Postanoxic Akinesia with Bilateral Pallidal Lesions: A PET Study

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Abstract

A 70-year-old woman developed marked akinesia after an anoxic event related to bronchiectasia. Magnetic resonance imaging studies revealed lesions in the bilateral globus pallidus and, to a lesser extent, in the putamen. Positron emission tomography studies with ¹⁸F-6-fluoro-L-dopa and ¹¹C-N-methylspiperone showed a decreased pre- and post-synaptic uptake in the striatum. Consistent with previous reports, the present case demonstrated the basal ganglia, particularly the globus pallidus, to be selectively susceptible to anoxic insults. Furthermore, a PET study indicated a disrupted presynaptic integrity of the dopaminergic terminals and decreased dopamine D₂ receptor binding, which together appear to underlie the pathophysiology of post-anoxic akinesia, at least in the present case.

Key words: Parkinsonism, akinesia, anoxia, globus pallidus, dopamine, positron emission tomography

Introduction

Anoxia is a cause of brain damage distinct from ischemia and other neurotoxic insults, such as carbon monoxide poisoning. The clinical details of anoxic brain injury remain unclear, because anoxia often accompanies ischemia and only on rare occasions causes purely anoxic brain injury, including accidents during anesthesia, drowning, altitude disease, and respiratory failure. We herein report a patient who suffered from severe anoxia and developed akinesia. We studied her anatomic lesions by magnetic resonance imaging (MRI) and dopamine transmission with positron emission tomography (PET) using ¹⁸F-6-fluoro-L-dopa (¹⁸F-DOPA) and ¹¹C-N-methylspiperone (¹¹C-NMSP) as tracers.

Case Report

A 70-year-old woman developed massive hemoptysis. Prior to this event, she was ambulatory with a normal intellect. She had no remarkable past medical history except for having suffered from bronchiectasia for 30 years. On arrival, she was cyanotic and comatose with feeble respiration. The results of the initial arterial blood gas examination showed a pH of 6.74, PaCO₂ of 114 mmHg and PaO₂ of 34.6 mmHg. Her blood pressure was maintained at a normal level. She gradually regained consciousness within two days. A CT study four days after the onset exhibited a low density area in the bilateral lentiform nuclei. Two years after the event, she was referred to our department with a chief complaint of gait disturbance. A general examination revealed fine crackles in the lower lung fields. A full blood count indicated microcytic hypochromic anemia, but the results of other routine blood tests were unremarkable, including the plasma copper and ceruloplasmin level. Neurologically, she was conscious and well oriented. Her intelligence score on the Wechsler Adult Intelligence Scale Revised (WAIS-R) scale was 79 (verbal IQ 79, performance IQ 78) and she had 23/26 correct responses in Raven’s Colored Progressive Matrices test (RCPM). She showed severe akinesia and an impaired postural reflex. Her muscle rigidity was minimal. She showed frequent gait freezing, particularly on initiation and turning. Her gait freezing markedly improved when she walked on stripes drawn on the floor. Her voice was se-
An MRI study showed T2 high and T1 low signal lesions in the bilateral globus pallidus, and to a lesser extent in the putamen (Fig. 1). A magnetic resonance angiography study revealed no significant stenosis in the major vessels. PET studies with \(^{11}\text{C}\)-NMSP and \(^{18}\text{F}\)-DOPA were conducted on separate days in the absence of dopaminergic treatment (HEADTOME-JV, Shimazu, Kyoto, Japan). The radioactivity in six regions of interest (ROIs; bilateral caudate nucleus, anterior and posterior parts of the putamen) was sampled (1). The uptake in each ROI was compared to the non-specific retention in the cerebellum at 90 minutes for \(^{11}\text{C}\)-NMSP and at 120 minutes for \(^{18}\text{F}\)-DOPA. When compared with healthy control subjects (n=5; age 68.8±8.3 [mean ± SD]), the \(^{11}\text{C}\)-NMSP uptake ratios of our patient were markedly decreased bilaterally in all ROIs (p<0.01, t-test; Fig. 2, top). For the \(^{18}\text{F}\)-DOPA PET study, the control group included subjects with a wide range of ages (n=9; age 20 to 81; 38.7±26.8 [mean ± SD]), because age does not influence the \(^{18}\text{F}\)-DOPA PET data in any of the ROIs used in this study (p>0.17, Pearson’s test). The \(^{18}\text{F}\)-DOPA uptake ratios of our patient were significantly lower than those of the control group in all ROIs (Fig. 2, bottom).

