CASE REPORT

CANVAS SYNDROME: A COMPREHENSIVE CASE REPORT ON RARE ATAXIA

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Abstract

Introduction: Cerebellar ataxia with neuropathy and vestibular areflexia syndrome (CANVAS) is characterized by cerebellum, vestibular system, and sensory pathways impairments. It progresses slowly compared to other ataxias like Friedreich's ataxia, and its genetic basis is complex and under investigation.

Case Report: A 34-year-old male presented with worsening imbalance over the past year, vertigo, slurred speech, and hand tremors. Physical examination revealed bidirectional nystagmus, dysmetria, and cerebellar atrophy on MRI. Vestibular tests were abnormal, and neuropsychological assessments showed memory and executive function deficits. Sensory nerve conduction studies were normal.

Discussion: The patient's symptoms of ataxia, vestibular areflexia, and sensory neuropathy are consistent with CANVAS. Cerebellar atrophy and Purkinje cell degeneration contribute to motor coordination deficits. Sensory neuropathy involves dorsal root ganglia degeneration. Despite supportive clinical features, genetic testing is necessary to confirm the diagnosis and exclude other genetic ataxias.

Conclusion: CANVAS is a rare ataxia syndrome with autosomal recessive inheritance affecting the cerebellum, vestibular, and sensory systems. The patient's symptoms and MRI findings suggest CANVAS, but further genetic testing is required for definitive diagnosis.

Keywords: CANVAS, cerebellar ataxia, cerebellar atrophy, sensory neuropathy, vestibular areflexia

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Introduction

Cerebellar ataxia with neuropathy and vestibular areflexia syndrome (CANVAS) is a recently recognized ataxic disorder that affects three key components of balance regulation: the cerebellum, vestibular system, and sensory pathways. This condition impairs three of the four cardinal balance components, with vision being the only unaffected modality. Compared to other ataxias, such as Friedreich's ataxia or spinocerebellar ataxia type 3, CANVAS progresses at a relatively slow rate. The underlying genetic etiology of CANVAS remains under investigation, although emerging evidence suggests that the

disorder may be associated with multiple causative genes, indicating a complex inheritance pattern. [1]

CANVAS is classified as a rare neurological disorder with an autosomal recessive inheritance pattern. There is no predictable sequence in the onset of its three cardinal features—cerebellar impairment, bilateral vestibular hypofunction, and somatic sensory deficits. Patients may present with only two of these three features for several years before fulfilling the minimum diagnostic criteria for CANVAS. Pathologically, CANVAS is characterized by neuronopathy affecting multiple cranial nerves and dorsal root ganglia, alongside a consistent pattern of cerebellar atrophy.[2]

In 2016, proposed diagnostic criteria for definitive CANVAS included the presence of an abnormal visually enhanced vestibulo-ocular reflex (VVOR) detected via video-oculography, videonystagmography, or rotational chair testing. Additionally, MRI findings demonstrating cerebellar atrophy, particularly involving the anterior and dorsal vermis as well as the lateral hemispheres (primarily affecting crus I), provide further diagnostic support. Neurophysiological evidence of neuronopathy (ganglionopathy) is also required, along with the exclusion of genetically testable ataxias, particularly spinocerebellar ataxia type 3 (SCA3) and Friedreich's ataxia.[3]

Case Report

A 34-year-old male presented with progressive imbalance over the past year. He reported difficulty maintaining balance while walking, which was absent when standing or sitting. He also experienced episodic vertigo, particularly when changing positions from lying to standing. Over the past six months, he developed slurred speech and hand tremors, especially while typing on a keyboard. He denied nausea, vomiting, hearing loss, tinnitus, facial numbness, headaches, or unilateral weakness.

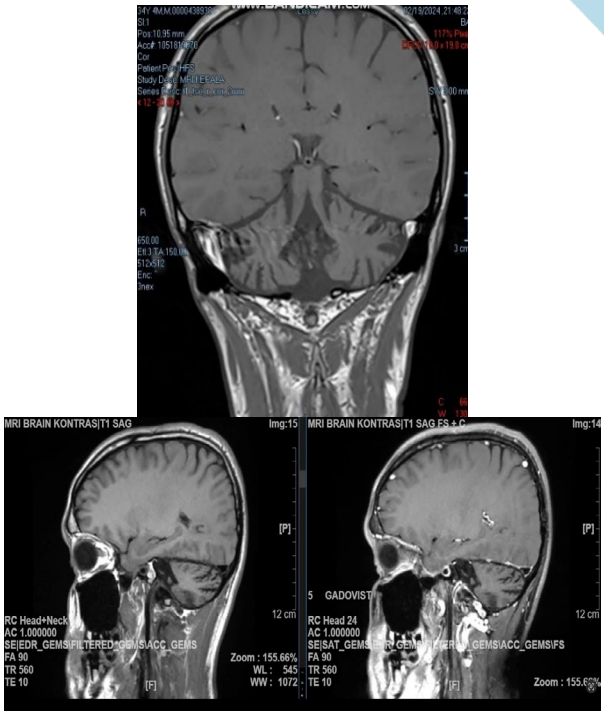
On examination, the patient was alert with a Glasgow Coma Scale (GCS) score of E4M6V5. Vital signs were stable (BP: 112/85 mmHg, HR: 85 bpm, RR: 18 breaths/min, Temp: 36.5°C). Neuro-ophthalmologic evaluation revealed corrected visual impairment and bidirectional horizontal nystagmus with rebound nystagmus. Saccadic dysmetria was observed in the left eye, while the right eye exhibited normal saccades.

