





# Cirrhosis Presenting as Parkinsonism: Two Cases

## Parkinsonizm ile Prezente Olan Siroz: İki Olgu

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**ABSTRACT** Acquired hepatocerebral degeneration is a heterogeneous neurological disorder resulting from chronic liver disease. Neuropsychiatric, cerebellar and extrapyramidal findings in different combinations may be observed in this clinical table. Cirrhosis presenting as parkinsonism is a rare and interesting subset of acquired hepatocerebral degeneration. In this paper we aimed to report two patients with advanced liver disease, who were diagnosed after new onset parkinsonism. Patients were admitted to our outpatient clinic with symmetrical parkinsonism and later diagnosed to have cirrhosis with portal hypertension. Patients had characteristic Cranial Magnetic Resonance imaging abnormality of symmetrical T1 hyperintensity in lenticular nuclei and anterior midbrain. Here we would like to emphasize that hepatocerebral degeneration should be kept in mind in middle-aged patients presenting with new onset symmetric parkinsonism, especially in the absence of resting tremor.

**Keywords:** Seconder parkinsonizm; hepatocerebral degeneration; kriptojenik siroz

**ÖZET** Edinilmiş hepatoserebral dejenerasyon, kronik karaciğer hastalığı nedeniyle oluşan ve heterojen nörolojik bozukluklardan oluşan bir tablodur. Nöropsikiyatrik, serebellar ve ekstrapiramidal bulgular değişik kombinasyonlarla görülebilir. Parkinsonizm olarak ortaya çıkan siroz edinilmiş hepatoserebral dejenerasyonun nadir görülen ve ilgi çekici bir alt grubudur. Bu yazıda yeni başlayan parkinsonizm sonrasında tanı konulan ilerlemiş karaciğer hastalığı olan iki olguyu sunmayı amaçladık. Olgular polikliniğimize simetrik parkinsonizmle başvurdu ve sonra portal hipertansiyonun eşlik ettiği siroz tanısı konuldu. Olguların T1 ağırlıklı incelemelerinde, lentiküler çekirdek ve orta beynin ön kısmında simetrik hiperintens sinyal değişikliğine yol açan karakteristik Kranial Manyetik Rezonans görüntüsü bulunmakta idi. Bu olgu sunumunda, orta yaşlı hastalarda, yeni başlayan, özellikle istirahat tremoru olmayan simetrik parkinsonizm tablosunun hepatoserebral dejenerasyon ile ilişkili olabileceğini vurgulamak istedik.

**Anahtar Kelimeler:** Sekonder parkinsonizm; hepatoserebral dejenerasyon; kriptojenik siroz

**A**cquired hepatocerebral (or hepatolenticular) degeneration (AHD) is a heterogeneous neurologic disorder which occurs secondary to chronic liver disease and is characterized by neuropsychiatric, cerebellar and extrapyramidal disorders.<sup>1</sup> This entity is a neurodegenerative disorder that effects lenticular nuclei and was first described by von Woerkom in advanced liver disease cases that were unrelated to Wilson's Disease. AHD is usually reported in patients who were known have chronic liver diseases with a porto systemic shunt and previous history of acute hepatic encephalopathy episodes.<sup>1-3</sup> On the other hand, chronic liver diseases can

rarely be presented with neurological findings.<sup>4</sup> In this paper, we have reported two patients with advanced liver disease who were diagnosed after clinical signs of new onset parkinsonism has occurred.

## CASE REPORTS

### CASE 1

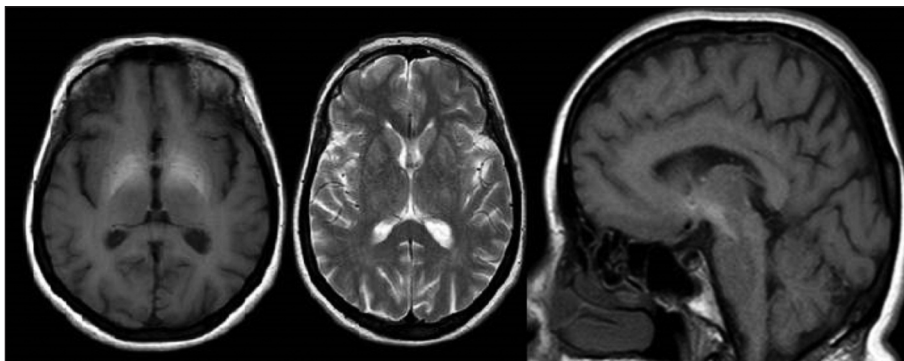
Sixty-two years old woman was admitted to our outpatient clinic with bradykinesia and dysarthria for the last three months. There was nothing remarkable other than hypertension in her medical history. No family history of systemic or neurological diseases were present. She was not under any medication that may trigger extrapyramidal symptoms. Neurological examination revealed bradymimia, postural instability, bilateral bradykinesia and rigidity. Her speech was slow and dysarthric. There was no sign of resting tremor. No motor weakness, sensory loss, ataxia or pyramidal signs were noted. Physical examination revealed no other findings except hepatosplenomegaly.

