Spastic Ataxia with Sensory Neuropathy Sans Cerebral Leukodystrophy in Probable Adult Polyglucosan Body Disease

Dear Sir,

Adult polyglucosan body disease (APBD) is a neurogenetic disorder characterized by progressive spastic paraparesis, distal sensory deficit in the legs, and neurogenic bladder with age at onset in the fifth or sixth decade. The presence of polyglucosan bodies in skin, muscle, or nerve tissues suggests the diagnosis of APBD.[1] Hereby, we report a 54-year-old lady who presented with spastic ataxia of 3 years duration with distal upper and lower limb sensory symptoms. Nerve biopsy showed the presence of polyglucosan bodies, which was diagnostic of APBD.

A 54-year-old lady presented with a history of difficulty in walking of 3 years duration and sensory symptoms in the form of tingling and burning paresthesia in distal upper and lower limbs of 1 year duration. The patient had walking difficulty in the form of stiffness in both lower limbs and imbalance while walking. There was no diurnal variation in the gait imbalance. She had tingling paresthesia in the hands and feet in a non-length-dependent topography. There was no sensory loss in the limbs. She had urinary urgency with occasional urge incontinence of 1 year duration. There was no motor weakness in the limbs or craniobulbar symptoms. There was no history of seizures, cognitive impairment, speech disturbance, tremors of limbs, or thinning of limbs. There were no similar complaints in his siblings or parents. Systemic examination was unremarkable. Neurological examination showed normal cognition, speech, and cranial nerves, including fundus. There was no nystagmus, normal saccades, and pursuits. Motor examination showed

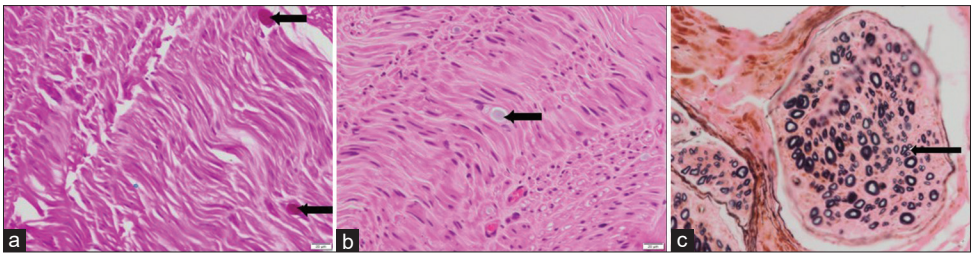

Figure 1: Histopathology of superficial peroneal biopsy (a) PAS stain showing polyglucosan bodies (black arrow); (b) Hematoxylin and eosin stain showing polyglucosan bodies (black arrow); (c) Kpal stain showing non-uniform loss of myelinated fibers with regenerating clusters (black arrow)

spasticity in both lower limbs (grade 3 according to modified Ashworth scale), normal tone in upper limbs, grade 3+ knee jerk, 2+ in upper limbs with absent ankle jerks, and normal muscle power. Sensory examination showed impaired proprioception in distal lower limbs with normal touch and pain sensation. Plantar responses were extensor, and Romberg sign was positive. There were no cerebellar signs. Gait was of spastic-ataxic type. A clinical possibility of myeloneuropathy was considered. Complete blood count, renal, hepatic, and thyroid function tests were normal. Serum vitamin B12, folate, and copper levels were normal. Serological tests for human immunodeficiency virus and syphilis were non-reactive. Brain and spine magnetic resonance imaging (MRI) did not show any atrophy or signal changes. Nerve conduction studies showed features of sensory neuropathy in lower limbs. Cerebrospinal fluid analysis was normal. Somatosensory evoked potentials showed absent cortical responses from tibial nerve stimulation. Superficial peroneal nerve biopsy showed polyglucosan bodies in axons with non-uniform loss of myelinated axons and regenerating clusters, suggestive of chronic axonal neuropathy [Figure 1]. The patient was treated with baclofen (10 mg/day) and gabapentin (300 mg/day). A final diagnosis of spastic-ataxic syndrome due to APBD was considered.

APBD was first described by Salvatore DiMauro *et al*.[2] in 1980 in four adult patients with progressive upper and lower motor neuron signs, sphincter disturbances, sensory loss in the lower limbs, and cognitive decline. The neuropathological examination shows the presence of intra-cellular accumulation of polyglucosan bodies containing amylopectin like polysaccharides in the central and peripheral nervous systems. Polyglucosan bodies have been shown in glycogen storage disorders (GSDs) like GSD type IV (Andersen disease), GSD type VII (Tarui disease), and GSD type XV (glycogenin deficiency). Polyglucosan bodies are round to oval, amphophilic to slightly eosinophilic, ground-glass hyaline bodies, deeply periodic-Schiff (PAS)-positive bodies.

