Psychotic Disorder in Neurodegeneration with Brain Iron Accumulation

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Introduction

Neurodegeneration with brain iron accumulation (NBIA) refers to a group of disorders that are characterized by iron accumulation, particularly in the basal ganglia (1). This process results in progressive dystonia, spasticity, Parkinsonism, neuropsychiatric abnormalities, optic atrophy or retinal degeneration. The worldwide prevalence of NBIA has been estimated at 1:1,000,000. The neuroaxonal dystrophies—pantothenate kinase-associated neurodegeneration (PKAN), which is now classified as NBIA type 1, and PLA2G6-associated neurodegeneration (PLAN), which is now classified as NBIA type 2—are the two main syndromes that account for most NBIA cases. Nevertheless, additional causative genes have been recently recognized to underlie much of the infrequent NBIA syndromes (2). The changes that are observed in patients with NBIA on cranial magnetic resonance imaging (MRI) are characteristic and virtually diagnostic. MRI changes demonstrate bilateral hyperintense signals within a hypointense region in the medial globus pallidus on T2-weighted images. These characteristic MRI findings are known as the eye-of-the-tiger sign. In most PKAN cases, the abnormalities are restricted to the globus pallidus and substantia nigra, with 100% having an eye-of-the-tiger sign. In a minority of PKAN cases, there is hypointensity of the dentate nuclei (3).

Treatments for NBIA are palliative and include pharmacologic treatment of spasticity and seizures, botulinum toxin or the intraventricular delivery of baclofen for focal dystonia and L-dopa treatment, which is beneficial in rare cases. In addition, there are therapies that are under investigation, including deep brain stimulation and iron chelation. Interest in iron chelation has re-emerged with data on the use of deferiprone, but iron chelation agents have been tried in the past without benefit (2).

Although many of the neurologic aspects of NBIA are clearly known, the understanding of its psychiatric aspects and comorbidity is limited. In this case report, we present a case of NBIA with prominent psychotic features.

Case

M.Y., a 33-year-old married male caretaker of a school and a father of two, was referred to the emergency psychiatry service because of his beliefs that the schoolmaster and some other strangers wanted to kill him. He claimed that he saw the schoolmaster spying on him through the window and that his own children and family would hurt him. Psychotic symptoms were present for two weeks. He was refusing to eat and drink because of his persecutory thoughts, thereby consuming a very limited amount of food. His sleep and communication were very limited. His symptoms had appeared insidiously over two weeks. He had not used any medications before his symptoms emerged. In addition, he was agitated and had difficulty in his speech and walking due to dysarthria, rigidity and dystonia. His family reported that

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he was an apathetic individual at baseline. His speech was sluggish, and, since his twenties, he could only move his upper extremities with difficulty caused by rigidity. The family also reported that his gait was impaired at the time of symptom onset, and he sometimes had facial grimaces. In addition, he had poor memory and difficulty with comprehension. All of these symptoms had slowly progressed over the last few years and had worsened since his twenties. The amnesia and rigidity symptoms became markedly worse when the psychiatric symptoms emerged. Although he had been able to work in the past, he had occupational impairments over the previous five years caused by his motor and cognitive symptoms.

A psychiatric examination of the patient revealed poor self-care and mild psychomotor agitation. His affect was anxious. He was mostly withdrawn and apathetic during the evaluation; however, intermittently, his affect was noted to be labile. His mood was anxious, but there were no manifestations of symptoms of a manic or depressive episode. His thought content was poor and he answered questions with single words. He had delusions of persecution and visual hallucinations. A neurological examination revealed rigidity in all of his extremities, and dystonia was particularly prominent in the upper extremities. He had moderate dysarthria. He was alert and there was no apparent confused state or fluctuation of the consciousness.

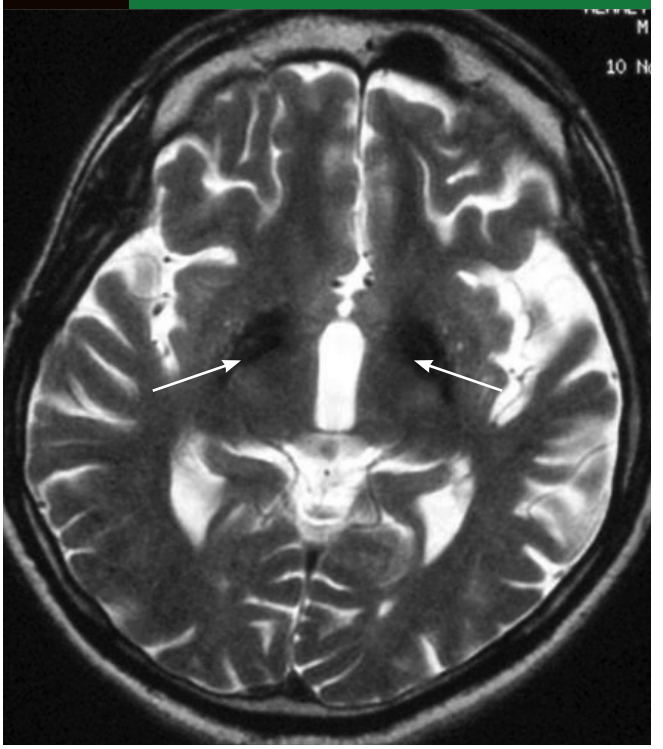
Fluctuations of consciousness were not apparent. All deep tendon reflexes were hyperactive, and his plantar responses were bilaterally extensor. He had urinary incontinence. There was bilateral pes cavus. Fundoscopic examination was normal. He had no history of substance/alcohol use or general medical problems. His family history was negative for any psychiatric and neurologic disorders.

