

# Chronic Manganese Intoxication Due to Methcathinone (Ephedron) Abuse: A Case Report

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## Abstract

*Known as an occupational disease, chronic manganese intoxication is recently being observed among abusers of psychoactive substances. Methcathinone hydrochloride is obtained by combining ephedrine/pseudoephedrine and potassium permanganate. Various neuropsychiatric symptoms have been reported among Ephedron users.*

*Our patient is a 29 year old male, who was referred to our hospital from a state general hospital with a diagnosis of Conversion Disorder. He was hospitalized and preliminary diagnoses of Facititious Disorder, Conversion Disorder, Psychiatric Disorder due to a General Medical Condition and Antisocial Personality Disorder. He was abstinent from any substance for five years upon referral to our hospital and had a history of methcathinone abuse for 4.5 years. The backache dated back to 6 years ago and a disturbance of gait was added to the clinical picture. A speech disturbance, falling while walking downhill and walking on tiptoe were added in the last 2-3 years. In the neurological examination, extrapyramidal system findings, gait disturbance and the report on use of manganese compounds were found. The setting was changed from psychiatric ward to neurology ward and evaluated by consultant neurologist. The case was diagnosed as 'Manganese Intoxication'.*

*The aim of this report is to demonstrate and emphasize the importance of questioning the presence of manganese compounds in case of history of substance abuse. Other areas of interest are the shortage of data on the intravenous use of manganese and the cases reported in the literature coming from the former Soviet Union.*

*Key Words: Manganese, Methcathinone, Ephedron, Substance Abuse*

## INTRODUCTION

Chronic manganese intoxication resulting from manganese intake above the daily requirement or contact of long duration is known as an occupational disease observed mostly in industrial workers (Perl and Olanow, 2007). On the other hand, intoxication due to chronic parenteral use of manganese in psychoactive substances is increasingly encountered as a problem that causes serious neurological impairment.

Manganese intoxication in recreational psychoactive substance users mainly results from intravenous use of methcathinone hydrochloride, known as ephedron in Europe, which is prepared by users in countries that were once part of the former Union of Soviet Socialist Republics (USSR) (de Brie et al. 2007). Ephedron is derived via the

oxidation of ephedrine/pseudoephedrine with potassium permanganate. This psychostimulant mixture, known as a 'Russian Cocktail' in Turkey, is prepared by mixing potassium permanganate and acetyl salicylic acid and is taken intravenously (Çitçi et al., 2003). Long-term parenteral use of ephedron by recreational psychoactive substance users causes parkinsonism (Sikk et al., 2007). Similar cases were reported by neurology clinics in Turkey and Canada (Çitçi et al., 2003; de Brie et al., 2007; Meral et al., 2007). This condition, which is caused by manganese, is reported to be resistant to levodopa and to cause permanent damage (Cersosimo and Koller, 2006; de Brie et al., 2007).

As a result of immigration and Internet use, ephedron use has spread beyond the borders of the former USSR and is becoming an international public health problem

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(de Brie et al., 2007). Herein we present a patient that had psychiatric findings in addition to psychoactive substance use and a history of psychiatric treatment that was referred to our psychiatric clinic following neurological evaluation. This case of chronic manganese intoxication due to substance abuse was observed to have no other pathological findings other than the findings of neurological examination. Our aim was to draw attention to the fact that this may be a clinical condition encountered in psychiatric clinics and may be underdiagnosed.

## CASE

The patient was a 29-year-old single male primary school graduate that was not working. He was referred to our hospital from the internal medicine clinic of a training hospital in Istanbul, where he was hospitalized with complaints that included the inability to walk, pain in both knee regions, and a depressed mood. The referral note stated that the electromyogram (EMG) obtained during neurological consultation was in the normal range. Cranial magnetic resonance imaging (MRI) was planned, but not performed, and a diagnosis of conversion disorder was considered upon psychiatric evaluation. When he presented at our hospital he complained of not being able to walk, pain in both knee regions, and easily induced crying. The patient stated that, "my brain wants to walk, but I can't walk". Interestingly, despite not being able to walk he could ride a bicycle. The patient was diagnosed with factitious disorder, conversion disorder, an organic (medical) condition, and Axis-II antisocial personality disorder; he was subsequently hospitalized in our clinic.

History provided by the patient and his family, and medical records revealed that behavioral problems began in childhood and adolescence, and that he engaged in criminal activity such as theft during these periods. He stated that 10 years prior to his presenting at our hospital he had been intravenously using a pseudoephedrine + potassium permanganate + acetyl salicylic acid mixture by dissolving it in 2 cc of water. He had learned about the mixture he called a 'Russian Cocktail' from a friend and used 2-3 doses every 2-3 weeks for 4.5 years; he had not used the mixture for the last 5 years.

