*. Because of the high Hunt and Hess grade, clipping was postponed until eight days after the initial haemorrhage. Following the angiography, the patient was initially neurologically intact. However, seven days after the initial haemorrhage, one day before the clipping was planned, the patient's neurological state acutely deteriorated, with a

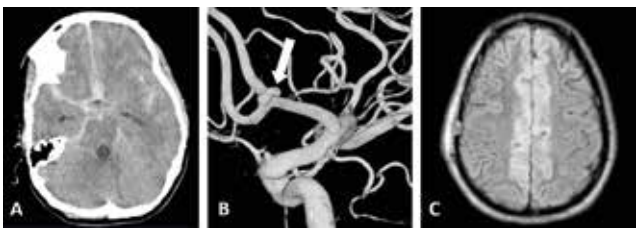

Figure 1. Brain CT, angiography and MRI of case 1. A: Noncontrast axial CT scan showing Hunt and Hess grade 3 and Fisher grade 3 subarachnoid haemorrhage. B: Cerebral angiography demonstrating a 4 mm anterior communicating artery aneurysm (arrow). C: Axial FLAIR MRI showing bilateral ischaemia of the medial frontal lobes after successful clipping of the aneurysm

Glasgow Coma Score (GCS) of 3. CT scan showed a rebleed with a Fisher grade 4 SAH. This was immediately treated with a right pterional craniotomy and clipping of the aneurysm. Postoperatively, the patient had her eyes open and followed the movements of persons around her bed, but she lay immobile, mute and unresponsive to commands or questions. The brainstem reflexes were intact. CTA revealed some mild bilateral carotid vasospasms. Hypertension was induced. Nevertheless bilateral ischaemia of the medial frontal lobes was seen on the fluid attenuation inversion recovery (FLAIR) MRI *(figure 1C)*. Five days after the rebleed, the patient moved her arms and sometimes she even followed simple commands with her hands. During the following weeks the patient evolved to an abulic state, with apathy, lack of spontaneous movements, spontaneous speech and social interaction. Thirteen months after the initial haemorrhage she had a Glasgow Outcome Scale – Extended (GOSE) of 5 (lower moderate disability).

Case 2: Left pericallosal artery aneurysm

A 47-year-old woman with an unremarkable medical history presented with a Hunt and Hess grade 4 and Fisher grade 4 SAH *(figure 2A)*. Initial CTA showed a small left pericallosal artery aneurysm. Cerebral angiography and successful coiling were performed the same day as the SAH. During the first days after admission, the patient was comatose, with a GCS of 3, but she also received intravenous midazolam because of a seizure. After stopping the midazolam, the patient opened her eyes, but there was no verbal and motor output. Hypertension therapy was started. MRI showed bilateral ischaemia of the medial frontal lobes and part of the genu of the corpus callosum *(figure 2B and 2C)*. Three weeks after admission the patient showed a fluctuating GCS, between following simple commands and no motor output at all, not even after a painful stimulus. Most of the time she lay immobile and mute, but followed movements of the people around her. In the following months she improved slowly. After six months she had a GOSE of 6 (upper moderate disability).

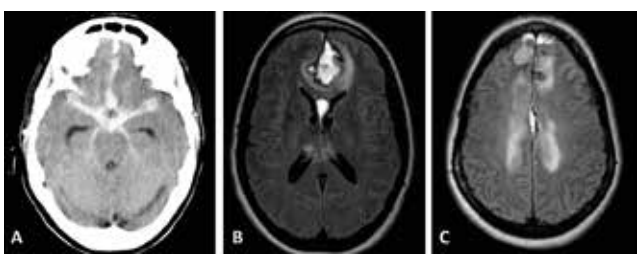

Figure 2. Brain CT and MRI of case 2. A: Noncontrast axial CT scan showing Hunt and Hess grade 4 and Fisher grade 4 subarachnoid haemorrhage. B and C: Axial FLAIR MRI showing ischaemia of the genu of the corpus callosum (B) and bilateral ischaemia of the medial frontal lobes (C)

