CEREBELLAR ATAXIA DUE TO ISOLATED VITAMIN E DEFICIENCY
S. JAYARAM, AAMOD SOMAN, SANJAY TARVADE, VIKRAM LONDHE

ABSTRACT
Ataxia is a common and important neurological finding in medical practice. Severe deficiency of Vitamin E can profoundly affect the central nervous system and can cause ataxia and peripheral neuropathy resembling Friedreich’s ataxia. Vitamin E deficiency can occur with abetalipoproteinemia, cholestatic liver disease or fat malabsorption. Ataxia with isolated Vit E deficiency (AVED) is an Autosomal Recessive genetic disorder with a mutation in the alpha tocopherol transfer protein gene (TTPA). This condition responds to high dose of Vit E and is one of the important causes of treatable ataxia.

We report a young patient with Ataxia with isolated Vit E deficiency (AVED) who responded partially to replacement of Vitamin E.

Key Words: Vitamin E, Ataxia, Alpha tocopherol transfer protein, Friedreich’s Ataxia, Ataxia with isolated Vitamin E deficiency

INTRODUCTION
Ataxia is a clinical neurological entity with wide range of etiological factors, very few of which are treatable. Vitamin E deficiency is one of the treatable causes of ataxia. It results in an ataxic condition similar to Friedreich’s ataxia. Early and prompt replacement of Vitamin E in such individuals can halt the progression of the disease and may at times result in complete recovery from ataxia. Though many cases of Vitamin E deficiency resulting in ataxia have been described in the western literature, reports from Indian literature could not be cited. This case underlines the significance of screening the selected patients of ataxia for Vitamin E deficiency and also points that the diagnosis of AVED should be considered in “mutation negative” Friedreich’s ataxia.

CASE REPORT
16-year-old female, came with history of imbalance while walking, ‘weakness’ in both lower limbs since 5 years and slurring of speech since 3 years. There was no history of tingling or numbness in upper or lower limbs.

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Table 5: Problems, Preventive/Corrective steps in the Phase I of the life cycle of medical equipment

<table>
<thead>
<tr>
<th>Stages</th>
<th>Problems identified</th>
<th>Preventive/Correctivesteps</th>
</tr>
</thead>
<tbody>
<tr>
<td>Purchase</td>
<td>Delay, Not as per Requirement, Irregularities</td>
<td>Ensure timely supply, Assess requirement. No diversion of funds, Follow laid down procedures</td>
</tr>
<tr>
<td></td>
<td>Inadequacy</td>
<td>Ensure adequacy of equipment</td>
</tr>
<tr>
<td></td>
<td>Defective equipment</td>
<td>Check for defects, spare parts, accessories and user manual</td>
</tr>
<tr>
<td>Inventory and</td>
<td>Absence of inventory, Palletage, Diversions</td>
<td>Timely and strict documentation, Proper storage, No diversions</td>
</tr>
<tr>
<td>documentation</td>
<td>Poor inventory, Palletage, Diversions</td>
<td>Allot adequate space, building</td>
</tr>
<tr>
<td>Installation</td>
<td>Delay: No Building, Faulty Site selection</td>
<td>Ensure power supply</td>
</tr>
<tr>
<td></td>
<td>No Electricity connection</td>
<td>availability of trained, qualified staff</td>
</tr>
<tr>
<td>Use</td>
<td>No staff</td>
<td>Availability of accessories, chemicals</td>
</tr>
<tr>
<td></td>
<td>No Accessories</td>
<td>Well framed policy and guidelines for use</td>
</tr>
<tr>
<td></td>
<td>No Framed policy</td>
<td>Ensure support services</td>
</tr>
<tr>
<td></td>
<td>No Support services</td>
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various stages of the life cycle.

REFERENCES
and no history of slipping of chappals. She had difficulty in combing hair and buttoning clothes. There was no history of exposure to heavy metals, or chronic ingestion of drugs.