He stated that 7 years ago he was imprisoned for 9 months for injuring someone with a weapon, and he began to experience back pain began while he was in prison. The patient began mandatory military service 6 years earlier. He engaged in self-damaging acts in order to obtain a medical leave form the military. He began experiencing difficulty walking during this period and he was followed-up in the military hospital after presenting with back pain and difficulty walking. Cerebrospinal

fluid examination, EMG, and cerebral computerized tomography (CT) performed in the military hospital were within normal ranges, and he was found to be unsuitable for military service during his seventh month in the military. He was diagnosed with antisocial personality disorder and substance addiction.

Due to the patient's back pain that began 7 years earlier, he could only walk while holding his back with his hand. He developed a speech disorder 2-3 years ago; his speech was slurred and he could not be understood. During the last 2 years his walking disability worsened and he began riding a bicycle after falling down a hill while he was walking. The patient's medical history was normal.

Physical examination of the patient revealed superficial cuts on the skin of both arms, a tattoo on his right shoulder, scars indicative of injections on both forearms. He was conscious, cooperative, and fully oriented. His appearance was normal for his age; he was of medium height and well built. His hygiene was suitable for a person of his socioeconomic level. He was respectful towards the interviewer. His affect was restricted. He was occasionally inappropriate, had normal associations with normal speed, and dysarthric speech. No delusions were observed in his thought content, but intense depressive themes were dominant. He had an inappropriate laugh while talking. Impairment of perception and judgment was not observed; he had normal insight.

Neurological examination revealed that his cranial nerves were normal. Muscle strength in the extremities was full. Deep tendon reflexes were hyperactive. There were no pathological reflexes. Examination of the cerebellar and the sensory systems revealed normal findings.

Extrapyramidal system (EPS) examination revealed bradymimia, bradykinesia, and evident increase in lower extremity tonus. He had postural instability. The patient walked with crutches and both knee joints hyperextended while walking, the right knee to a greater extent. Routine chemistry, blood count, and erythrocyte sedimentation rate, thyroid hormones, and serum manganese levels were in the normal range. Other laboratory findings included anti-HBC total (+), anti-HBS (+), VDRL (-), and anti-HIV (-). Electroencephalogram and cranial MRI were in the normal range.

Neuropsychological examination revealed mild verbal and non-verbal memory impairment, accompanied by frontal axis findings. The memory impairment detected was frontal type (spontaneous recall phase impaired, whilst recognition phase normal). Psychological evaluation, during which the Minnesota Multiphasic

Personality Inventory and Rorschach tests were assessed together, revealed immature, dependent, inadequate, and intellectually restricted personality features, as well as difficulty with impulse control and situational depression. Hamilton Depression Rating Scale score was 18, Hamilton Anxiety Rating Scale score was 10, and Mini Mental Test score was 28.

Following the patient's examination, a neurological consultation was requested, especially for his difficulty walking and back pain; his history of permanganate use, mask-like face, dysarthric speech, and increase in DTRs suggested an organic pathology. Result of the neurological consultation were as follows: His speech was dysarthric, muscle strength was complete, DTRs increased in the lower extremities, bradymimia and bradykinesia, cerebellar tests normal, muscle tone increased in the lower extremities, spastic gait and cock-walk gait; there were no sensory defects. When the examination findings were combined with the patient's history of substance use, it was agreed that they could be assessed as intoxication due to intense manganese use and the diagnoses of conversion disorder and factitious disorder were excluded.

Based on the patient's complaints, clinical findings, psychometric examination, and rating scale scores, the patient was diagnosed with major depression and chronic manganese intoxication due to psychoactive substance use. Fluoxetine 20 mg/day was started. Because of medication compliance problems and complaints of sleep impairment, amitriptyline 25 mg/day and diazepam 5 mg/day were added to the treatment. The patient was transferred to the neurology clinic on the 20th day of hospitalization. Carbamazepine 200 mg/day was started because of his impulsive behavior. The patient was discharged from the neurology clinic with the diagnosis of manganese intoxication, and Selenium-ACE tablets 1 × 1, piracetam 2400 mg/day, carbamazepine 400 mg/day, fluoxetine 20 mg/day, and L-dopa + carbidopa 187.5 mg/day were prescribed.

## DISCUSSION

Diagnosis in our case was made based on history and examination findings, rather than laboratory tests and other investigations. Manganese intoxication has been associated with neuropsychiatric findings, including euphoria, emotional incontinence, masked face, monotonous speech, hyperesthesia, cock-walk gait, increase in muscle tone, weakness in lower and upper extremities, eyelid tremor, exaggerated movements of the knee joint, difficulty walking, loss of libido, and progressive parkinsonism (Yamada, 1986). It is suggested that parkinsonism due to manganese (MP) intoxication can be distinguished from

Parkinson's disease (PD) by impairment in walking and standing, some differences in tremor and dystonia, bilateral findings, and low-level response to levodopa treatment (Calne et al., 1994; Cersosimo and Koller, 2006).

