

Ocular findings of oculomotor apraxia/ataxia type 1: case report

Early-onset ataxia with oculomotor apraxia or oculomotor apraxia/ataxia type 1 (AOA-1) is a recessive progressive neurodegenerative disease that is clinically characterized by progressive diffuse ataxia, dysarthria, hand and head tremors, chorea, and dystonia.¹ The onset may occur as growth retardation primarily between the ages of 1 and 20 years. Cognitive impairment, mental retardation, peripheral axonal neuropathy, distal atrophy, superficial and deep sensory insufficiency, and hypo-/areflexia are seen in the progression of the disease along with movement disorders. Clinical ophthalmologic findings include gaze-evoked nystagmus, oculomotor apraxia, hypometric saccades, saccadic impairment, fixation failure, and excessive blinking. Progressive external ophthalmoparesis, which begins with upward gaze paralysis, may mask the signs of apraxia.¹

Laboratory findings include hypoalbuminemia, hypercholesterolemia, and frequently observed increased creatine kinase levels, although an increased alpha-fetoprotein level is observed infrequently.² In nerve conduction studies, findings are compatible with sensorimotor axonal neuropathy. Cerebellar atrophy, brain stem atrophy, and, in later stages, cortical atrophy are observed with magnetic resonance imaging.²

In this correspondence, we report the ocular findings of AOA-1 disease, which is rare, supported by genetic testing and neurologic clinical and laboratory findings.

A 28-year-old male was admitted to neurology clinic with complaints that first started at the age of 2 years as instability and frequent falls while walking. There was a delay in speaking, and dysarthric speech was present. At age 10 years, the patient started to be mobilized with a wheelchair because he could not walk without support. His parents are distantly related, and there are no findings in his older sister and brother. His uncle's daughter has ataxia that started at the age of 10 years, but there are no findings in his uncle or aunt (for pedigree, see Fig. 1).

In the neurologic examination, dysarthric speech, dysmetria, and dysdiadokinesis were present (Video 1, available online); loss of grade III proximal strength in both lower extremities, distal muscular atrophy in the lower extremities, and drop foot also were noted. No extrapyramidal signs or choreiform movements were observed in the patient. Deep tendon reflexes could not be obtained in all extremities. Plantar reflex could not be obtained in both lower extremities. Electromyography showed no motor and sensory response in the bilateral lower extremities, spontaneous activity was not observed in the muscles of the right lower extremities, superficial sensation was normal, and demyelinating and axonal motor neuropathy findings were detected.

There was evidence of cerebellar atrophy on cranial magnetic resonance imaging (Fig. 2). Scoliosis was detected on direct digital radiography. Cognitive impairment was found in the Mini-Mental State Examination (21/30).

Laboratory findings were hypoalbuminemia (3.48 g/dL), elevation in creatine kinase (434 U/L), a slight elevation in the level of alpha-fetoprotein (5.85 U/mL), and cholesterol was at normal levels (189 mg/dL).

On ophthalmologic examination, the best-corrected visual acuity in both eyes was bilateral 0.9 with the Snellen decimal chart (both eyes had mild myopic astigmatism). No pathology was detected on anterior segment and fundus examination. The macula and optic disc were normal in appearance. Intraocular pressure was normal. The patient's ocular fixation was weak. Smooth-pursuit eye movements were poor but enough (about maintaining target fixation), and saccadic eye movements were hypometric in the horizontal axis (Video 2, available online). During the volitional smooth pursuit, fixation could be achieved with the support of head movement, and oculomotor apraxia was observed (Video 2, available online). Blinking was increased. Conjugated eye movement was impaired, and saccadic eye movements were delayed and were slowed down especially in horizontal gaze. The macula and optic disc were considered normal by optical coherence tomography (Spectralis OCT, Heidelberg, Germany), and a multifocal electroretinogram (Metrovision Vision Monitor MonPackONE, Perenchies, France) was evaluated as artefactive because it was difficult to achieve fixation. Amplitude and latency were normal in the visual evoked potential test (Metrovision Vision Monitor).

Genetic analysis with whole-exon sequencing revealed a P. Lys328SerfsTer2 (c.982_998del) mutation in the *APTX* gene as homozygous. The same mutation was found to be heterozygous in the patient's father, older sister, and brother.

