CASE REPORT

SPINOCEREBELLAR ATAXIA TYPE 2 IN A TURKISH FAMILY

Kadriye Ağan[1], Deniz Kutlu[1], Nazlı Başak[2], Önder Us[1], Dilek İnce-Günal[1]

[1]Marmara University, School of Medicine, Department of Neurology, Istanbul, Türkiye [2]Boğaziçi University, Molecular Biology and Genetics, Istanbul, Türkiye

ABSTRACT

Spinocerebellar ataxias are classified according to the clinical signs, affected neuroanatomical regions and genetic features. Spinocerebellar ataxia type II (SCA 2) is characterized by gait and limb ataxia, dysarthria, ophthalmoplegia, and polyneuropathy . Extrapyramidal system signs and dementia are observed at late clinical stages. SCA 2 is caused by an expanded (CAG) trinucleotide repeat on the chromosome 12 resulting in production of abnormal protein called ataxin-2. Here we report a family who was affected by SCA 2 for three generations. Gait ataxia was the first symptom in all cases, followed by dysarthria and ophthalmoplegia respectively. None of the patients had extrapyramidal signs or cognitive decline. Axonal polyneuropathy was established with EMG in one patient and brain MRI showed pure cerebellar atrophy in all patients. An autosomal dominant cerebellary ataxia was the preliminary diagnosis on the virtue of family history, neurological examination and laboratory and scaning techniques. Genetic studies disclosed a mutation on the SCA 2 locus. Spinocerebellary ataxias are a group of disorders classified according to associating clinical signs and symptoms.Therefore, it is important to establish an accurate clinical classification as it would lead to a clue for the discovery of new gene locuses.

Keywords: Ataxia, Spinocerebellar ataxia, Autosomal dominant

SPİNOSEREBELLAR ATAKSİ TİP 2 İLE İZLENEN AİLE SUNUMU

ÖZET

Spinoserebellar ataksiler, ataksiye eşlik eden diğer nöroanatomik yapıların etkilenip etkilenmemesine ve genetik özelliklerine göre sınıflandırılır. Spinoserebellar ataksi tip II (SCA-2) yürüyüş ve ekstremite ataksisi ile başlayan, dizartri, oftalmopleji, periferik sinir tutulumu ile şekillenen geç klinik evrelerde ekstrapiramidal sistem bulguları ve demansında eklendiği bir SCA tipidir. İlk bulguların 3-4. dekadda başladığı SCA-2 12. kromozoma lokalize edilmiş, ataksin-2 genini kodlayan bir trinükleotid tekrar hastalığıdır. Bu yazıda 3 kuşak boyunca etkilenimin olduğu bir aile sunulacaktır. Tüm olgularda yürüyüş ataksisi ile başlayan semptomlara sırası ile dizartri ve oftalmoplejinin eklendiği gözlendi. Piramidal, ekstrapiramidal ve kognitif etkilenim saptanmadı. Bir hastanın EMG'sinde aksonal tutulumun ön planda olduğu polinöropati saptandı. Üç hastada yapılan kranial görüntülemelerde saf serebellar atrofi bulundu. Klinik, radyolojik ve elektrofizyolojik çalışmaların sonucu ve aile öyküsü nedeni otozomal dominant spinoserebellar ataksi düşünülen hastalarda gerçekleştirilen genetik çalışmada SCA-2 lokusunda mutasyon saptandı. Spinoserebellar ataksiler, serebellar bulgulara eşlik eden nörolojik semptomlara göre sınıflanan ve her yeni tanımlanan semptoma göre yeni bir lokusun bulunduğu bir hastalık grubudur. Hastaların klinik bulgularının iyi sınıflandırılması lokusun saptanması için önemlidir.

Anahtar Kelimeler: Ataksi, Spinoserebellar ataksi, Otozomal dominant

INTRODUCTION

Spinocerebellar ataxias are classified according to the clinical signs, affected neuroanatomical regions and genetic features. Spinocerebellar ataxia type II (SCA 2) is characterized by gait and limb ataxia, dysarthria, ophtalmoplegia, and polyneuropathy[1,2]. Extrapyramidal system signs and dementia are observed at late clinical stages.

