Cerebellar ataxia and nystagmus with GAD antibodies in a woman from the West Indies : a video demonstration

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A 72-year-old Afro-Caribbean woman presented with diplopia, vertigo, intermittent vomiting, progressively worsening ataxia ([video 1](#)) and nystagmus ([video 2](#), segment 1) over a period of 4 months. There was a 2-year history of type 2 diabetes mellitus and hypothyroidism being treated with oral metformin 500 mg, gliclazide 80 mg two times per day and L-thyroxine 0.1 mg daily. She denied exposure to chemicals or recreational drugs. Social, family and sexual history were insignificant.

Her body mass index was 24 kg/m². The Mini Mental State Examination (MMSE) score was 30/30. Cerebellar gait ataxia with an ample sustentation base was present. This worsened over 4 weeks, leading to a score of 26/40 on the scale for the assessment and rating of ataxia (SARA). Dysmetria and dysdiadochokinesis were also prominent in all limbs. Bilateral gaze-evoked nystagmus was noted in the primary position, in horizontal, upbeat and down beat directions but this was not torsional ([video 2](#), segment 1). Dysarthria, intention tremor, spinal cord long tract signs and rigidity were absent. The rest of the physical examination was normal.

Extensive medical investigations ruled out underlying endocrine, autoimmune, vasculitic, infectious and neoplastic illnesses. Glycosylated haemoglobin (Hb1Ac) level of 5.5% was normal. Haematologic and metabolic status, hepatic and renal function tests, collagen vascular tests, tumour markers, retroviral and syphilitic serological tests and cerebellar antibody panel for neoplasm were normal. High levels of glutamic acid decarboxylase antibodies (GAD-Abs) at 502.4 U/mL (reference range positive above 10 U/mL) with mildly elevated anti-thyroid antibodies (TPO AB) at 37.18 IU/mL

Video 2 Segment 1 recorded before treatment showed a jerk type severe bilateral nystagmus noted in the primary position and was of mixed directions such as horizontal, upbeat and down beat but not torsional. The nystagmus was not affected by the position of the patient's body. The phenomenon's periodicity was of approximately 60 s. Segment 2 recorded 4 months after treatment showed a gaze-evoked bilateral nystagmus that were horizontal, upbeat and down beat but not torsional and was not seen in the primary eye position. There was an impaired gaze holding but no rebound, spontaneous peripheral vestibular phenomenon or Brun's nystagmus. There was a significant improvement in the severity, duration and impairment due to the phenomenon.

(reference range, 0–35 IU/mL) were noted. MRI of the brain with angiography and venography, MRI of the spinal cord, computerised tomographic scans of the chest, abdomen and pelvis, mammography, oesophgogastroduodenoscopy and colonoscopy were normal. Positron emission tomography scan and islet cell antibody testing were unavailable. Other immune-mediated cerebellar ataxias including gluten ataxia, paraneoplastic cerebellar degeneration, Hashimoto's encephalopathy and other differentials were also considered ([table 1](#)).

GAD-Abs associated cerebellar ataxia with nystagmus was diagnosed based on the neuroclinical manifestations, elevated serum GAD-Abs, MRI findings, exclusion of other diseases with further support from the patient's clinical and biochemical response to immunomodulation. Treatment with steroids and azathioprine over 4 months demonstrated an improvement of nystagmus ([video 2](#), segment 2), partial resolution of diplopia, vertigo, dysmetria, dysdiadochokinesis and ataxia with an increase in the SARA score to 35/40. GAD-Abs level decreased to 318.4 U/mL after 6 months treatment.

Video 1 Segment 1 showed moderate cerebellar ataxia with ample sustentation base and poor coordination on assisted ambulation. Segment 2 showed a positive dysmetria test.

