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CORRESPONDENCE

Parkinsonism Caused by Viral Encephalitis Affecting the Bilateral Substantia Nigra

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Introduction

Post-encephalitic Parkinsonism is a relatively rare type of Parkinsonism [1]. It usually occurs several years after encephalitis, but it may also occur in the acute phase of encephalitis [2]. Post-encephalitic Parkinsonism is caused by damage to the substantia nigra [3] and the Parkinsonian symptoms could be markedly relieved by low-dose levodopa [2]. Lesions in the substantia nigra can be identified by magnetic resonance imaging (MRI) in some patients with post-encephalitic Parkinsonism. The substantia nigra is located in the midbrain, which is a relatively small part of the brainstem containing multiple structures with diverse functions. Therefore, midbrain damage affecting these neighboring structures could cause diverse manifestations. It is easy to distinguish damage to these structures based on clinical manifestations but it is usually confusing to distinguish them merely based on MRI. This article describes a patient who had Parkinsonism during the acute phase of viral encephalitis with lesions to the bilateral substantia nigra on MRI, and briefly discusses the pathogens, pathophysiology, clinical manifestations and treatment of post-encephalitic Parkinsonism. Also differentiated are three syndromes with similar imaging features, which might be confused with damage to the substantia nigra.

Case Report

A 22-year-old woman presented to the neurology department with a 7-day history of rhinorrhea and headache followed by a 3-day history of fever, dysphagia, bradykinesia, limb rigidity, and urination disturbances. At admission, the patient was unable to make any movements except blink the eyes. The patient had no history of drug abuse or family history of inherited diseases. Neurological examination revealed neck rigidity, hypomimia, dysarthria, and lead-pipe hypertonia, without tremor or ocular dyskinesia.

Magnetic resonance imaging (MRI) revealed lesions in the bilateral substantia nigra characterized by hyperintensity on T2-weighted sequences and fluid-attenuated inversion recovery (FLAIR) sequences, and hypointensity on T1-weighted sequences (Fig. 1). Cerebrospinal fluid test showed increased leukocyte counts (29×10^6/l, among which 86% were lymphocytes), and normal protein and glucose levels. No bacteria, mycobacteria or fungi were found in the patient's cerebrospinal fluid microscopically or by germiculture. Electroencephalography and X-ray films of chest were normal. Blood count revealed slightly increased leukocytes: 9.95×10^9/l (normal range 3.5–9.5×10^9/l), among which 79% were neutrophils (normal range 45–75%). The basic metabolic panel was normal and human immunodeficiency virus (HIV) antibody, cytomegalovirus antibody and Epstein-Barr virus antibody tests were all negative.

The patient was treated with acyclovir and levodopa and benserazide hydrochloride tablets for 14 days, and all of the symptoms were alleviated. Levodopa and benserazide hydrochloride tablets treatment was continued for an additional 16 days before the patient was discharged with all symptoms relieved and cerebrospinal fluid abnormalities resolved; however, the lesions on MRI remained (Fig. 2). The patient continued to receive levodopa and benserazide hydrochloride tablets treatment for 2 months, and no Parkinsonian symptoms reappeared after levodopa and benserazide hydrochloride tablets withdrawal; however, MRI still showed blurry lesions in the bilateral substantia nigra, especially on the left side (Fig. 3). The patient did not have any Parkinsonian symptoms 6 months after discharge but she refused to undergo MRI because she was trying to become pregnant.