APBD is an autosomal recessive glycogenosis caused by a homozygous or compound heterozygous pathogenic variant in *GBE1* gene. The phenotypic profile varies from liver disease in infancy to neuromuscular disease and APBD in adults based on the residual level of the glycogen-branching enzyme activity.[3] The underlying pathomechanism of APBD is not known, but these inclusions cause mechanical disruption of normal cellular functions such as intra-cellular transport. The first case series from India were the description of seven cases in 2007. Patients were diagnosed based on the presence of polyglucosan bodies in nerve axons or sweat glands. Cognitive and pyramidal involvement was the most common symptom, followed by neuropathy. There were white matter changes on brain MRI in four out of five patients.[4] Our patient did not have cognitive disturbances or white matter lesions on MRI. Mochel *et al*.[5] (2012) reported 50 APBD patients from four countries and found that neurogenic bladder, spastic paraplegia with vibration loss, and axonal neuropathy were the most common manifestations. Nerve conduction studies showed sensorimotor polyneuropathy and homozygous p.Y329S *GBE1* variant was the most common genetic abnormality. Brain MRI showed atrophy of the medulla, spinal cord, and cerebellar vermis and signal changes in periventricular white matter, internal and external capsules, middle and inferior cerebellar peduncles, and the medial lemniscus of the medulla and pons. Hellmann *et al*. (2015) reviewed 30 patients of APBD and found similar symptoms as reported by Mochel *et al*.[5] The atypical presentations of APBD include stroke-like episodes, motor neuron disease (MND) phenotype, atypical parkinsonism with MND, frontotemporal dementia with MND, and so on.[6]

Our patient had spastic paraparesis, overactive bladder with sensory neuropathy sans cognitive deficits, and brain MRI changes of leukodystrophy. Nerve biopsy showed the presence of intra-axonal polyglucosan bodies. The genetic testing of Glycogen Branching Enzyme (GBE) activity was not done, and the level of GBE activity was not determined. The absence of cerebral leukodystrophy may lead to the non-suspicion of the diagnosis. APBD should be considered in patients with spastic ataxia with sensory neuropathy sans cerebral leukodystrophy.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Rohan Mahale, Sridhar Shashi, Anitha Mahadevan[1], Raviprakash Singh, Vivek Potluri, Hansashree Padmanabha, Pooja Mailankody, Mathuranath S. Pavagada

Departments of Neurology and [1]Neuropathology, National Institute of Mental Health and Neurosciences (NIMHANS), Bengaluru, Karnataka, India

Address for correspondence: Dr. Rohan Mahale, Department of Neurology, National Institute of Mental Health and Neurosciences (NIMHANS), Bengaluru - 560 029, Karnataka, India.
E-mail: rohanmahale83@gmail.com

References

1. Lossos A, Meiner Z, Barash V, Soffer D, Schlesinger I, Abramsky O, *et al*. Adult polyglucosan body disease in Ashkenazi Jewish patients carrying the Tyr329Ser mutation in the glycogen-branching enzyme gene. Ann Neurol 1998;44:867-72.
2. Robitaille Y, Carpenter S, Karpati G, DiMauro SD. A distinct form of adult polyglucosan body disease with massive involvement of central and peripheral neuronal processes and astrocytes: A report of four cases and a review of the occurrence of polyglucosan bodies in other conditions such as Lafora's disease and normal ageing. Brain 1980;103:315-36.
3. Souza PVS, Badia BML, Farias IB, Pinto WBVR, Oliveira ASB, Akman HO, *et al*. GBE1-related disorders: Adult polyglucosan body disease and its neuromuscular phenotypes. J Inherit Metab Dis 2021;44:534-43.
4. Chickabasaviah Y, Anadure R, Mahadevan A, Bhoi K. Seven cases of adult polyglucosan body disease (APBD): Expanding the clinical spectrum, and the role of skin biopsy. Ann Indian Acad Neurol 2007;10:26-7.
5. Mochel F, Schiffmann R, Steenweg ME, Akman HO, Wallace M, Sedel F, *et al*. Adult polyglucosan body disease: Natural history and key magnetic resonance imaging findings. Ann Neurol 2012;72:433-41.
6. Hellmann MA, Kakhlon O, Landau EH, Sadeh M, Giladi N, Schlesinger I, *et al*. Frequent misdiagnosis of adult polyglucosan body disease. J Neurol 2015;262:2346-51.

Submitted: 13-Aug-2023 **Revised:** 30-Aug-2023 **Accepted:** 12-Sep-2023
Published: 07-Nov-2023

DOI: 10.4103/aian.aian_725_23