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Manganese Induced Parkinsonism
: A Case Report

Manganese (Mn) intoxication is known to induce parkinsonism. Mn-induced parkinsonism preferentially affect the globus pallidus in contrast to idiopathic parkinsonism where degeneration predominantly involves the nigral pars compacta. We describe a 51-year-old man who had been occupationally exposed to Mn. He had parkinsonian features including masked face, resting tremor, and bradykinesia. He also had a cock walk and a particular propensity to fall in a backward gait. There was no sustained therapeutic response to levodopa. A fluorodopa PET scan was normal. This case indicates that Mn-induced parkinsonism can be differentiated from idiopathic parkinsonism in that the former has unique clinical features and a normal fluorodopa PET scan.

Key Words : *Manganese; Parkinson's disease; Globus pallidus; Tomography, emission-computed*

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INTRODUCTION

Manganese (Mn) is an essential element for biologic function in humans and animals, but excessive exposure can be toxic. The most obvious manifestations of Mn intoxication are expressed as neurologic deficits (1). Mn intoxication is well known to induce parkinsonism (2, 3). However, a careful analysis of patients with Mn-induced parkinsonism reveals important clinical, pharmacologic, and imaging differences from idiopathic parkinsonism (IP) (4, 5). Despite widespread occupational exposures to Mn-containing products, there has been few reports on manganese poisoning in Korea (6). In 1986, there was an outbreak of manganese intoxication among workers preparing materials for welding rods in Korea. We encountered a patient who was exposed to Mn during the outbreak, and developed parkinsonism. He had unique clinical features of Mn-induced parkinsonism. We report the case with fluorodopa positron emission tomography (PET) finding.

CASE

A 51-year-old male patient had been occupationally exposed to Mn for almost one year. He was employed in a factory producing raw materials for manufacturing welding rods in 1985. His job was mixing strong acetic acid with crushed Mn powder in a poorly ventilated room. Almost one week after he started his work, he first noticed mild dizziness and frequent epistaxis. Ten months later, he began to have difficulty in walking, particularly when he tried to take his first step. Generalized weakness and slurred speech was also noticed. He stopped work one year after employment. Two months after his retirement, he noticed tremor in his left hand which spread to his left foot. Thereafter, he also experienced frequent falling in a backward gait and propulsion. The neurological deficits had gradually progressed for several years.

On examination, July 1997, he had parkinsonian features including masked face, resting tremor in both hands, more prominent in the right side, and bradykinesia. He also had hypophonia and monotonous speech. Rapid alternative movement was impaired in both hands. There was severely impaired postural stability. He showed decreased arm swing and the so-called "cock walk" in his gait. There was a particular propensity to fall in a backward gait. Dystonia was noticed in his left hand and foot. In the beginning, there was a mild response to levodopa which was not sustained. Magnetic resonance image (MRI) showed nothing remarkable. Fluorodopa PET scan revealed normal uptake in the striatum (Fig. 1).

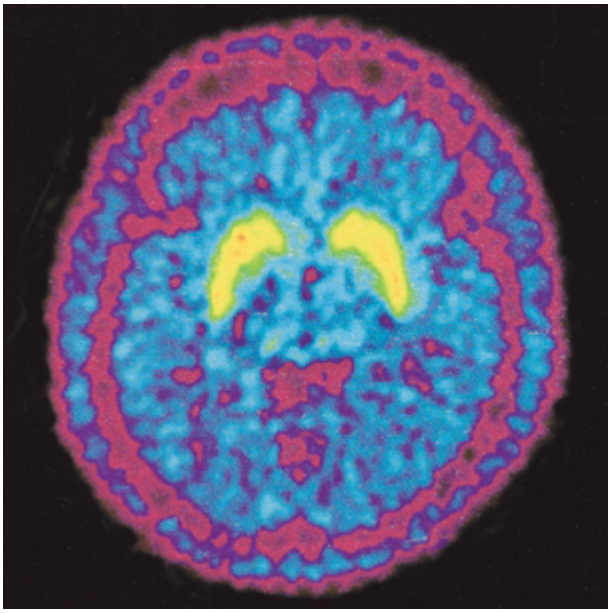

Fig. 1. ^{18}F-dopa PET scan shows a normal uptake in the striatum.