She was diagnosed with parkinsonism and further evaluation was carried out. Cranial magnetic resonance imaging (MRI) revealed increased signal intensity in bilateral lenticular nuclei and midbrain on T1-weighted images, which were isointense on T2 weighted images, characteristics to hepatolenticular degeneration (Wilson's disease) (Figure 1). There was no evidence of corneal Kayser-Fleischer (K-F) ring in Slit lamp examination. Urine and blood copper levels were normal. Serum biochemical and hematologic tests were within normal lim-

its. The level of serum ammonia was normal. Hepatitis markers were negative. Ultrasound examination demonstrated coarse heterogeneous texture of liver accompanied with increased size and irregular margins. Cavernous transformation of portal vein with collateral vessels around portal and splenic veins suggested portal hypertension originating from chronic liver failure. Levodopa treatment was initiated, and she was consulted to department of gastroenterology for the etiology of chronic liver disease; though specific etiology for cirrhosis could not be found in this case (cryptogenic). The patient was also evaluated by the department of gastroenterology and started on treatment with propranolol and diuretic drugs. In follow-up examinations of the patient, there was a partial improvement in the features of parkinsonism especially in bradykinesia.

### CASE 2

Sixty-eight years old man was admitted to our outpatient clinic with a six months history of forgetfulness, fatigue, and slowing in movements. There was nothing remarkable other than chronic obstructive pulmonary disease in his medical history. He was not using any medication that may trigger extrapyramidal symptoms. No family history of systemic or neurological diseases were reported. Neurological examination revealed postural instability, bradymimia, bilateral symmetric bradykinesia and rigidity. And also he was walking slowly with short shuffling steps. There was no sign of resting tremor. No motor weakness, sensory loss, ataxia or pyram-



**FIGURE 1:** Cranial MRI revealed increased signal intensity in in bilateral lenticular nuclei and midbrain on T1-weighted images, which were isointense on T2 weighted images, of Case 1.

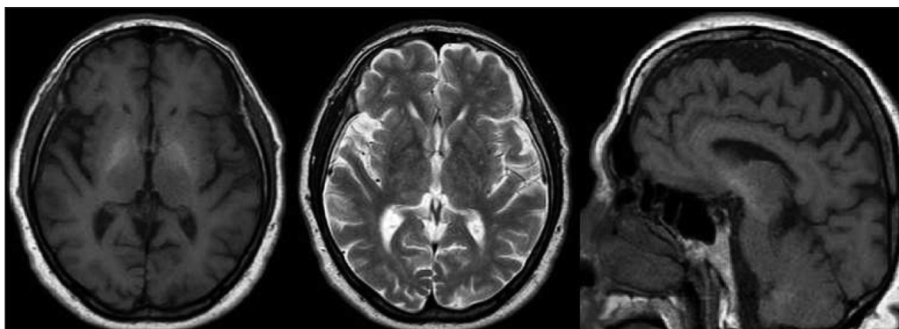
idal signs were noted. On physical examination we noticed his palmar eritem and icterus. Secondary parkinsonism was diagnosed and further evaluated. Cranial MRI revealed increased signal intensity in basal ganglia bilaterally on T1-weighted images, which were iso- intense on T2 weighted images (Figure 2). Because of symmetrical findings and cranial MRI features, the patient was diagnosed with hepatocerebral degeneration. In laboratory investigation; coagulation tests and liver function tests were abnormal (PT:26,5 sec (9,8-13,3), APTT: 39 sec (23-35 sec), INR: 1,5 (0,8-1,2), total bilirubin: 2,85 mg/dl (0,3-1,2 mg/dl), AST: 45 U/L (0-35 U/L), ALT:42 U/L (0-35 U/L)). Hepatitis markers were negative. Urine and blood copper levels were normal. Abdominal ultrasound examination revealed hepatosteatosis, hepatomegaly and mild heterogeneous texture of liver parenchyma. Dilatation of portal and splenic veins were suggestive for portal hypertension. He was consulted to department of gastroenterology and diagnosed with chronic liver disease. Specific etiology for cirrhosis could not be found (cryptogenic), as for the previous patient. Levodopa was administered for the treatment of parkinsonism, and also put under medical treatment with propranolol and diet regulation by department of gastroenterology. In follow-up period of the patient, there was a partial improvement in walking and bradykinesia.

## DISCUSSION

Here we reported two cases of cirrhosis presenting with parkinsonism. Acquired hepatocerebral degeneration is a neurodegenerative disorder that ef-

fects lenticular nuclei and was first described by Von Woerkem in cases of advanced cirrhosis which were unrelated to Wilson's disease.<sup>5</sup> The clinical presentation of chronic liver disease is widely variable. Chronic liver disease usually emerge with systemic symptoms; but although rare, neurological and psychiatric symptoms may also be seen as the presenting feature. In the literature, most of the reports were of patients with cirrhosis related parkinsonism, who were already known to have liver disease.<sup>4,6,8</sup> In contrast, our cases were presented to the neurologist with clinical features of parkinsonism without prior history of liver disease.