Neuro-otologic examination confirmed vestibular dysfunction. Dix-Hallpike testing elicited downbeat nystagmus without latency, lasting >30 seconds, and was non-fatiguable. No spontaneous nystagmus was observed in a sitting position. Gaze-evoked nystagmus was present in horizontal but not vertical fields. Rebound nystagmus was positive bilaterally, and head-shaking testing revealed cross-coupled nystagmus. Hearing examination revealed no abnormalities. However, balance assessment showed that the patient had a stable stance with both feet together (Romberg test). When performing the sharpened Romberg test with eyes open, the patient fell.

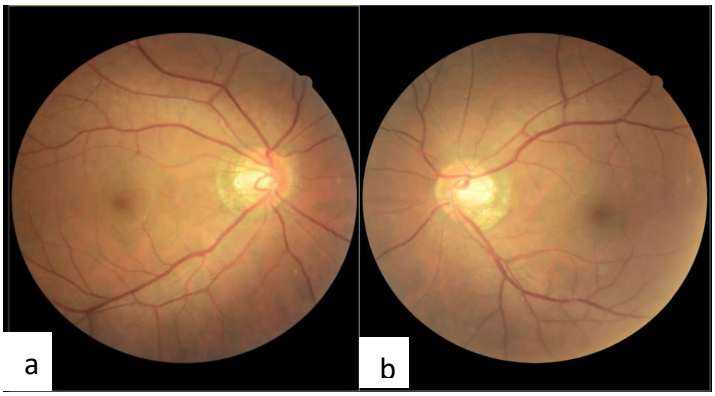
Figure 1. Gait Pattern in Cerebellar Ataxia

Tandem walking assessment revealed impairments. In the finger-to-finger coordination test, the patient exhibited positive dysmetria. The knee-to-heel test also showed disturbances. Vestibulo-ocular reflex (VOR) testing was positive on both sides, and the VOR suppression test was impaired in both right and left directions. Bilateral bradykinesia was observed, with greater severity on the left side. Visual dynamic acuity testing showed bilateral impairments.

Additional examinations, including somatosensory evoked potentials (SSEP) and nerve conduction studies (NCS), revealed no abnormalities. Higher cognitive function assessment using MMSE, MoCA-Ina, CERAD, TMT A, and TMT B indicated memory dysfunction (impairment in verbal and visual delayed recall) and executive function deficits (including difficulties in calculation and abstraction). Contrast-enhanced brain MRI revealed cerebellar atrophy, predominantly affecting the vermis. No atrophy was observed in the brainstem, cerebral cortex, or spinal cord.



Figures 2. Contrast-Enhanced Brain MRI: Coronal and Sagittal Views



Figures 3. Fundoscopy Images: (a) Right Eye, (b) Left Eye

Discussion

The clinical manifestations observed in this patient, including ataxia, vestibular areflexia, and sensory neuropathy, are highly suggestive of Cerebellar Ataxia, Neuropathy, and Vestibular Areflexia Syndrome (CANVAS). A characteristic pattern of cerebellar atrophy often precedes the full clinical presentation, manifesting as ataxia, motor coordination impairment, and nystagmus. In CANVAS, Purkinje cells in the cerebellum exhibit increased susceptibility to degeneration, which plays a crucial role in motor coordination. The progressive loss of Purkinje cells leads to cerebellar atrophy, contributing to the ataxic symptoms experienced by the patient. This condition is strongly associated with a biallelic AAGGG repeat expansion in the RFC1 gene, a mutation that results in the production of aberrant proteins, ultimately leading to neuronal dysfunction and degeneration.[4]

