Cerebral Infratentorial Large B-Cell Lymphoma Presenting as Parkinsonism

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Though rare, primary intracranial tumors can present with Parkinsonian symptoms, and diagnosis can be delayed unless there is a high index of suspicion. We herein present an 81-year-old man who was seen in our neurology clinic due to acute onset of unsteady gait and altered consciousness. Parkinsonism was initially diagnosed because of the typical manifestations. Levodopa was prescribed; however, there was a limited effect on his symptoms. Upon detail history and neurological examination, left sided hemiparesis was disclosed. Cerebral imaging studies revealed a solid mass over the right infratentorial para-midbrain area leading to reactive obstructive hydrocephalus. Work-up including chest and abdominal CT scanning, upper and lower GI endoscopy, and tumor marker studies failed to uncover any abnormalities. A neurosurgeon was consulted and a shunt procedure and biopsy of the infratentorial mass were performed. Histopathological examination of the biopsy tissue revealed tumor diffusely intermixed with large cells consistent with large B-cell lymphoma. The patient and his family declined further treatment. Though rare, cerebral tumors can present with Parkinsonian features and represent a diagnostic challenge. Clinicians should be aware of the possibility of cerebral neoplasms causing Parkinsonism, and include them in the differential diagnosis, especially for patients presenting with atypical Parkinsonian features, or those not responsive to initial therapy.

Keywords: levodopa; parkinsonism; large B-cell lymphoma; pyramidal signs; infratentorial area

Clinical Findings

An 81-year-old man was seen in our neurology clinic because of the rapid development of an unsteady gait beginning a few days prior. In addition, he had begun to stutter when speaking and his voice had become hypophonic and slurred. He was prescribed levodopa by his family physician under the assumption of Parkinsonism. He received little improvement from the levodopa, so was brought to our clinic. His medical history was significant for chronic obstructive pulmonary disease and peptic ulcer disease. When seen in our clinic, he denied any headache or blurred vision. Examination revealed an upright stance with a broad based gait, marked difficulty in gait initiation, and constant freezing in block motion. Postural instability was evident in the pull test. There was marked facial hypomimia with reduced blinking, his speech was very hypophonic, and he was disoriented to time and space. Cranial nerve testing revealed a masked face with slight dysarthria and dysphagia. A bilateral resting tremor was observed when he...
was asked to place his hands on the table. Cogwheel rigidity was detected bilaterally over the elbows and wrists. Ophthalmologic investigation revealed no ocular involvement. On motor system testing, his left side extremities were weak (left-sided hemiparesis with Medical Research Council scale R/L of 5/4). Initial non-enhanced cranial computed tomography (CT) revealed a solid mass in the right posterior midbrain causing mild dilatation of lateral and the 3rd ventricles (Fig. 1).

Upon admission, routine laboratory studies including tumor marker surveys were performed, but failed to uncover any abnormalities. Cerebrospinal fluid (CSF) examination was normal. Serology for human immunodeficiency virus (HIV) was negative. Abdominal sonography, bone scan, chest and abdominal CT and X-ray, and upper and lower gastrointestinal (GI) panendoscopy were all unremarkable. Gadolinium-enhanced cerebral magnetic resonance imaging (MRI) was performed which revealed a sizable para-midbrain tumor and reactive obstructive hydrocephalus (Fig. 2). MR spectroscopy revealed an increased choline/N-acetyl-aspartate (NAA) ratio and an amount of lactate indicating an active energy consumption/hypervascular state (Fig. 3).

A neurosurgeon was consulted to manage the hydrocephalus, and a ventriculo-peritoneal shunt was inserted and a biopsy of the para-midbrain mass was performed. Grossly, the tissue specimen had a smooth contour with superficial hypervascularity, and had been tightly adherent to the midbrain. Microscopic examination revealed tumor cells diffusely intermixed with large cells, suggesting lymphoid differentiation (Fig. 4).

Family members declined radiotherapy or chemotherapy, and he was transferred to hospice for further care.