Case 3: Left pericallosal artery aneurysm

A 59-year-old man with an unremarkable medical history presented with a Hunt and Hess grade 4 and Fisher grade 4 SAH *(figure 3A)*. CTA was negative. Because of an obstructive hydrocephalus secondary to the intraventricular haemorrhage, emergency placement of an external ventricular drain was necessary. The initial diagnostic angiography showed some irregularity of the left pericallosal artery, but no aneurysm. A repeat angiography after one week showed the same irregularity, but still no aneurysm. MRI and magnetic resonance angiography showed bilateral ischaemia of the medial frontal lobes, but also a structure suspected to be a thrombosed aneurysm *(figure 3B and 3C)*. Exploratory surgery confirmed the presence of a large thrombosed aneurysm of the left pericallosal artery. The aneurysm was clipped and the haematoma was evacuated. Four days after hospital admission, the patient opened his eyes, he looked focused and followed movements, but he was unresponsive to commands or questions. Ten days after the haemorrhage, the patient followed simple commands, but his condition fluctuated greatly. From the akinetic mutistic state he slowly evolved in an abulic state. After one month he spoke for the first time. After five months he had a GOSE of 3 (lower severe disability)

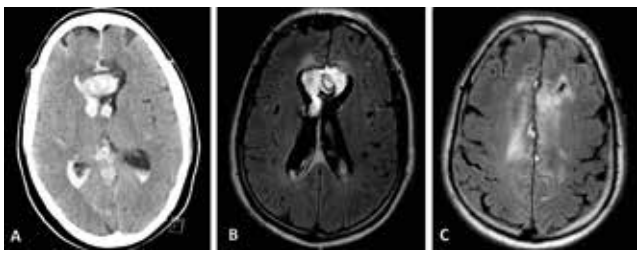

Figure 3. Brain CT and MRI of case 3. A: Noncontrast axial CT scan showing Hunt and Hess grade 4 and Fisher grade 4 subarachnoid haemorrhage with bleeding in both lateral ventricles. B: Axial FLAIR MRI showing a thrombosed aneurysm of the left pericallosal artery. C: Axial FLAIR MRI showing bilateral ischaemia of the medial frontal lobes

Discussion

Akinetic mutism is a neurological condition characterised by akinesia (inability to move) and mutism (inability to speak). The inability to move is not the result of a paresis or paralysis, but it is caused by a complete or nearly complete loss of spontaneity and initiative, resulting in lack of action, ideation, speech and emotions. Patients with akinetic mutism sporadically follow commands but this can show considerable fluctuation. There is a normal sleep-wake cycle.[1,2,7]

Pathophysiology

Akinetic mutism is generally associated with bilateral lesions of the centromedial part of the brain from the anteromedial frontal lobes down to the upper brain stem. There are specific areas involved such as the frontal lobes (cingulate gyrus, supplementary motor area and dorso-lateral border zone), basal ganglia (caudate, putamen), diencephalon (thalamus, hypothalamus) and mesencephalon. These sites are located along

pathways that originate in the mesencephalon (substantia nigra) and project widely to dopamine receptors in the spinal cord, brainstem, diencephalon, striatum and mesiofrontal lobe.[8,9]

In our three cases there was bilateral ischaemia of the medial frontal lobes, in particular of the cingulated gyrus. The cingulated cortex is involved in various functions. First, it has a role in premotor function and shares many features with the premotor areas. Electrical stimulation of the anterior cingulated cortex elicits primitive gestures, for example rubbing, kneading, sucking, lip-smacking or pressing fingers together. Second, the cingulated cortex is involved in vocalisation; for example involuntary vocalisation or speech arrest is common in cingulated seizures. Electrical stimulation can cause dysphasia, perseveration or change in speech volume. Third, emotions are in part mediated by the cingulated cortex. Electrical stimulation evokes different emotions, including fear, pleasure and agitation. During cingulated seizures emotional changes are common, for example laughing, crying or irritability.[9] The cingulated cortex is also involved in the way we respond to pain. Foltz and White[10] successfully treated patients with chronic pain with cingulumotomy. They report that the patients still feel the pain, but it does not bother them or trigger any adverse emotional reaction.