**Discussion**

Our patient developed marked akinesia and postural disturbance after severe hypoxia. The results of the WAIS-R and RCPM indicated that her cognitive functions were relatively preserved. Therefore, her akinesia cannot be explained by cognitive impairment or decreased motivation, but likely were attributable to parkinsonism due to basal ganglia lesions. Similar cases have been reported with isolated lesions in the bilateral globus pallidus (GP), particularly in the external globus pallidus (GPe) (2-4). The clinical course and the results of neuroimaging studies suggest that other causes of akinesia are unlikely, including normal pressure hydrocephalus, idiopathic and drug-induced parkinsonism, progressive supranuclear palsy, corticobasal degeneration, and Wilson’s disease.

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According to the standard physiological model of the basal ganglia, the GPe is a key station of the indirect pathway,
and its damage would lead to a net reduction in the basal ganglia output to the thalamus through disinhibition of the subthalamic nucleus and increased excitation of the internal segment of GP (GPI) (5, 6). Therefore, akinesia due to GPe lesions can thus be explained by this model. On the other hand, GPI lesions apparently ameliorate parkinsonism, as proven by therapeutic pallidotomy in Parkinson disease patients. In our patient, it was difficult to specify the lesions responsible for the akinesia because of the presence of other lesions in the basal ganglia (Fig. 1B). Based on the pathophysiological theory of parkinsonism, we speculated that the adverse effect of GP lesions may have overwhelmed the anti-parkinsonian effect of the GPe lesions in this patient. Previous studies of anoxic brain damage have also showed that akinesia is associated with GP lesions, while dystonia patients tend to have lesions in the putamen (7, 8).

Besides the anatomical lesions in the basal ganglia, the PET study performed on our patient revealed the functional blockade of dopamine transmission. Striatal D2 receptor binding was decreased in our patient, which is in contrast to the findings observed in Parkinson’s disease patients who show increased striatal D2 receptor binding in the absence of dopaminergic treatment (9, 10).

The striatum and globus pallidus are also susceptible to neurotoxic insults by carbon monoxide, cyanide, and manganese (8, 11, 12). However, little is known about dopamine transmission in these clinical settings. Yoshii and colleagues conducted a 11C-NMSP PET study with a victim of carbon oxide (CO) poisoning with bilateral pallidial lesions (13). Unlike our case, the parkinsonism of their patient responded well to bromocriptine treatment, and a PET study revealed an increased D2 receptor binding potential in the striatum. The responsiveness to dopaminergic treatment may therefore be variable in postanoxic and neurotoxic akinesia, perhaps depending on the severity, lesioned structures, and etiologies. Dopamine PET may therefore predict the responsiveness to dopaminergic treatment for akinesia.

Hypoxia is also known to cause parkinsonism in association with nigral damage. Diffusion-weighted MRI in postanoxic patients showed decreased regional Apparent Diffusion Coefficient in the substantia nigra, thus indicating cytotoxic edema (14, 15). The substantia nigra (SNc) may be vulnerable to hypoxia because of its high iron content and direct binding of carbon monoxide to heme iron. It is also possible that the decreased 18F-DOPA uptake reflects some degree of anoxic damage in the SNc.

In summary, postanoxic parkinsonism may result from damage to multiple brain structures, including the GP, putamen, and SNc. Dopamine PET may be useful in future studies to clarify how the various forms of postanoxic parkinsonism correlate with the clinical manifestations and drug responsiveness.

The authors state that they have no Conflict of Interest (COI).

References