The patient's sensory neuropathy presents as glove-and-stocking hypesthesia, a hallmark feature of CANVAS. One of the primary neuropathological findings in CANVAS is dorsal root ganglia (DRG) degeneration, which results in axonal degeneration with secondary demyelination of the posterior columns. The progressive neural loss within the DRG supports the clinical suspicion of peripheral sensory deficits in CANVAS.[5] Similarly, the patient's vestibular areflexia manifests as impaired coordination, balance disturbances, vertigo, nystagmus, and abnormal VVOR. One of the key pathological mechanisms underlying CANVAS is vestibular ganglion neuron degeneration, which reduces vestibular input to the brain, ultimately resulting in vestibular areflexia.[5,6]

Based on the patient's symptomatology, the clinical findings strongly align with a clinically probable diagnosis of CANVAS. Supporting evidence includes abnormal VVOR and cerebellar atrophy observed on MRI. However, NCV did not reveal significant sensory abnormalities, which does not support a definite diagnosis of clinically probable CANVAS, despite the presence of glove-and-stocking hypesthesia. To establish a more definitive diagnosis, genetic testing is essential to exclude other hereditary ataxias, such as spinocerebellar ataxia type 3 (SCA3) and Friedreich's ataxia.[1]

Spinocerebellar ataxia type 3 (SCA3), also known as Machado-Joseph disease, is the most common form of autosomal dominant spinocerebellar ataxia, caused by a CAG trinucleotide repeat expansion in the *ATXN3* gene. Clinically, it is characterized by progressive cerebellar ataxia accompanied by pyramidal signs, extrapyramidal features such as dystonia or Parkinsonism, peripheral amyotrophy with generalized areflexia, progressive external ophthalmoplegia, and action-induced facial or lingual fasciculations.[7,8] In the present case, SCA3 was considered due to the presence of progressive ataxia, vestibular dysfunction, and sensory neuropathy. However, the absence of typical features including pyramidal or extrapyramidal involvement, ophthalmoplegia, and a family history of autosomal dominant inheritance makes this diagnosis unlikely. Instead, the clinical profile of prominent vestibular areflexia and sensory neuronopathy is more

consistent with CANVAS. Nevertheless, definitive exclusion of SCA3 requires molecular confirmation of CAG repeat expansion in the *ATXN3* gene.

Friedreich's ataxia (FRDA) is a slowly progressive autosomal recessive degenerative disease involving both neural and extraneural systems, most commonly caused by GAA repeat expansion in the FXN gene. It usually manifests in childhood or adolescence with gait ataxia, dysarthria, sensory loss, and areflexia, and is frequently associated with systemic features such as hypertrophic cardiomyopathy, scoliosis, and diabetes mellitus. Neurologically, FRDA consistently involves three major systems: (1) large fiber sensory pathways, leading to proprioceptive loss and absent reflexes, (2) cerebellar coordination systems, resulting in gait ataxia, impaired limb coordination, and dysarthria, and (3) corticospinal tracts, which may cause progressive lower extremity weakness and spasticity. [9,10] In the present case, FRDA was considered as a differential diagnosis due to the presence of progressive ataxia and sensory neuropathy. However, the patient's age of onset in late adulthood, absence of cardiomyopathy, scoliosis, or diabetes, as well as the presence of vestibular areflexia, which is not characteristic of FRDA, make this diagnosis unlikely. Moreover, while clinical features can suggest the possibility of FRDA, a definitive diagnosis requires genetic confirmation of biallelic *FXN* mutations, typically GAA repeat expansion testing.[9] Genetic testing has not yet been performed in this patient and is strongly recommended to definitively rule out FRDA.

Further diagnostic assessments should be considered to refine the diagnosis. Referral to the otolaryngology (ENT) department for video head impulse testing (vHIT) could provide additional confirmation of vestibular impairment. Additionally, vestibular-evoked myogenic potentials (VEMP), sympathetic skin response (SSR), sinus rhythm (SR), and RR interval variability should be evaluated in the neurophysiology department. Moreover, transcranial magnetic stimulation (TMS) could be explored in the context of neurorestorative interventions.

Conclusion

CANVAS (Cerebellar Ataxia, Neuropathy, and Vestibular Areflexia Syndrome) is a rare neurodegenerative disorder affecting the cerebellum, vestibular, and sensory systems, following an autosomal recessive inheritance pattern. The primary clinical manifestations observed in the patient, including ataxia, motor coordination impairment, vertigo, and nystagmus, strongly support a diagnosis of CANVAS. This is further reinforced by radiological findings demonstrating cerebellar atrophy and visual-vestibular dysfunction. Although the clinical presentation is highly suggestive of CANVAS, additional diagnostic assessments are required for confirmation. Genetic testing is recommended to exclude other hereditary ataxias.

Conflict of Interest

The authors declared no conflict of interest.

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