She was born of second-degree consanguineous marriage but none of the family members had similar complaints.

Examination revealed averagely built and nourished female with normal vital signs. She had slurred speech, and nystagmus. Cognition was normal. Fundoscopic evaluation was normal. There was no skin, hair or skeletal system abnormality. Both the lower limbs had rigidity. Power was normal in both lower limbs as well as upper limbs but coordination was impaired. Finger nose finger and Heel knee shin test were impaired indicating Ataxia. Romberg's test revealed increased swaying on closing eyes. Her gait was ataxic. Vibration sense and Joint position sense were impaired in the lower limbs. Bilateral knee and ankle reflexes were absent while other reflexes were normal.

Her investigations revealed the following: Hemoglobin – 98 gm/L. White Blood Cell count – 6.7 X 10^9/L (N: 60%, L: 38%, E: 02%, B: 00%, M: 00%). Electrolytes, Blood Sugar, Renal Function test, and liver function tests were normal. MRI and CT Brain were normal. Thyroid function tests were normal.

Serum Vitamin E – 11 µmol/L [N: 18 – 29 µmol/L]. Serum Lipid Levels were normal: Triglycerides 1.37 mmol/L, S. Cholesterol 4.78 mmol/L, and LDL cholesterol 3.0 mmol/L. Stool fat excretion was normal. There were no gastrointestinal abnormalities. In view of this, it was concluded that our patient had isolated vitamin E deficiency. We could not do the genetic studies for Ataxia with isolated Vitamin E deficiency (AVED).

Patient was treated with Vitamin E (400 mg three times a day). Patient registered objective improvement over 2 weeks and was discharged. At the end of two months of follow up the patient had significant objective improvement in gait, upper limb ataxia, and sensory signs of the lower limb. But the investigations could not be completed due to the financial constraints.

**DISCUSSION**

Friedreich’s ataxia is one of the most common forms of Autosomal Recessive ataxia. Vitamin E deficiency can result in ataxia with clinical presentation similar to Friedreich’s ataxia – Ataxia with isolated Vitamin E deficiency (AVED).

Vitamin E is one of the most important lipid-soluble antioxidant nutrients. Cystic fibrosis, chronic cholestatic liver disease, abetalipoproteinemia, short-bowel syndrome, isolated vitamin E deficiency syndrome, and other malabsorption syndromes all may cause varying degrees of Vitamin E deficiency.

Neurologic findings in Vit E deficiency follow a pattern of progression that can be divided into early and late stages. Early findings include hyporeflexia, decreased proprioception, decreased vibratory sense, distal muscle weakness, nystagloia (night blindness), and normal cognition. With continued deficiency neurologic symptoms progress and patients can develop truncal and limb ataxia and diffuse muscle weakness. Further eye problems may develop, including limited upward-gaze nystagmus and dissociated nystagmus and rarely Retinitis pigmientosa. Late manifestations include dysphagia and dysarthria, cardiac arrhythmias, ophthalmpoplegia, and possible blindness. Cognition may be affected in later stages, and dementia can also occur.[1]

Isolated vitamin E deficiency syndrome is caused by an Autosomal Recessive genetic disorder involving chromosome arm 8q that involves a mutation in the Alpha Tocopherol Transfer Protein gene (TTPA). The mutation was first described by Ouahchi et al in 1995.[2] Ouahchi et al. reported three mutations of the TTPA gene and 744delA mutation was found in 68% of 17 families studied.[3,4] Neurologic findings develop within the first or the second decade of life but presentation as late as 4th or the 6th decade has been described.[3,4] It is difficult to clinically distinguish it from Friedreich’s Ataxia. The patients with Friedreich’s ataxia have a mutation in the frataxin gene. However, in the absence of such a mutation, Vitamin E deficiency should be considered. Thus ataxia with vitamin E deficiency may present as “mutation negative” Friedreich’s ataxia.[5]

Vitamin E replacement can influence outcomes significantly; therefore, screening for Vitamin E deficiency is beneficial for patients with Ataxia of unknown cause.