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Table 1 Differential diagnosis and investigations

Differential diagnosis	Investigation	Results and conclusion
Stroke	History, T2W and DWI/ADC MRI	Insidious onset of symptom, sudden vascular event unlikely, 4-month time needed to full establishment of the syndrome. Upper motor, reflex and sensory examinations normal. No focal lesions
Space occupying lesion of brain and spine	T2W MRI	No mass lesions. Minimal cerebral atrophy. No cerebellar atrophy. No evidence of intracranial hypertension or middle shift
Multiple sclerosis	T2W MRI	No paraesthesia or sensory abnormalities. No evidence of demyelination disseminated in time/space on MRI fails to satisfy MacDonald's criteria
Multiple system atrophy	History, T2W MRI	Autonomic features at presentation were absent and a pure cerebellar syndrome is not common such as in our patient. The absence of typical MRI features such as 'hot cross bun sign'
Paraneoplastic syndrome	History, FDG-PET, onconeural antibodies	No clinical pointer to malignancy. FDG-PET was not available. Onconeural antibodies were negative
Inherited spinocerebellar ataxia	History, SCA6 genetic testing	There were no signs of dysarthria, peripheral neuropathy, spasticity, areflexia, vegetative symptoms or fasciculations. SCA6 Genetic testing was unavailable
A toxic or metabolic cerebellar syndrome	History, biochemistry	Unlikely without alcohol or recreational drugs consumption, exposure to chemicals or radiation, or medication history (eg, lithium, phenytoin). Absent ophthalmoplegia is seen in thiamine deficiency or areflexia and proprioception loss in vitamin E deficiency. Serum vitamin B ₁₂ , folate levels and haemoglobin were normal
Creutzfeldt-Jacob disease	History	No additional features such as rapidly progressive dementia, psychiatric disturbance, myoclonus and sensory symptoms
Hashimoto's encephalopathy	History, GAD-Abs, anti-thyroid antibodies	Steroid-responsive encephalopathy with autoimmune thyroiditis that could not be confirmed by elevation of anti-TPO or anti-thyroid microsomal antibody and/or anti-thyroglobulin. No additional features such as seizures, myoclonus or tremor, chorea, dystonia and psychosis. When ataxia is the only manifestation, it can easily be missed or mistaken for degenerative ataxia, however GAD-Abs were positive
Autoimmune cerebellar syndrome	History, GAD-Abs	Clinical manifestations were typical of the disease and were associated with nystagmus, hypothyroidism and diabetes. GAD-Abs were strongly positive in serum. Consent for lumbar puncture was not obtained

DWI/ADC MRI, diffusion-weighted imaging/ apparent diffusion coefficient magnetic resonance imaging; FDG-PET, fluorodeoxyglucose-positron emission tomography; GAD-Abs, glutamic acid decarboxylase autoantibody; SCA6, spinocerebellar ataxia type 6; T2W MRI, T2-weighted magnetic resonance imaging.

Subsequently, human immune globulin and/or plasmapheresis treatment was declined.

GAD-Abs spectrum disorder includes limbic encephalitis, opsoclonus-myoclonus-ataxia syndrome, palatal myoclonus, epilepsy, stiff person syndrome, encephalomyelitis with rigidity, Guillain-Barré and myasthenia like syndromes, cerebellar ataxia with or without nystagmus and is considered part of

the group of polyglandular autoimmune illnesses, that includes diabetes mellitus, myasthenia gravis, thyroiditis and pernicious anaemia. The cerebrospinal fluid analysis may be normal or may show oligoclonal bands, mild pleocytosis and intrathecal synthesis of GAD-Abs, in some cases. Cerebellar ataxia associated with GAD-Abs is rare, particularly when accompanied by nystagmus.¹⁻³

This report represents the first documented case of this clinical entity from the West Indies.

Learning points

- ▶ Glutamic acid decarboxylase antibodies (GAD-Abs)-associated cerebellar ataxia is a part of an expanding spectrum of neurological disorders associated with the GAD enzyme needed to convert the excitatory amino acid glutamate into the inhibitory neurotransmitter gamma-aminobutyric acid.
- ▶ Cerebellar ataxia associated with GAD-Abs can be diagnosed based on the neuroclinical manifestations and elevated GAD-Abs, with further support from the patient's response to immunomodulation.
- ▶ Cerebellar ataxia with or without nystagmus associated with GAD-Abs is a potentially treatable syndrome using immunomodulation.
- ▶ GAD-Abs should be sought not only in patients with polymorphic, persistent or refractory neurological syndromes but also with associated cancer and polyglandular autoimmune illnesses.

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