Results of hemograms, biochemistry, sedimentation rates, thyroid functions, total Ca^{2+} levels, parathyroid hormone levels, Cu^{2+} levels, ceruloplasmin levels, iron and iron binding capacity, a venereal disease research laboratory test, human immunodeficiency virus, hepatitis B surface antigen, B12, folic acid and electroencephalography were within normal limits. A Porteus Maze test indicated a current IQ of 70. A neuropsychological evaluation revealed severe memory and visuo-spatial dysfunction and severe diffuse cognitive disturbance that was characterized by significant impairment in executive functions.

MRI of the patient revealed symmetrical hypointense signal intensity changes bilaterally along the globus pallida, and these were characteristic of the eye-of-the-tiger appearance (see Figure 1).

The patient was diagnosed with neurodegeneration with brain iron accumulation (NBIA) based on the clinical picture and the characteristic radiographic findings. He was hospitalized and started on quetiapine, 50 mg per day. His visual hallucinations completely resolved, and his persecution delusion was partially improved in three weeks. The patient was discharged from the hospital with outpatient psychiatry and neurology follow-up. He was compliant with the medication during the follow-up period for six months. We did not determine any psychiatric symptoms during this period, but the symptoms of dystonia, dysarthria and cognitive deterioration progressed markedly. The symptoms did not progress simultaneously with the quetiapine treatment, but they progressed over a few months. After six months, he moved to another town to be near his brother and his family. His family reported that six months after his psychiatric hospitalization, the patient developed acute swallowing and breathing difficulties with confusion. His general condition deteriorated in a few days. He was hospitalized in the intensive care unit at the local hospital. Two days later, he died due to respiratory arrest according to the medical records.

Figure 1 **Axial TSE T2-Weighted Image Reveals a Small Hyperintensity of the Globus Pallida, Surrounded by a Marked Hypointensity Giving a Characteristic Eye-Of-The-Tiger Appearance**



Discussion

In this case report, we describe a patient with NBIA and severe psychotic symptoms. NBIA is a collection of con-

genital neurologic conditions in which iron accumulates in the basal ganglia, resulting in progressive dystonia, spasticity, Parkinsonism and neuropsychiatric abnormalities. Nine types and their associated genes have been documented. The age of onset can range from infancy to late adulthood; the rate of progression also varies. There is cognitive deterioration in some subtypes, but, frequently, cognition is somewhat spared (4). According to the time of onset and rate of progression, two subgroups can be distinguished in PKAN: the classic type or the atypical type. In the classical form, symptoms begin within the first decade of life and exhibit rapid progression. The predominant findings are extrapyramidal symptoms. Cognitive decline and corticospinal tract involvement are generally seen in this group, and pigmentary retinopathy and a loss of consciousness are the early symptoms of the classical disease. The atypical form appears in the second or third decade, with slower progression. Extrapyramidal dysfunction is frequent but less severe. Speech disorders and psychiatric features are frequent in the atypical form, whereas the clinical evidence of retinopathy is much less common (1, 5).

The current case report contributes to the knowledge of the psychiatric aspects of NBIA, which is relatively ambiguous in the literature.

The clinical features of our case were compatible with the atypical form. The prevalence of psychosis in basal ganglia diseases (6) is well known, but case reports of NBIA with psychotic symptoms are extremely rare (7, 8). Previous reports on the psychiatric symptoms have included bouts of rage, depression, nervousness and irritability (9-11). Vansteenkiste et al. have described a patient who had initially been diagnosed with conversion disorder (12). The psychiatric features, including depression and psychosis, have been reported to be more common in patients with the atypical subtype (5, 13). Our case, which can be classified as the atypical form, supports this claim.

The basal ganglia are important in the pathogenesis of psychiatric symptoms. The basal ganglia project to many cortical areas, including the frontal, prefrontal, inferotemporal and posterior parietal cortices; thus, the basal ganglia and cortical regions are connected by multiple and different circuits. Cognitive, affective and motor symptoms in schizophrenia can be explained by alterations in a single site, the substantia nigra pars reticulata, and all of these symptoms can result from abnormal nigral output to the cingulate, orbitofrontal, dorsolateral prefrontal and temporal cortical areas. The pathogenesis of the psychotic symptoms in NBIA can be dıscussed in parallel with subcortical dementias with psychotic symptoms (14).

When NBIA and psychiatric symptoms coincide, appropriate assessments may prove challenging (9). The current case report contributes to the knowledge of the psychiatric aspects of NBIA, which is relatively ambiguous in the literature.

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