An important feature in the presented case was the change in clinical picture over time due to chronic manganese intoxication. Psychiatric symptoms due to manganese intoxication may present earlier than neurological findings and remit after 3 months, depending on the dose used. EPS findings, on the other hand, present later and in most cases are permanent, even if exposure to manganese stops (Huang et al., 1998; Sikk et al., 2007). Foot dystonia and dystonic gait similar to Wilson's disease has also been observed. Patients walk with a cock-walk gait, characterized by the feet not completely contacting with the ground; patient walks on their toes and there is a tendency to fall while walking backwards. This type of walking found similar to a cock's walk because of the heels being up in the air, and the special posture of the trunk and arms, is characteristic of MP (Kim et al., 1998; Cersosimo and Koller, 2006). Our patient presented with cognitive and emotional changes, parkinsonism, postural instability, and cock-walk gait. Information concerning the patient's psychiatric signs during the early period of ephedron use was limited, but the patient did previously present to a psychiatry clinic. Of particular note was that even though the presented case last used ephedron 5 years ago, his symptoms continued to worsen and the clinical signs continued, irreversibly.

The number of manganese intoxication cases due to ephedron use is increasing. Most cases are reported from neurology clinics because of irreversible MP that develops as a result of long-term exposure; however, psychiatric signs are observed during the prodromal phase of the disease (Yamada, 1986). Such cases of psychoactive substance use may present first to psychiatric clinics, rather than to neurology clinics. These cases may present with comorbid or psychiatric impairment related to substance use. Furthermore, medical investigations and long-term follow-up among such patients are difficult to perform because motivation for treatment is low. There may be a specific ephedron user group due to the mixture being legally available outside the former USSR, and at low cost. Antisocial personality disorder, depression, and other psychiatric diagnoses and co-diagnoses, in addition to an abundance of social stressors may complicate the diagnostic process, as in the presented case.

In psychiatric history of our case, there were some important features that can make the clinician to think a psychiatric disorder represented with physical signs such as conversion disorder or factitious disorder. Maladapt-

tive abilities to social stressors, personality features, and avoidance of social responsibilities of the patient might lead to evaluate these physical symptoms as a psychiatric findings. Furthermore, because the patient had suffered of back pain which cannot be explained by neuroimaging test results and he had ability to ride a bicycle despite not being able to walk, and neuro-imaging and medical test results within normal ranges, all these findings and symptoms might also reinforced the tendency to make a psychiatric diagnosis. For example, a restricted or inappropriate affect may be confused with *la belle indifférence* in such patients. In our case, the affect that was not appropriate to his mood may have been interpreted by the primary physician as a sign of *la belle indifférence*.

The diagnostic process in manganese intoxication cases is complicated by the fact that imaging and other medical tests do not always yield pathological findings. Active users have high serum and urine manganese levels and, consistent with the clinical picture, bilateral hyperintensity in the striatal regions in T1 sections of cranial MRIs, especially the medial segment of the globus pallidus and the reticular portion of the substantia nigra. Despite the fact that MRI may be normal or hyperintensity in MRI may decrease following discontinuation of exposure to manganese, this improvement may not be reflected in the clinical picture (Huang et al., 1998; Cersosimo and Koller, 2006; Stephens et al., 2008). Similarly, cases have been reported in which serum manganese levels were within the normal range, although clinical signs and symptoms continued after discontinuation of ephedron use (Stephens et al., 2008). Positron emission tomography (PET) appears to be helpful in the diagnosis (Calne et al., 1994; Olanow, 2004); however, as with MRI, PET results are likely to return to

normal after discontinuation of ephedron use (Kim et al., 1998; Cersosimo and Koller, 2006). Çitçi et al. (2003) reported that MRI results were within the normal range in a manganese intoxication case due to ephedron use. It has been recommended to assess the manganese level in pubic hair or scalp hair for the diagnosis of chronic manganese intoxication (Huang et al., 1998), but if a considerable amount of time has passed since discontinuation, false negative results may be obtained. The presented case discontinued ephedron use 5 years earlier; therefore, the MRI findings were normal, and the serum manganese level was within the normal range. The manganese level was not assessed in the hair of our patient because a clinical diagnosis was made, the patient discontinued ephedron use 5 years earlier, and the patient declined to have his hair examined.

In such cases detailed history taking and directly questioning if manganese compounds were used are important in the diagnostic process. The clinician must have information on manganese intoxication and ephedron use. Neurological signs may be missed in earlier stages of manganese intoxication, may not be clear in the clinical picture, and no findings may be observed in imaging and medical tests in the later stages of intoxication. Signs may be interpreted as drug side effects or PD; however, early diagnosis and treatment of this condition, which causes irreversible damage, are critical.

The presented case was reported because manganese intoxication might be increasing in prevalence among substance users and diagnosis may take years. Additionally, there is a possibility of misdiagnosis because there is limited information in the psychiatric literature and limited data on the intravenous use of manganese.

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