Akinetic mutism after right internal watershed infarction

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ABSTRACT

We describe a 72-year-old man who developed akinetic mutism following a cerebrovascular accident involving his right internal watershed area and responded well to dopaminergic agonists. We discuss this rare condition and the unusual unilateral location of the lesion.

Keywords: akinetic mutism, cerebrovascular accident, dopaminergic agonist, subcortical infarction

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INTRODUCTION

Akinetic mutism is a neurological disorder characterised by diminished voluntary movement, speech and thought, without disturbance of arousal. The term was initially used in 1941 by Cairns et al in their presentation of a patient with an epidermoid cyst of the third ventricle.[1] This uncommon disorder has since been described in patients with stroke, typically involving bilateral frontal lobes or bilateral paramedian reticular formations, and has only rarely been described in unilateral lesions. We present a case of akinetic mutism in a 72-year-old man following unilateral right internal watershed infarction.

CASE REPORT

A 72-year-old right-handed man had a background history of hypertension, dyslipidaemia, and a previous stroke in 1997 with residual left-sided weakness. Post-stroke, he had been able to ambulate independently but slowly and was able to communicate normally. He was admitted to the stroke unit of a tertiary hospital in Singapore in January 2006 for recurrent left-sided weakness. On examination, he was alert with a left-sided hemiplegia. However, he was apathetic, with absence of verbal output and paucity of movement of the right limbs. He was able to track objects and occasionally nodded his head to questions.

Unenhanced limited axial magnetic resonance imaging with diffusion-weighted sequences of the brain showed multiple acute infarctions in the right middle cerebral artery and watershed territories, involving the right corona radiata, and cortical and subcortical white matter of the right fronto-parietal-occipital lobes. In addition, there were old infarctions in the left medulla and left cerebellum, and an area of gliosis at the right occipital pole (Fig. 1). There was no obvious involvement of the cingulate gyrus. Magnetic resonance angiography demonstrated occlusion of the right internal carotid artery. Subsequently, Doppler ultrasonography of the carotid arteries confirmed severe stenosis of the distal right internal carotid artery.

He was transferred to the hospital's rehabilitation unit two weeks later. On arrival, he was maximally dependent in all activities of self-care, transfers and locomotion, incontinent of urine and bowel, and required nasogastric tube feeding. He was diagnosed with akinetic mutism, with depression as a possible confounding factor. A therapeutic trial of Madopar (L-dopa 100 mg, benserazide 25 mg) 62.5 mg three times daily, and Fluoxetine 20 mg once daily was commenced; and subsequently titrated up to Madopar 125 mg three times daily and Fluoxetine 40 mg once daily. He also underwent concurrent physical, occupational and speech therapy.

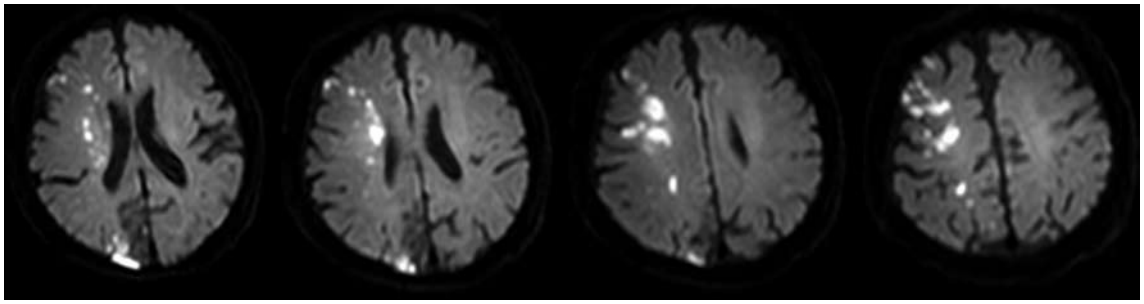

Fig. 1 Series of diffusion-weighted MR images of the brain show multiple acute infarctions in the right middle cerebral artery and watershed territories.

Over the course of six weeks in the rehabilitation unit, neurological and functional improvements were noted. There was improved eye contact, increased frequency of shaking or nodding his head to simple questions, increased participation in therapy sessions with occasional utterance of monosyllabic responses to simple questions, and he was successfully weaned onto full oral feeding with modified diet and thickened fluids. By the time of discharge, he was able to ambulate using a walking aid with minimal to moderate assistance of one helper. However, he was still generally apathetic, inconsistent in his interaction and required moderate assistance in all activities of self-care and transfers.

