Case Report

Myelopathy in Two Brothers with Respiratory Chain Disorder—Severe Complex 1 Deficiency with Atlantoaxial Dislocation and Long Spinal Arachnoid Cyst: A New Unreported Association

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Billion of years ago bacteria is believed to have entered a eukaryotic cell and converted to mitochondria. The respiratory chain present in it supplies ATP to all cells and therefore the diseases can have any phenotype. Diagnosis may be difficult to confirm by the conventional methods including genetics. Two brothers born to consanguineous parents had global delay, mild visual impairment and drooping of eyelids since birth in the elder child and dysmorphism in the second one. Both had progressive myelopathy due to retroflexed odontoid, large arachnoid cyst and tethered cord. Muscle biopsy with special stain was normal but respiratory chain assay revealed severe complex 1 deficiency. Elder child underwent surgical decompression of the arachnoid cyst with duroplasty with significant improvement. Atlantoaxial dislocation and large arachnoid cyst as cause of myelopathy is not reported in literature in patients with respiratory chain disorders to the best of our knowledge.

Keywords: Arachnoid cyst, atlantoaxial dislocation, respiratory chain disorder

INTRODUCTION

It is postulated that a billion years ago, aerobic bacteria entered eukaryotic cells resulting in a symbiotic relationship and the bacteria became the mitochondria. Spinal cord involvement in mitochondrial diseases is relatively less recognized than brain, muscle, peripheral nerves, and other system involvement. Mostly postmortem examination has shown spinal cord involvement in clinically asymptomatic patients. Patients with Leigh syndrome, Kearns–Sayre syndrome, and mitochondrial encephalopathy with ragged red fiber syndrome have been occasionally reported with spinal cord involvement. Leukoencephalopathy, brain stem and spinal cord involvement, and lactic acidosis (LBSL) is a classical syndrome caused by mutation in the DARS2 gene, encoding mitochondrial aspartyltransfer ribonucleic acid synthetase, and it presents as spasticity, ataxia, deafness as well as posterior column features. Mitochondrial recessive ataxia syndrome (MIRAS) is caused by POLG1 mutation, and it presents with cognitive dysfunction, behavioral problems, ataxia, and spinal cord involvement.

Atlantoaxial instability and compressive myelopathy

Atlantoaxial instability (AAD) can be due to bony abnormalities, soft tissue disorders, or both. It is usually congenital and occasionally acquired. In patients with hypotonia due to various causes, AAD is observed, but mostly it is asymptomatic and occasionally symptomatic. The common examples are Down syndrome, Ehlers–Danlos syndrome, and related collagenopathies, where they are due to

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 laxity at ligaments levels. Females are more affected than males.

**Respiratory chain diseases and spinal cord**

The respiratory chain supplies energy in the form of Adenosine tri phosphate. Mitochondrial respiratory chain was first identified in 1962.[7] It comprises a spectrum of rare disorders. The symptoms are mostly non specific. It can affect any system, affect persons of all age group, can be inherited in any pattern and screening tests and even mutation analysis can be normal leading to delay in diagnosis even after clinical suspicion.[8] Approximately 25 nuclear genes have been found to be associated with respiratory chain disorders and many remain undetected.

**Subjects and Methods**

Patient 1 is currently a 15-year-old boy born to second-degree consanguineous parents, who presented to us at the age of 11 years with the following complaints. He was born naturally at full term but had fetal distress, poor sucking, and global delay. He had symmetrical non-fatigable drooping of both eyelids since birth. Examination revealed optic atrophy in both eyes [Figure 1]. From the age of 10 years, he was noticed to be dragging both legs, which progressively worsened with tendency to buckle. He had exaggerated reflexes and extensor plantar response as well as impaired posterior column sensations, which was followed by bladder involvement. He had kyphoscoliosis at upper thoracic region. He was investigated with repetitive nerve stimulation, anti-Acetyl choline receptor antibody, lactate (13.2 mg/dL), ammonia (71 mcg/dL), and creatine kinase (132 U/L). Tandem mass spectrometry was normal. Electro myography showed myopathic pattern and left biceps biopsy showed normal architecture, including modified Gomori’s trichrome stain [Figure 2]. However respiratory chain assay showed severe complex 1 deficiency [Figure 3]. Magnetic resonance imaging (MRI) showed retroflexed dens with cervicomedullary compression, poorly developed anterior arch of atlas, brachycephaly, long arachnoid cyst with dural ectasia from cervical to lumbar region with anterior displacement of cord, and low lying cord tethered at L4 [Figure 4]. In view of the high risk involved in anesthesia, he was managed symptomatically but he became bed bound. His height was 146 cm and neck length was 10 cm and height/neck ratio was 14.6 at the present admission. He underwent lumbar drain placement, L2 left hemilaminectomy, and repair of dural defect, and at 2 months of follow-up, he is presently ambulant, and his postoperative imaging showed significant relief of compression [Figure 5]. His younger brother had similar history but did have drooping of eyelids. He did not undergo muscle biopsy; however, his MRI showed similar features [Figures 6 and 7].

**Result**

We report two brothers who presented with global delay and compressive myelopathy. The elder child was histopathologically proven case of complex 1 deficiency, and biopsy was not conducted in the younger one but he shared the same phenotype.

**Discussion**

Clinical features of spinal cord involvement are seen in LBSL, Leighs syndrome (LS), Mitochondrial Encephalopathy with ragged red fiber syndrome (MERRF). Infantile onset spinocerebellar ataxia (IOSCA). Pontocerebellar hypoplasia (PCH). Mitochondrial Multiorgan Dysfunction syndrome (MIMODS). Mito chondrial Encephalopathy and
stroke like syndrome (MELAS). Chronic External Ophthalmo plegia syndrome (CPEO). Lebers Hereditary Optic Neuropathy (LHON). They present in varying combinations of posterior column, corticospinal tracts, spinocerebellar tract, and autonomic involvement in association with central nervous system features. Though scoliosis is reported due to neuromuscular involvement, to the best of our knowledge, bony anomaly of odontoid and arachnoid cyst are not reported in literature. Surgical decompression of the arachnoid cyst gave excellent results.

**Conclusion**

This is the first report of the novel association of two brothers having autosomal-recessive inherited
Figure 4: Preoperative MRI of patient 1 showing (A) retroflexed odontoid, (B) arachnoid cyst in thoracic region, (C) spinal cord pushed anteriorly and laterally, and (D) tethered cord

Figure 5: (A) Cord atrophy. (B) Partly decompressed lumbar cord. (C) Partly decompressed thoracic cord
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respiratory chain disorder with compressive myelopathy due to AAD, arachnoid cyst, and tethered cord [Figure 8]. Awareness of this association helps in judicious use of safe drugs so that mitochondrial crisis is avoided during surgery and postoperative management.

Limitation
Genetic testing was not carried out due to financial constraint.

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.

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Figure 6: Patient 2 showing dysmorphic features without ptosis

Figure 7: MRI of patient 2 showing (A) retroflexed odontoid, (B) arachnoid cyst in dorsal cord, (C) arachnoid cyst extending along root sleeves, and (D) arachnoid cyst in lumbar region
Conflicts of interest
There are no conflicts of interest.

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