Autosomal recessive ataxia is a group of neurodegenerative diseases. The early-onset progressive cerebellar AOA clinical phenotype was first distinguished from other ataxias by Aicardi et al.³ A mutative *APTX* gene causes cell death by preventing transcriptional activities in neurons. Fibroblasts from AOA-1 patients are more susceptible to oxidative damage than normal fibroblasts, and increased oxidative DNA damage was found in the cerebellum of AOA-1 patients.⁴ Neuropathologically, severe Purkinje cell loss and neuronal loss in the dorsal root ganglia and anterior horn were detected. This is caused by a mutation in the *APTX* gene, which encodes the aprataxin protein. Aprataxin protein is a nuclear protein required for single-stranded DNA repair. The loss of function of this protein causes the repair of single-stranded DNA damage not to be restored.⁵

Although cortical atrophy was not observed in our patient, cerebellar atrophy was detected. Ophthalmologically, oculomotor apraxia was quite evident in head tracking,

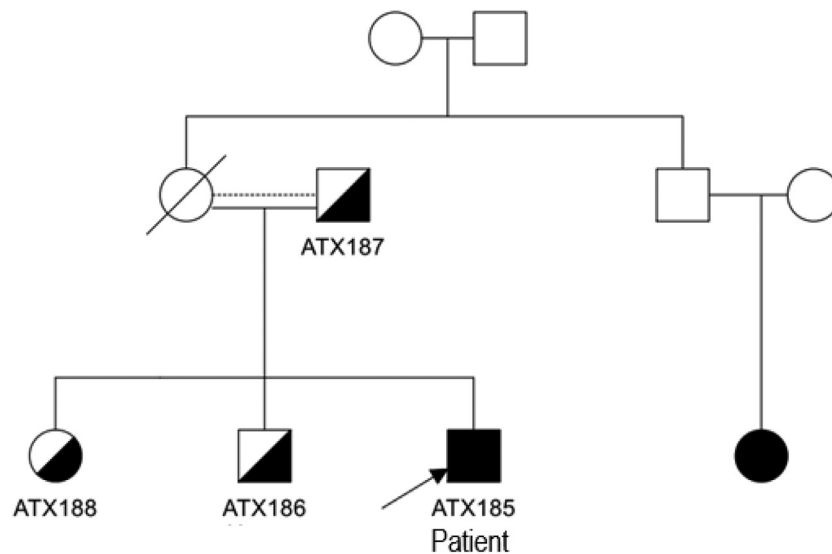


Fig. 1—Pedigree of the patient.

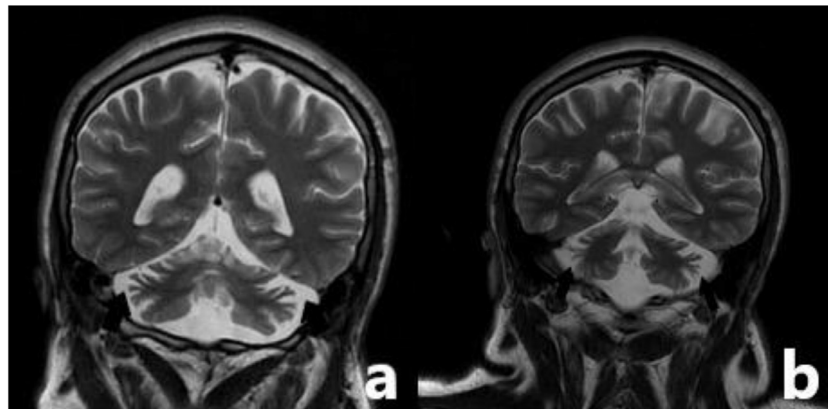


Fig. 2—Cranial magnetic resonance T₂-weighted images of our patient. Bilateral cerebellar atrophy is clearly seen in the images.

increased blinking, fixation failure, and saccadic hypometry. No retinal and optic nerve pathology was observed in electrophysiologic tests. Ocular findings were present, mostly in the form of ocular movement disorder.

A previous study found oculomotor apraxia, gaze-evoked nystagmus, and extraocular ophthalmoplegia at an earlier age and at a higher rate in patients with the homozygous c.689_690insT mutation.⁶ Although it is thought that there is a correlation between genotype and phenotype, this case has severe ataxia and oculomotor apraxia with severe genome deletion. Head thrust and abnormal eye movement are recognized as initial symptoms in <10% of cases, although gaze-evoked nystagmus is reportedly present in >70% of AOA-1 cases.⁶ It has been reported that apraxia was not present in 34.5% of AOA-1 cases and that it may finally progress to external ophthalmoplegia.⁶

In conclusion, our patient has a very rare case of AOA-1 published in Turkey that is supported by genetic testing. Our purpose in presenting this case is to show that oculomotor apraxia is the predominant ocular finding in this patient with severe cerebellar and neuropathic findings.

Online-only material: This article includes online-only material. Videos 1 and 2 can be found on the CJO web site at <http://pubs.nrc-cnrc.gc.ca/cjo/cjo.html>. They are linked to this article in the online contents of the xxx 2022 issue.

Supplementary materials

Supplementary material associated with this article can be found in the online version at [doi:10.1016/j.jcjo.2022.06.006](https://doi.org/10.1016/j.jcjo.2022.06.006).

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Footnotes and Disclosure

The authors have no proprietary or commercial interest in any materials discussed in this correspondence.