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Late-onset Tremor and Ataxia Syndrome: Fragile X-Associated Tremor/Ataxia Syndrome and Neuroimaging Findings

Geç Başlangıçlı Tremor Ataksi Sendromu: Frajil X Tremor Ataksi Sendromu ve Nörogörüntüleme Bulguları

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Dear Editor,

A man aged 60 years presented to our clinic with symptoms of progressive vertigo, difficulty in walking, loss of balance, and impaired hearing, which he had had for 3 months. His family history revealed a diagnosis of premature ovarian failure in the daughter. Systemic examination findings were normal. Neurologic examination revealed bilaterally reduced hearing that was more remarkable on the right, dysmetria and dysdiadokinesia, bilateral intentional tremor in upper extremities, ataxic gait, diminished patella and Achilles reflexes on both sides, and diminished vibration sense on all four sides. The neuropsychiatric examination was normal.

Laboratory examinations including complete blood count, C-reactive protein, serum electrolytes, liver and kidney function tests, blood glucose, thyroid function tests, iron, iron binding capacity, levels of vitamin B12, folic acid, and complete urine analysis resulted as normal. Brain magnetic resonance imaging (MRI) revealed mild cerebral atrophy, and increased symmetrical T2 hyperintense lesions in the middle cerebellar peduncle (MCP) (Figure 1). No diffusion restriction was seen in these areas in diffusion-weighted imaging. Cardiac testing also proved normal, and genetic testing revealed 108 CGG repeats in the Fragile X mental retardation 1 (*FMR1*) gene compatible with premutation (55-200). The patient was clinically diagnosed as having fragile X-associated tremor/ataxia syndrome (FXTAS) and followed up. Genetic analysis of the family members showed that the patient's daughter and brother's daughter also had premutations in the *FMR1* gene.

FXTAS has a clinical picture characterized by parkinsonism, cerebellar signs (ataxia and tremor), peripheral neuropathy, autonomic symptoms, cognitive impairment, and psychogenic problems such as anxiety, mood disorders, sleep disorders (1). Signs of the syndrome are associated with high CGG trinucleotide repeat counts in the *FMR1* gene (2). The normal number of repeats in alleles is 5-54. Approximately 55-200 repeats are seen in premutation or carriership, whereas Fragile X-related mental retardation protein (FMRP) cannot be synthesized (2,3,4). Neuropathologic studies have shown ubiquitin-positive eosinophilic intranuclear inclusion bodies in neurons and astrocytes, as well as spongiform white matter changes with axon and myelin loss (4).

Symmetrically increased intensity in MCP seen in MRI is deemed as a definite diagnostic criterion of FXTAS; however, only 42-64% of patients have this finding, and it is not specific for FXTAS (3,4,5). Furthermore, cerebral and cerebellar global atrophy, hippocampal and amygdala atrophy, and corpus callosum thinning may also accompany MRI findings of FXTAS. Loesch et

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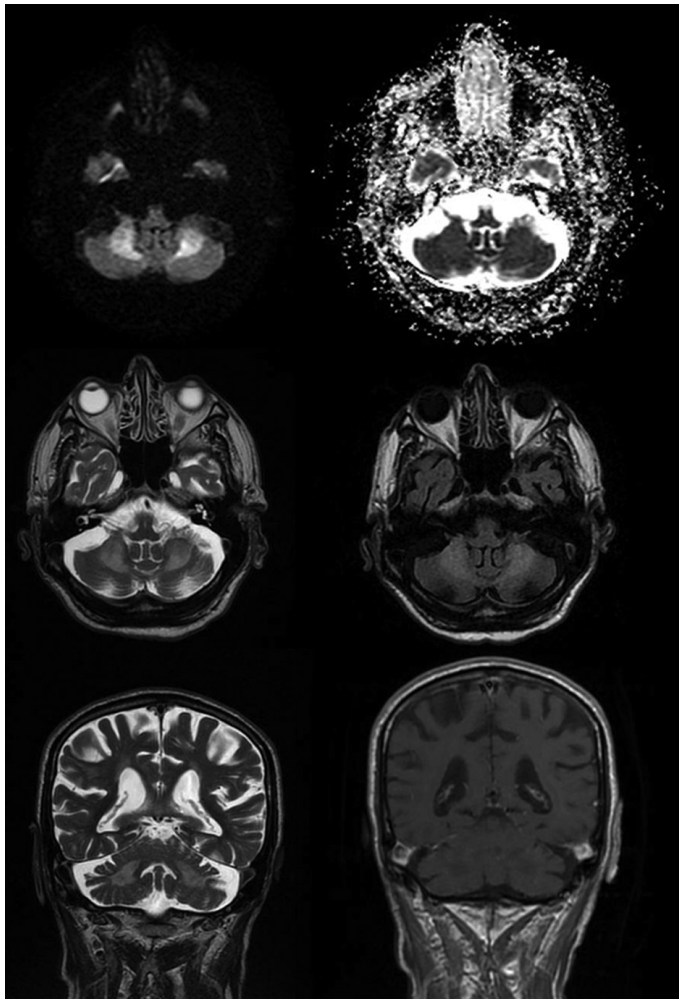

Figure 1. Mild cerebral atrophy and bilaterally increased T2 signal intensity in middle cerebellar peduncles in brain magnetic resonance imaging. No diffusion restriction was seen in diffusion-weighted imaging

al. (5) reported that an increased number of CGG repeat counts was associated with reduced brain volume in MRI. FXTAS should be noted as a diagnostic possibility in patients with typical MRI findings who present with ataxia/tremor at advanced age.

Ethics

Informed Consent: Consent form was filled out by all participants.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Levent Öcek, Onural Tümer, Figen Tokuçoğlu, Concept: Levent Öcek, Figen Tokuçoğlu, Yaşar Zorlu, Design: Levent Öcek, Figen Tokuçoğlu, Data Collection or Processing: Levent Öcek, Onural Tümer, Figen Tokuçoğlu, Özgür Öztekin, Analysis or Interpretation: Levent Öcek, Figen Tokuçoğlu, Özgür Öztekin, Yaşar Zorlu, Literature Search: Levent Öcek, Figen Tokuçoğlu, Yaşar Zorlu, Writing: Levent Öcek.

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