Causes

Several different pathologies can cause akinetic mutism, but always with involvement of the frontal lobes, basal ganglia, the mesencephalon or thalamus:

- Infarction, for example bilateral anterior cerebral artery infarction with frontal lobe damage or bilateral thalamus damage, due to percheron artery infarction[11]
- Frontal lobotomy[12]
- Thalamus and hypothalamus damage secondary to hydrocephalus[8,13]
- Creutzfeldt-Jacob disease[14]
- Traumatic brain injury[15]
- Tumours, for example astrocytoma with bilateral basal ganglia invasion[16]
- Induced by medication, for example tacrolimus [17]
- Anterior communicating artery aneurysm[2]
- Carbon monoxide intoxication with bilateral frontal lobe damage[18]
- Anoxia.[19]

In our cases akinetic mutism was caused by a ruptured aneurysm of the anterior communicating artery or the pericallosal artery, with secondary ischaemia of the medial frontal lobes. In our cases, in spite of hypertensive treatment, there was no improvement.

Differential diagnosis

The diagnosis is important as akinetic mutism can be mistaken for minimally conscious state, delirium or even locked-in syndrome. The differential diagnosis between akinetic mutism and minimally conscious state can be difficult, since the two conditions generally share the features of diffuse motor deficit, fluctuations in obeying simple orders and the presence of eye tracking and sleep-wake cycle. Sometimes the differentiation only becomes clear after an MRI scan.[7] There are two clinical phenomena that can help to differentiate between akinetic mutism/abulia on the one hand and minimal conscious state on the other hand. The first is the telephone effect, in which patients speak more or sometimes almost fluently on a telephone. Unfortunately not all patients show this effect, but in abulic patients some improvement of the speech on a telephone is common. The second clinical phenomenon in patients with akinetic mutism or abulia is the paradoxical performance, in which patients suddenly express complex and correct ideas, for a few seconds or minutes.[1,3,15] We did not observe these phenomena in our patients.

A delirium fluctuates more than akinetic mutism, with some good periods in contrast to akinetic mutism. Moreover, a patient with a delirium could improve with medication, for example neuroleptics.

To distinguish akinetic mutism from locked-in syndrome, it is very important to look at the eyes of the patient. Someone with locked-in syndrome has voluntary eye movements, especially vertical eye movements are spared.

Cerebellar mutism is another syndrome that should be in the differential diagnosis. It consists of mutism, emotional lability, hypotonia, and ataxia. Typically it starts one to two days after resection of a midline posterior fossa tumour, mostly in children; however, it has also been described after trauma or cerebellar haemorrhage. The difference with akinetic mutism is that patients with cerebellar mutism can still move, although with ataxia.[20]

Treatment

There is little information about the treatment of akinetic mutism, except treating the underlying and concurrent medical conditions. Most case reports have presented patients with akinetic mutism successfully treated with dopamine receptor agonists.[8,13,21,22] However, there are also case reports about patients with akinetic mutism being successfully treated with olanzapine, atomoxetine and levodopa.[23-25] Most of the reported cases are hydrocephalus patients. There are no reports about treatment response in patients with akinetic mutism due to SAH. We did not try the above-mentioned medications in our patients.

Prognosis

There is little known about the prognosis of akinetic mutism. In our group, one patient showed only a very small improvement from a GOSE of 2 to 3. However the other two patients showed a more significant improvement from an initial GOSE of 2 to a GOSE of 5-6.

Conclusion

Akinetic mutism is a neurological condition characterised by the lack of verbal and motor output in the presence of preserved alertness. It has been described in a number of neurological conditions including trauma, malignancy and cerebral ischaemia. In our cases akinetic mutism was caused by a ruptured aneurysm of the anterior communicating artery or the pericallosal artery, with secondary ischaemia of the medial frontal lobes. It is important to recognise akinetic mutism and not to mistake it for a minimally consciousness state.

Disclosures

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