SCA 2 is caused by an expanded (CAG) trinucleotide repeat on the chromosome 12 resulting in production of abnormal protein called ataxin-2[2]. The symptoms usually begin in the third or fourth decade of life[2].

Here we will report a Turkish family who was affected by SCA 2 for three generations.

İletişim Bilgileri:
Kadriye Ağan
e-mail: kagan@marmara.edu.tr
Marmara University Faculty of Medicine, Neurology, Istanbul, Türkiye

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CASE REPORT

The index case (II-1) was a 49 year old female. Her symptoms began in the fourth decade of life with dysequilibrium and dysarthria respectively. Two years later clumsiness in fine finger movements and writing has been developed. The family history is depicted in Figure 1. Her minimental status test score was 29/30. Neurological examination revealed dysarthria, bilaterally restricted upward and lateral eye movements, limb and gait ataxia. Magnetic resonance imaging (MRI) showed cerebellar atrophy (Figure 2). Electrophysiological studies revealed axonal sensory polyneuropathy.

The second patient (III-1) was a 26 year old son of the index case. He was complaining of head titubation which started approximately a year ago. Neurological examination revealed dysarthria, bilaterally restricted lateral eye movements and limb ataxia. MRI showed cerebellar atrophy (Figure 3)

The brother (II-3) of the index case was a 47 year old man. He experienced dysequilibrium which began in the fourth decade.

The mother (I-4) of the index case was 69 years old. Her history of dysequilibrium and explosive speech began in the sixth decade. MRI of this case showed cerebellar atrophy, too.

