Autosomal Recessive Parkinson's Disease with Early-Onset in a Turkish Family

Bir Türk Ailesinde Erken Başlangıçlı Otozomal Resesif Parkinson Hastalığı

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ABSTRACT

Parkinson disease is a progressive, neurodegenerative disease with an increasing incidence of age. It is thought that genetic factors in etiology may be the underlying cause together with environmental factors. Sporadic cases are seen in 85 %, familial forms in 10-15 %, and single gene inheritance in 5 %. In this article, we present a patient with early-onset Parkinson disease who had family history but negative genetic analyses. Genetic mutations of autosomal recessive early-onset parkinsonism are more frequently evaluated in clinical practice and are directed to be analyzed more frequently in a selected group of patients.

Key Words: Parkinson disease, autosomal recessive, early-onset

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ÖZET

Parkinson Hastalığı insidansı yaş ile artan ilerleyici, nörodejeneratif bir hastalıktır. Etiolojide genetik faktörlerin çevresel faktörlerle birlikte altta yatan neden olabileceği düşünülmektedir. Sporadik nedenler % 85 oranında görülürken, ailesel formlar % 10-15 tek gen katılımı ise % 5 oranında görülmektedir. Bu yazıda, aile hikayesi olan ancak genetik analizleri negatif olan erken başlangıçlı parkinson hastasını sunduk. Otozomal resesif erken başlangıçlı parkinsonizmin genetik mutasyonları klinik pratikte daha sık değerlendirilmekte olup ve seçili hasta grupları daha sık analiz edilmek üzere yönlendirilmelidir.

Anahtar Sözcükler: Parkinson hastalığı, otozomal resesif, erken başlangıçlı

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INTRODUCTION

Parkinson disease is a progressive, neurodegenerative disease with an increasing incidence of age. It is thought that genetic factors in etiology may be the underlying cause together with environmental factors. Sporadic cases are seen in 85 %, familial forms in 10-15 %, and single gene inheritance in 5 %. In this article, we present a patient with early-onset Parkinson disease who had family history but negative genetic analyses.

CASE REPORT

A 64-year-old female patient was admitted to hospital with progressive gait difficulty and balance problems for 6 months. She had hypertension and Parkinson disease for 10 years in her past medical history. She was treated with levadopa 125mg 3x1. But she feeled worsen end of the dose for 1 year. She had decreased facial expression, bradykinesia, mild extremity rigor, but no tremor ve rigidty. Myerson, glabellar tap and bilateral palmomental reflexes are positive.

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Her gait had decreased step lenght with decreased speed. The patient's parent were not consanguineous. She had 2 sisters and 3 brothers, A 44-year-old brother who had Parkinson disease. Also her 75-year-old uncle was diagnosed with Parkinson disease and 3 aunts had demantia. The patient was hospitalized for regulation for medical theraphy. Brain MRI showed widening of bilateral cerebral hemisferes due to atrophy. (figure 1) Result of standartized mini mental state examination test was 18/30. Analysis of the *PARK2, PARK 6, PARK 7, PARK 9* mutation by DNA were negative. Rasajilin 1 mg and levadopa HBS form added to the medical theraphy. Donepezil 10 mg and memantine 20 mg were started for dementia, fluoxetine 20 mg and quetiapine 100 mg for anxiety and sleep disorder. After the new medical medicaton, the patient had better ability to move, gait and balace. Psyhchiatric and sleep disorders were benefit from medical theraphy, too.

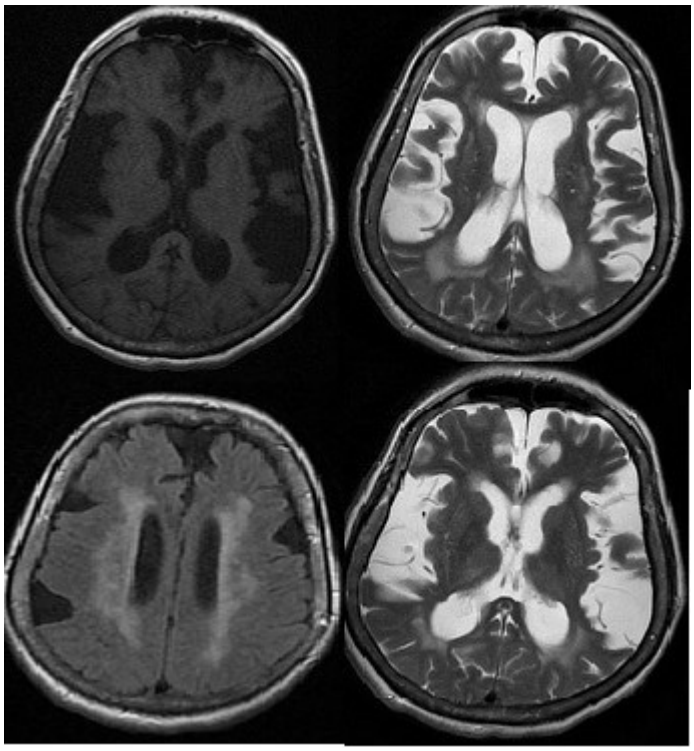

Figure 1. Brain MRI showed widening of bilateral cerebral hemisferes due to atrophy

DISCUSSION

The majority of patients who get Parkinson disease are over the age of 60. When a patient who is 21-50 old receives a diagnosis with Parkinson disease, it is defined as early onset Parkinson disease. Our patient had diagnosed with Parkinson disease at the age of 54. We thought that the symptoms of the patient started earlier. Since the patient had a severe familial history, the patient was considered an early-onset Parkinson disease. Autosomal dominant and autosomal recessive patterns are seen in familial Parkinson Disease.

The autosomal recessive form was found to be responsible for PARK2-type *PARKIN* gene, PARK6 for *PINK1* gene, PARK7 for DJ-1, and PARK9 for *ATP13A2* gene (1,2,3). When molecular pathology occurs, incorrectly synthesized and damaged proteins reveal the phenotypeof early-onset Parkinson disease.

PARK2 had wide phenotypic features. Also late onset, tremor dominancy, fluctuations during the day, early dyskinesia due to levodopa with dystonia being rare. So it is difficult to differ the patients with PARKIN from sporadic cases (2). Our patient who had not *PARKIN* gene mutation, had not tremor dominancy and early dyskinesia but had wearing off.

PINK1 mutation with Parkinson patients is characterized by early-onset, dystonia and/or psychosis, slowly progression. Recent study showed that PARKIN and PINK1 positive cases had learning, memory abnormalities and weaking of circadian rythms (4). Our patient had slowly progression, memory abnormalities. We had not detected PINK1 mutation.

Mutations in the DJ-1 gene have been reported to be rare from autosomal recessive parkinsonism patterns (3). Early-onset, symmetrical involvement, slowly progression, levodopa responsive form are seen in DJ-1 positive cases (5). Our patient had symmetrical involvement, slowly progression but no DJ-1 mutation.

Clinical characteristics of patients with PD-associated *ATP13A2* mutations were varied. Respective frequency of features: rigidity, bradykinesia, postural instability, supranuclear upgaze paresis, cognitive impairment, dystonia, resting tremor, hallucination, and myoclonus (6). Different studies in several countries with *ATP13A2* mutations were detected early-onset (6). Our patient had no *ATP13A2* mutation.

As pathogenesis is identified with genes and proteins associated with Parkinson, new treatment options can occur (7). Genetic mutations of autosomal recessive early-onset parkinsonism are more frequently evaluated in clinical practice and are directed to be analyzed more frequently in a selected group of patients.

Conflict of interest

No conflict of interest was declared by the authors.

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