Although reminiscent of idiopathic Parkinson disease (PD), several features such as absence of resting tremor, symmetrical extrapyramidal findings and early gait impairment allow PD to be reasonably ruled out in our patients. Wilson disease is the most frequent cause of secondary parkinsonism. Vascular, toxic, metabolic and drug induced parkinsonism are the other reasons.<sup>4,9</sup> Similarities in lesion type on cranial MRI, distribution and localization has led to the suspicion of undiagnosed Wilson's disease in these patients.<sup>4</sup> However, the late onset clinical table and absence of Kaiser-Fleischer rings in these patients suggested that this possibility is unlikely. It was then suggested that this clinical table represents a distinct subset of patients with hepatocerebral degeneration; and indeed, brain lesion distribution closely resembles to those observed in patients with Wilson Disease.<sup>3</sup> Symmetric T1 hyperintensity in the lenticular nuclei and anterior midbrain on MRI was consistently ob-



**FIGURE 2:** Cranial MRI revealed increased signal intensity in in bilateral lenticular nuclei and midbrain on T1-weighted images, which were isointense on T2 weighted images, of Case 2.

served in our patients. On the other hand, Wilson disease was unlikely for our patients on seventh decade who had no Kaiser-Fleischer rings and normal serum and urine copper levels.

The prevalence of AHD has been reported 1-20% of patients with liver cirrhosis.<sup>4,10</sup> Studies in AHD have shown that the neurological findings are not linked to the etiology of underlying liver disease. Porto-systemic shunting consequent to hepatic dysfunction permits neurotoxic substances, particularly manganese, to enter the systemic circulation and therefore the brain.<sup>1,4</sup> Studies in humans and experimental animals have shown that toxic exposure to manganese results with a clinico-radiological picture resembling AHD.<sup>11</sup> It has been proved that manganese is cleared by the hepatobiliary system and whole blood and cerebrospinal fluid manganese concentrations in some patients with AHD are several fold above the reference range. The deposition of manganese in the brain is postulated in patients with AHD, which may induce diffuse degeneration in parenchymal brain. Microscopically, neuronal loss, Alzheimer type II astrocytes and cytoplasmic glycogen granules in basal ganglia are characteristic.<sup>12</sup> Unfortunately level of manganese could not be investigated in blood or cerebrospinal fluid in our patients.

AHD develops gradually and the symptoms become progressively worse. Medical treatment is often disappointing. But it has been reported that some patients with AHD are responsive to branched chain amino acids or levodopa therapy. Moreover, liver transplantation in selected cases could be curative. For these reasons, AHD might be accepted as a reversible and partially treatable disorder.<sup>4,13,14</sup> Our patients were also responsive to levodopa treatment in terms of parkinsonian symptoms. In follow up period there were not any complication related to cirrhosis.

In conclusion, this case report suggests that AHD should be considered in patients with a new onset of symmetrical parkinsonism with typical

neuroradiologic findings, even in the absence of a known liver disease or previous episodes of hepatic encephalopathy. Idiopathic Parkinson's disease usually presents with unilateral or asymmetric bilateral symptoms. Therefore, especially in these patients with a new-onset symmetrical bradykinesia without resting tremor, secondary causes should be evaluated in detail. It is also important to suspect of parkinsonism related to hepatocerebral degeneration in middle-aged patients presenting with a rapid onset of symmetric parkinsonism, as it is the main cause of secondary cases. A careful investigation for an evidence of underlying liver disease should be made and both clinical or neuroradiologic findings should be taken into consideration in differential diagnosis.

#### **Informed Consent**

*Was obtained from the patients.*

#### **Source of Finance**

*During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.*

#### **Conflict of Interest**

*No conflicts of interest between the authors and/or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.*

#### **Authorship Contributions**

**Idea/Concept:** Neslihan Eskut, Özge Yılmaz Küsbeci, Pınar Tamer; **Design:** Neslihan Eskut, Özge Yılmaz Kucukeci, Pınar Tamer, Ali Murat Koç; **Supervision/Consultancy:** Neslihan Eşkut, Özge Yılmaz Küsbeci; **Data Collection and/or Processing:** Neslihan Eskut, Pınar Tamer, Ali Murat Koç; **Analysis and/or Interpretation:** Neslihan Eskut, Özge Yılmaz Kucukeci, Pınar Tamer, Ali Murat Koç; **Source Browsing:** Neslihan Eşkut, Özge Yılmaz Kucukeci, Pınar Tamer, Ali Murat Koç; **Written by Makalenin:** Neslihan Eşkut, Özge Yılmaz Küsbeci; **Critical Review:** Özge Yılmaz.

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