PET measurement

The patient was given 100 mg of oral carbidopa one hour before scanning. PET scan was performed using the ECAT EXACT HR (Siemens/CTI, Knoxville, Tenn, USA). Fluoro (^{18}F) dopa (207 MBq) in normal saline solution was infused intravenously over 30 seconds. Parametric images of ^{18}F-dopa influx (Ki) were created using in-house software (MRC Cyclotron Unit, Hammersmith Hospital, London, UK). We used time frames from 25 to 94 min. postinjection with occipital counts as the input function (7). Region of interest (ROI) analysis was performed on the Ki images. The ROIs were placed on three contiguous planes containing caudate and putamen through image inspection. One circular ROI of 58.2 mm^2 (diameter=8.7 mm) was positioned on each caudate nucleus. One elliptical ROI of 141.4 mm^2 was placed on each putamen. The Ki values are as follows: right caudate 0.01202/min, right putamen 0.01230, left caudate 0.01274, left putamen 0.01240 (normal; caudate 0.0125±0.0013, putamen 0.0125±0.0019).

DISCUSSION

Mn is the fourth most widely used metal in the world, following iron, aluminium, and coppper. Inhalation of dust or fume is the major route of entry in occupational Mn poisoning. More than 90 percent of Mn is excreted in the bile into the intestinal tract to be eliminated in the feces and only a little Mn is excreted in the urine (8). The primary target organs of Mn toxicity are the brain and the lungs (9, 12). The toxicity to the brain is manifested as a chronic disorder resembling parkinsonism (10). However, there are dissimilarities between IP and Mn-induced parkinsonism both clinically and pathologically (5, 11). Neurodegeneration in IP primarily occurs in the substantia nigra pars compacta. In contrast, considerable evidence suggests that Mn intoxication preferentially affects the globus pallidus (5, 12). Therefore, clinical manifestations of these disorders are not identical.

The clinical reports (6, 13) vary somewhat, but it is generally considered that manganism starts gradually with nonspecific symptoms, often of a psychiatric nature, the so-called "manganese madness". After a few months, motor deficits somewhat similar to those of IP appear, but often including dystonia. A particularly characteristic finding is the so-called "cock walk" (14), in which patients strut on their toes. This is quite unlike the usual clinical picture of IP. It is notable, as in our case, that patients can develop the motor deficits of manganism without having experienced any phase of manganese madness (4). In our case, he showed dystonia in his left hand and foot. He also had a cock walk in his gait, quite an unique symptom in Mn-induced parkinsonism. A particular propensity to fall in a backward gait and a prominent postural instability, compared with the severity of other parkinsonian features, is considered another characteristic clinical feature in Mn-induced parkinsonism (5). Thus, some investigators do not consider manganism a form of parkinsonism. They maintain that manganism is predominantly a dystonic disease characterized by a postural instability of complementary muscle groups (15). In our case, he demonstrated propensity to fall backward in his gait as well as a prominent postural instability although the patient did not have any other features of advanced parkinsonism. Failure to achieve a sustained therapeutic response to levodopa is also helpful to discriminate between IP and manganism (1, 16). In our case, there was a mild response to levodopa in the beginning, which was not sustained. Fluorodopa PET scan provides informations of considerable value in discriminating between ID and manganism (17, 18). Fluorodopa PET scan allows an index of the integrity of the dopaminergic nigrostriatal pathway and is abnormal in IP (19). There is a reduced uptake of fluorodopa in the striatum (17, 18). This finding is in accord with the fact that there is a 40 to 60% loss of dopaminergic cells in the nigrostriatal pathway, the primary focus of neurodegeneration in IP. In manganism, the fluorodopa PET scan is normal (17), compatible with the pallidum being the epicenter for damage in manganism. In our case, PET scan revealed a normal fluorodopa uptake in the bilateral striatum

(Fig. 1), indicating preservation of the nigrostriatal dopaminergic system where IP preferentially affects. Recently, the usefulness of MRI to provide visual evidence of cerebral deposits of Mn has been described. T1-weighted MRI demonstrated high signal intensities in the regions of the striatum, globus pallidus, substantia nigra, and pituitary gland which disappeared after cessation of exposure to Mn (20). In our case, there was no signal change in the striatum over 10 years after cessation of Mn exposure. This finding suggests that the high signal intensity of T1-weighted image reflects recent exposure to Mn.

This case indicates that Mn-induced parkinsonism can be differentiated from IP in that the former has the cock walk, a particular propensity to fall in a backward gait, failure to achieve a sustained therapeutic response to levodopa, and a normal fluorodopa PET scan.

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