The pathological feature is central peripheral axonopathy in Friedreich’s ataxia while in ataxia with isolated vitamin E deficiency (AVED) there is slight-to-moderate axonal sensory neuropathy with normal to moderate decrease of large myelinated fiber density and important regeneration in nerve biopsy described as central distal axonopathy.[6]

In Japan, a unique mutation in the TTPA gene - His101Gln (H101Q) i.e substitution of glutamine for histidine in the protein has been described to be associated with increased incidence of Retinitis pigmentosa.[3,4] However recently the mutation of start codon of the Alpha -TTP gene has been reported to show retinitis pigmentosa.[7]

Patients with abetalipoproteinemia tend to have a predominance of eye problems, including decline in visual fields and pigmented retinopathy. The incidence of Retinitis pigmentosa is less in children with cholestatic disorders.

Replacement of Vitamin E is essential for the complete recovery of the ataxia in patients with AVED. However, late presentation results in incomplete recovery even after Vit E replacement. Recommendations for the replacement of Vitamin E are as follows:[8,9]
• Abetalipoproteinemia – 66 – 132 mg/kg/d
• Chronic cholestasis – 10 – 16 mg/kg/d
• Cystic fibrosis – 3 – 6 mg/kg/d
• Short-bowel syndrome – 132 – 2400 mg/d
• Isolated vitamin E deficiency – 533 – 2400 mg/d

This case underlines the significance of screening the selected patients of ataxia for Vitamin E deficiency as it is one of the treatable causes of Ataxia. It is recommended that all patients with ataxia of unknown cause should have vitamin E deficiency excluded. Similarly, neurologists should be aware that ataxia with vitamin E deficiency may present as “mutation negative” Friedreich’s ataxia.

REFERENCES

HYPERAMMONEMIA: AN UNUSUAL PRESENTING FEATURE OF MULTIPLE MYELOMA
A. S. SHAH, N. SHETTY, S. JAISWAL, B. C. MEHTA

ABSTRACT
A 76 year old lady presented with altered sensorium and was found to have hyperammonemia on evaluation. She had no evidence of liver disease. For her symptomatology of backache, evaluation by bone marrow study showed evidence of multiple myeloma. She was given chemotherapy for multiple myeloma, which resulted in improvement in her sensorium, along with this there was also a rapid decline in serum ammonia levels. Hyperviscosity and hypercalcemia are common causes of altered sensorium in a patient with myeloma but in this case hyperammonemia was the likely cause.

Key Words: Hypercalcemia, hyperviscosity, sensorium

INTRODUCTION
Hyperammonemia is commonly seen in liver disease, Reye’s syndrome, inborn errors of urea synthesis, severe urinary tract infections and induced by medications like valproate.[1] We had a patient who presented with disturbance of consciousness and flapping tremors. She was diagnosed to have hyperammonemia and multiple myeloma and there was a dramatic improvement in sensorium on treating her for myeloma with chemotherapy which paralleled the rapid decline in serum ammonia levels.

CASE REPORT
A 76 year old lady was admitted with fever and altered sensorium gradually worsening over past 3 weeks. A day prior to admission she had a fall and was unable to move right leg. She had backache since past 8 months for which she was evaluated by an orthopedic surgeon. MRI of the dorso-lumbar spine done at that time showed compression fracture of the second lumbar vertebra, degenerative changes at multiple levels and bone marrow edema. She was advised bed rest and treated with analgesics and Taylor’s brace. There was only partial relief with these measures. About 3 months back she was evaluated for generalized weakness, persistent backache, difficulty in walking, loss of appetite and intermittent irrelevant talks. Her investigations at that time were: hemoglobin 8.3 g/dL, white cell count 6800/cmm, platelet count 110, 000/