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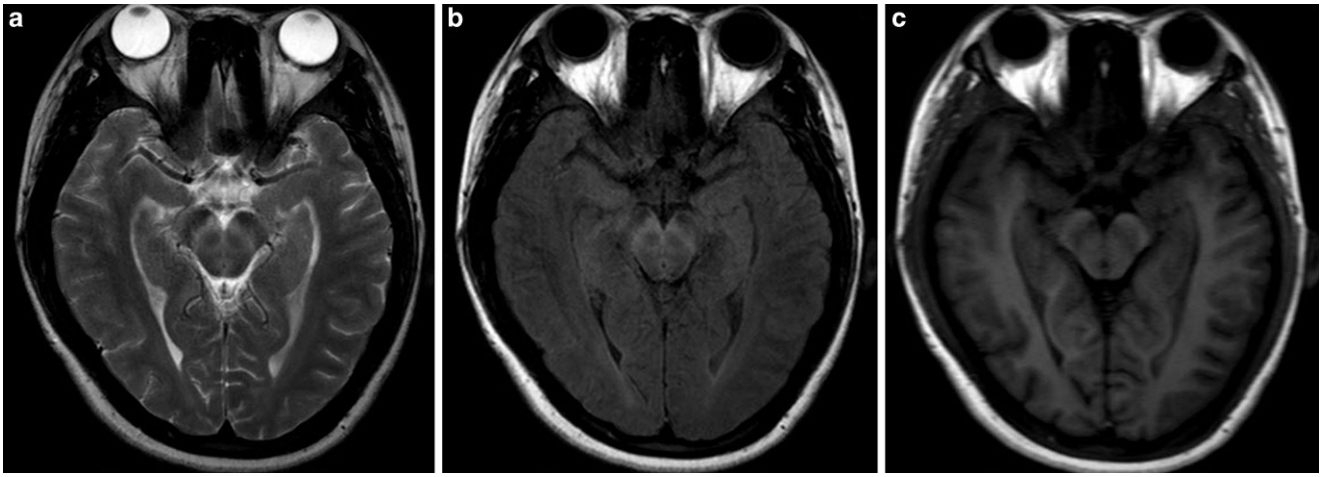

Fig. 1 Axial MRI images at admission show lesions in the bilateral substantia nigra characterized by hyperintensity on **a** T2-weighted imaging and **b** fluid-attenuated inversion recovery sequences. **c** Hypointensity on T1-weighted imaging

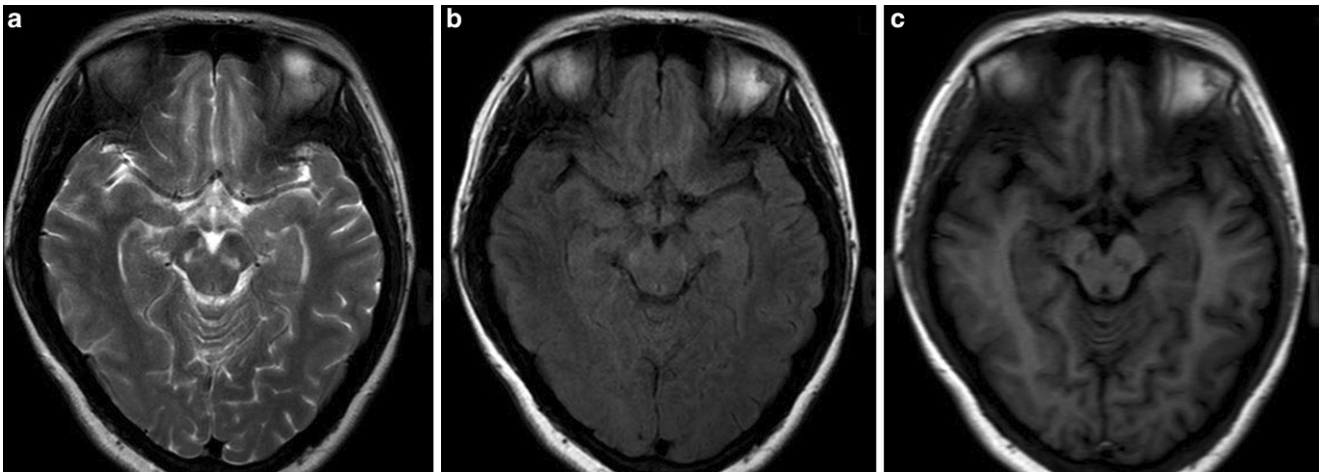

Fig. 2 **a** After treatment with acyclovir and levodopa and benserazide hydrochloride tablets, the hyperintense lesions in the bilateral substantia nigra on T2-weighted imaging decreased with clearer boundaries. **b** The lesions in the fluid-attenuated inversion recovery sequences decreased but became blurry. **c** T1-weighted imaging showed that the lesions in the bilateral substantia nigra became smaller with clearer boundaries after treatment