Discussion

Parkinsonism is an array of neurological symptoms which presents as a pattern of involuntary movement. Cardinal features include resting tremor, bradykinesia, cogwheel rigidity, and loss of postural stability. Idiopathic Parkinsonism accounts for the majority of the cases.
Infratentorial Lymphoma Presenting as Parkinsonism

Though uncommon, secondary Parkinsonism can occur and intracranial tumors are one of the causes. Primary central nervous system lymphoma (PCNSL) accounts for 0.85-1.5% of all primary central nervous system malignancies (Oliveras et al. 1988). They usually affect immunocompromised individuals, particularly those with acquired immunodeficiency syndrome or post organ transplantation.

The clinical presentation of PCNSL with movement disorders such as myoclonus, tic, chorea, or tremor uncommon. Sciarra and Sprofkin (1953) reported that 2.1% of patients with Parkinsonism had cerebral tumors and Tolosa and Vilato (1965) reported a frequency of 1%. Most of tumors which result in Parkinsonism involve the basal ganglia (Pramstaller et al. 1999), supplementary motor area (Haussermann et al. 2001), corpus callosum (Sánchez-Guerra et al. 2001), or frontal lobe (Bucciarelli and Cavaliere 1991; Krauss et al. 1995). Lesions in the infratentorial compartment have only been reported sporadically in the literature (Pohle and Krauss 1999).

Gherardi et al. (1985) was the first to report PCNSL arising from the infratentorial area and compressing the midbrain. The substantia nigra was infiltrated by the tumor and showed neuronal loss and extraneuronal pigment. Histological features included the presence of neurophagia–like nodules. It was speculated that the nodules might reflect a neuronotoxic activity of the lymphoma, and could be the origin of the Parkinsonism. Several possible pathophysiological mechanisms were thus proposed, including: 1) mechanical distortion of the rostral midbrain and the substantia nigra, 2) infiltration and destruction of the substantia nigra, and 3) impairment of the nigrostriatal pathways. None of these hypotheses, however, reached a general consensus.

In recent years, abnormalities in brainstem region, specifically the pedunculopontine nucleus (PPN), have been considered to be the critical factor in the development of the core signs of Parkinsonism (Galvan and Wichmann 2008). Anatomically, the PPN is tightly connected to the basal ganglia and stimulation of the PPN area could increase, or at least boost locomotion, whereas inhibition or destruction of the PPN might decrease motor function. In our patient, the occult tumor was located over infratentorial area (para-midbrain area), and he presented with Parkinsonism with left side hemiparesis. Since typical Parkinsonism will not manifest pyramidal signs/symptoms, acquired Parkinsonism should be taken into consideration. It could be argued that our patient might have been afflicted with coincidental idiopathic Parkinson’s disease; however, there was strong evidence to rule out paraneoplastic or idiopathic Parkinsonism on account of the rapid progression of symptoms and negative systemic workup. Additionally, in our patient, imaging studies were vital to the final diagnosis.

In our patient, we hypothesize that the hydrocephalus secondary to the cerebral mass also attributed to his Parkinsonism. Yoshimura et al. (2002) reported a 66-year-old woman who presented with 3-year history of progressive right-sided Parkinsonism. Cranial MRI showed a polycystic mass in the left side midbrain and reactive cerebral hydrocephalus. Physical factors, such as increased ventricular pressure near the upper midbrain and diencephalon, may cause shear, torsion, and ischemia of the nigrostriatal projection fibers. In patients with hydrocephalus caused by aqueductal stenosis, the compressive pressure of the enlarged ventricles may be easily transmitted to the nearby upper midbrain and its nigrostriatal projection fibers, resulting in Parkinsonism. Study using positron emission tomog-
raphy (PET) scanning (Remy et al. 1995) has shown the presence of a greater dysfunction of projections from the medial substantia nigra to the anterior striatum in comparison with idiopathic Parkinsonism patients.

Atypical Parkinsonism is a clinical diagnosis, and intracranial tumors can present as idiopathic Parkinsonism. Extrapyramidal symptoms can precede other symptoms, or remain isolated until the tumor has reached an advanced stage. A vigorous search for extra-long tract signs or focal neurological deficits is crucial, as diagnosis might be delayed resulting in irreversible damage. Neuroimaging studies are recommended in patients with atypical Parkinsonism or in those who do not respond to levodopa.

Acknowledgment

This work has received no funding from any organization. The first author would like to thank Dr. Tseng Ching-Ying for his vigorous contribution and image interpretations, Professor Leiyu Shi for invaluable guidance in epidemiology, and Dr. Peterus Thajeb for teachings regarding movement disorders.

References