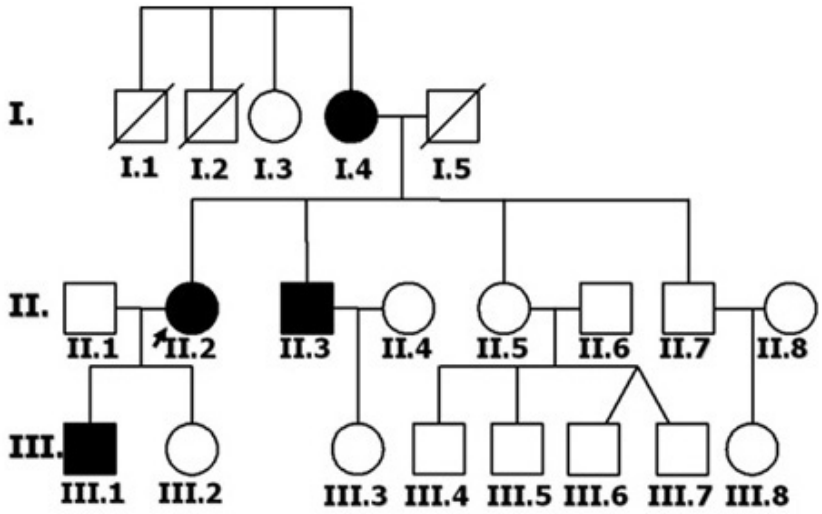

Figure 1: Family history

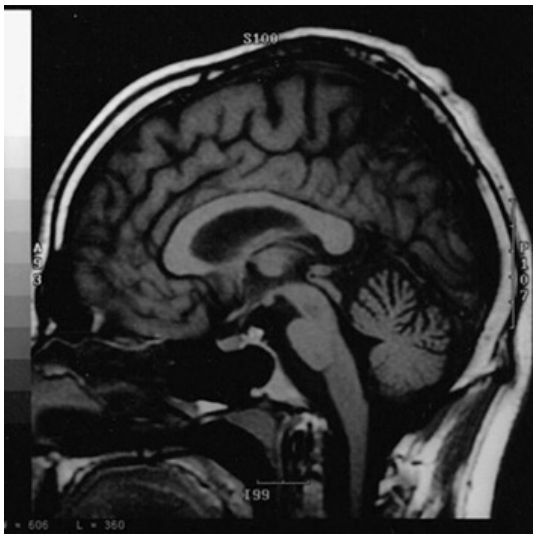

Figure 2: MRI shows cerebellar atrophy

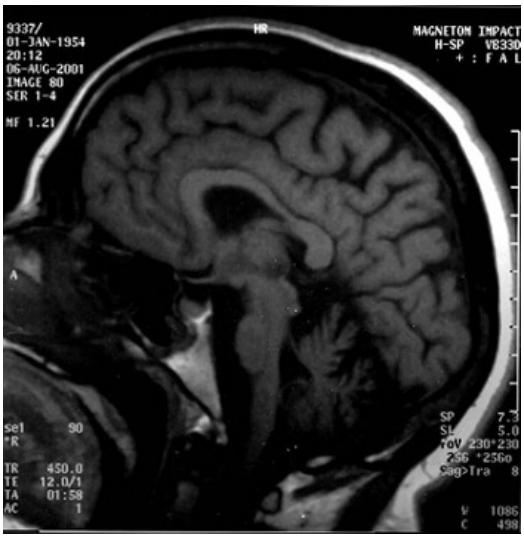

Figure 3: MRI shows cerebellar atrophy

Acquired vitamin E deficiency, vitamin B 12 deficiency, hypothyroidism, other familial and neurodegenerative diseases (multi-system atrophy, cerebellary malformations, stroke, multiple sclerosis, psychogenic disorders, Creutzfeldt-Jakob Disease, Behçet's Disease) were excluded by neurologic examination, laboratory and scanning techniques.

The family showed autosomal dominant inheritance and anticipation resulting in onset of symptoms, in the latest generation, in the third decade; earlier generations had onset in the fifth or sixth decade. The testing showed a normal CAG repeat of 23 on one chromosome and abnormally amplified CAG repeat of over 41 on the other chromosome in index case and her son III-1. Genetic studies disclosed an autosomal dominant cerebellary ataxia, SCA 2.

DISCUSSION

Spinocerebellar ataxia (SCA) type 2 is a CAG trinucleotide repeat disorder characterized by progressive ataxia. In 1982, Harding classified autosomal dominant cerebellar ataxias (ADCA) into three types[1]. ADCA I is characterized by ataxia with signs of neurodegeneration outside the cerebellum including pyramidal and extrapyramidal involvement, ophthalmoplegia, peripheral neuropathy, and dementia[1]. ADCA II represents ataxia with extracerebellar neurologic findings, plus retinal degeneration. ADCA III is a pure form of ataxia and degeneration restricted to the cerebellum[1]. SCA – 1, 2, 3 and 6 fit into the ADCA I clinical category[1]. SCA 2, 15% (13-40%) is the second common form of ADCA I and characterized by slowly progressive ataxia and dysarthria associated with the ocular findings of nystagmus, slow saccadic eye movements, and in some individuals ophthalmoparesis[3,4]. We describe a family with ataxia, dysarthria, ophthalmoplegia and peripheral neuropathy. There are studies which revealed dementia, L-dopa responsive Parkinsonism, fasciculations, dystonia, and/or chorea at SCA 2 patients[5]. The Parkinsonian phenotype is associated predominantly with a shorter abnormal range of CAG repeat lengths and older onset age[6]. In the present report all of the four patients had cerebellar dysfunction. Most patients began with dysarthria and gait ataxia. As the disease progressed, limb ataxia became more pronounced. Family members who were examined showed ophthalmoparesis and peripheral nerve involvement, and the clinical suspicion of SCA type 2 was confirmed by genetic study. One patient (III-1) showed head titubation, which was rarely reported in the literature[7] .

The SCAs show anticipation and different degrees of expansion in maternal or paternal transmission.[7]. There is a negative correlation between CAG repeat size and age of disease onset, therefore young patients suffer from more severe and rapidly progressing disease[8]. DNA analysis showed a normal CAG repeat of 23 on one chromosome and abnormally amplified CAG repeat of over 41 on the other chromosome in index case and her son III-1. Blood samples from the mother and brother of the index case were not available. Therefore, the degree of anticipation and the existence of paternal imprinting were not analyzed. The widest range of age onset is observed in individuals with allele numbers between 38-45 CAG repeats[9] .

Testing for dominant ataxias should be included in the evaluation of patients with ataxia, especially in cases with a positive family history for spinocerebellar ataxia. New gene locuses which are linked to SCA's, are discovered every other day. Genetic study is significant in defining SCA types which are common in our country.

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