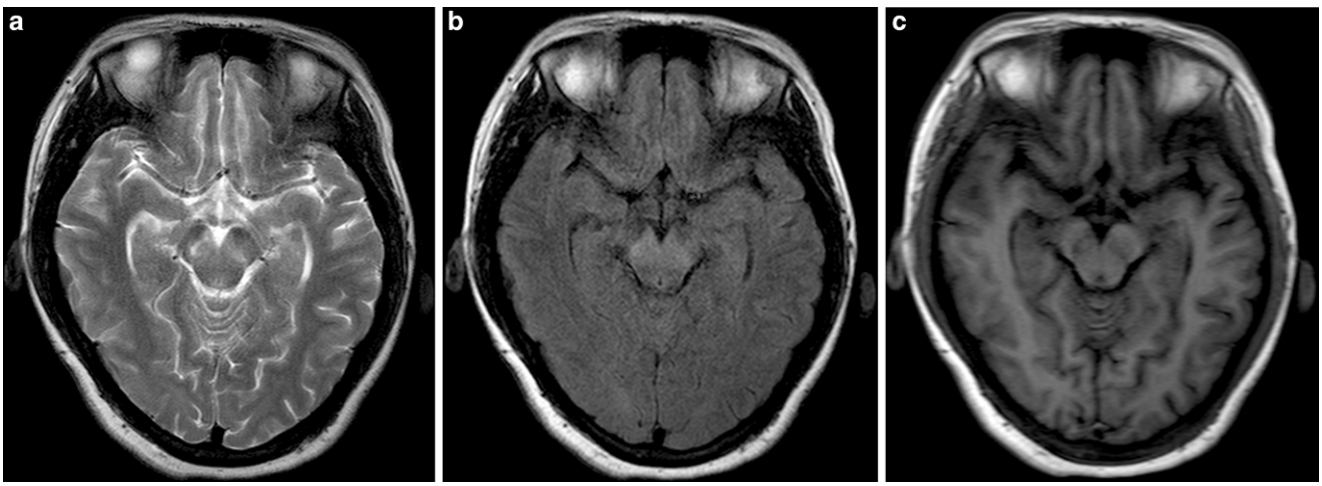

Fig. 3 **a** Two months after discharge, the hyperintense lesions in the bilateral substantia nigra on T2-weighted imaging became more blurred, especially the lesion on the left side. **b** The hyperintense lesions on the fluid-attenuated inversion recovery sequences also became more blurred. **c** The hypointense lesions in the bilateral substantia nigra on T1-weighted imaging also became more blurred

Discussion

Substantia nigra neurons, especially neurons of the substantia nigra pars compacta, synthesize and transfer dopamine to the striatum, including the putamen and caudate nucleus. This signaling pathway then passes through the globus pallidus, subthalamic nucleus and thalamus and finally to the motor cortex. When more than half of the dopaminergic nerves are lost, the symptoms of Parkinsonism emerge [4]. The loss of substantia nigra neurons is a typical pathological feature of Parkinsonism and manifests as bradykinesia, hypertonia, and gait dysfunction, with or without tremor [1, 5]. Parkinsonism is usually seen in the post-encephalitic phase, usually several years after encephalitis, but it occasionally occurs in the acute encephalitic phase [5]. Post-encephalitic Parkinsonism constitutes approximately 2.7% of all Parkinsonism cases [1], and it can be caused by various pathogens, including the influenza virus, coxsackie virus, Japanese encephalitis B virus, West Nile virus, Louis encephalitis virus, HIV, and *Plasmodium falciparum* [2, 3]. There are also cases reporting that post-encephalitic Parkinsonism can be caused by enteroviruses and dengue viral infections [6, 7]. Among these pathogens, Japanese encephalitis B virus is considered the predominant virus for inducing Parkinsonism [8]. In addition, there are also many cases of post-encephalitic Parkinsonism with an unclear pathogen etiology [3]. Patients with post-encephalitic Parkinsonism usually have influenza-like symptoms at onset and can rapidly progress to Parkinsonism. The Parkinsonian symptoms are often sensitive to low-dose levodopa [2, 9].

Substantia nigra is located in the midbrain, and it is close to the red nucleus, oculomotor nerves, cerebral peduncle and superior cerebellar peduncle [10]. As a relatively small area of the brain that contains multiple important structures, damage to the midbrain may cause various symptoms due to the impairment of different structures, including Benedict syndrome (red nucleus and oculomotor nerve impairment-induced involuntary movements and oculomotor paralysis), Claude syndrome (superior cerebellar peduncle and oculomotor nerve impairment-induced ataxia and oculomotor paralysis), and Weber syndrome (cerebral peduncle and oculomotor nerve impairment-induced limb paralysis and oculomotor paralysis) [10]. Having similar imaging features, these three syndromes should be differentiated from the substantia nigra damage in this case, especially when the clinical manifestations are not well-recognized. The clinical manifestations of these three syndromes are quite different from Parkinsonism and they mostly occur unilaterally; thus, it is relatively easy to distinguish them if neuroimaging and clinical manifestations are combined [10].

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Conflict of interest X. Liu, F. Deng and L. Chen declare that they have no competing interests.

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