DISCUSSION

The main differential diagnoses of this case were aphasia, aphemia, locked-in syndrome and severe depression. Our patient was initially thought to be globally dysphasic. Although this might account for his lack of verbal output, it did not explain his profound lack of effort to communicate or to follow non-verbal commands. It is also unlikely as aphasia is usually associated with left-sided lesions in patients who are right-handed, as is the case with our patient. Aphemia was ruled out as written communication was also absent. Locked-in syndrome was not a possibility as occasional, though rare, spontaneous movements of his right side were observed. Furthermore, the site of stroke is inconsistent with that of locked-in syndrome. Severe apathetic depression could not be excluded and hence, he was treated with anti-depressants. Overall, his clinical picture was most consistent with akinetic mutism, as he was alert and able to track objects visually but made no attempt to communicate verbally or non-verbally; moved his limbs spontaneously, albeit only rarely; and was eventually able to walk with assistance – indicating that the descending pathways were intact.

Akinetic mutism may arise from various causes including stroke, subarachnoid haemorrhage,[2] toxic encephalopathy,[3] carbon monoxide poisoning,[4] Creutzfeldt-Jakob disease,[5] malignancy,[6] and Behcet's disease.[7] In patients with stroke, sites involved may be grouped into the (1) medio-frontal, (2) midbrain and thalamus,[7,10] (3) basal ganglia,[11] and (4) subcortical regions,[7] and are usually bilateral involving one or more of these sites, e.g. bilateral anterior cerebral artery infarction,[8,9] and left anterior cerebral artery infarction with bilateral subcortical and basal ganglia lesions.[12] Unilateral lesions causing akinetic mutism have been infrequently described – including one patient with left anterior cerebral artery infarction,[13] one with left and another one with right capsular genu infarction,[14] and one with left thalamomesencephalic infarction.[15]

Akinetic mutism is thought to be a state of avolition in which the patient has no desire to think, speak or move, therefore resulting in the clinical picture as described above. It is proposed that this is caused by loss of frontal executive functions secondary to frontal lobe dysfunction – either due to bilateral frontal lobe lesions or disruption of the frontal-subcortical circuits; leading to lack of spontaneous thought, speech and motor activity, but with intact memory, sensory and motor pathways. This theory is supported by involvement of the frontal lobes and/or components of the frontal-subcortical circuits (the basal ganglia, internal capsules, thalami, hypothalamus, limbic lobes and mesencephalon) in patients with akinetic mutism due to stroke or other neurological disorders. It is further supported by a functional imaging study which showed reduced metabolism in both frontal and cingulate cortices and subcortical white matter, with preserved metabolism in the sensory-motor cortex, temporal lobes, basal ganglia and brainstem in a patient with akinetic mutism after carbon monoxide poisoning.[4]

In our patient, we believe that extensive right subcortical infarction resulted in disruption of his fronto-subcortical circuits leading to frontal lobe dysfunction and hence akinetic mutism. The old lesions in the contralateral medulla and cerebellum, sites not usually involved in akinetic mutism, were unlikely to have been a contributing factor although the possibility cannot be totally discounted. Unilateral lesions, such as those occurring in our patient, resulting in akinetic mutism are rarely reported. Why and how predominantly bilateral, and occasionally unilateral, dominant or non-dominant hemispheric lesions result in this rare condition remains to be elucidated. Further functional studies may be useful towards increasing our understanding of the nature of frontal executive functions and the pathophysiology of lesions of the frontal lobes and their subcortical connections.

Treatment of akinetic mutism involves treating the underlying and concurrent medical conditions, removal or reduction of pharmacological agents that may reduce motivation, pharmacological therapy and non-pharmacological therapy.[17] Pharmacological therapy includes mainly dopaminergic agents – dramatic improvement in patients with akinetic mutism after treatment with bromocriptine, pergolide or levo-dopa have been reported,[16] but no randomised controlled trials are available, possibly due to the rarity of the condition. It is postulated that as frontal-subcortical circuits comprise dopaminergic neurons, repletion of dopamine restores the function of these pathways. Other agents such as stimulants, activating anti-depressants, cholinesterase inhibitors, glutaminergic

agents and new psychotropic modafinil may also be helpful.[17] Non-pharmacological therapy includes environmental modification to increase interest and stimulation, and cognitive-behavioural therapy tailored to the patient's specific deficits.[17] Our patient responded to a levo-dopa/benserazide combination, a selective serotinergic receptor inhibitor and intensive rehabilitation.

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