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ATAXIA DUE TO VITAMIN E DEFICIENCY: TWO CASE REPORTS AND A MINI-REVIEW

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Abstract

The spectrum of hereditary ataxias includes various etiologies, among which isolated vitamin E deficiency stands out as a specific and treatable cause in children. This article presents a case report and a mini-review of ataxia due to isolated vitamin E deficiency, detailing the clinical and biological features observed in two siblings.

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1. Introduction :

Hereditary ataxia encompasses a wide range of neurological disorders characterized by the degeneration of the cerebellum and its associated pathways, leading to impaired coordination and balance.
Among these various forms, ataxia due to isolated vitamin E deficiency is particularly noteworthy as it represents a specific, identifiable, and treatable cause of ataxia in pediatric patients : Vitamin E plays a crucial role in maintaining neuronal integrity and function due to its antioxidant properties, which protect cell membranes from oxidative stress. Such deficiency of this vital nutrient can result in significant neurological impairments, particularly affecting motor coordination [1,2].

This article provides a concise case report alongside a review of particular genetic disorder.

2. Cases Presentation :

A 5-year-old girl presented with progressive ataxia and dysarthria, accompanied by diffuse hyporeflexia/areflexia for the past 12 months. Her somatic and neurological examinations were otherwise normal, except for these symptoms. Her 2-year-old brother exhibited right lateral hyporeflexia, with their mother reporting several spontaneous falls. Genetic testing for the frataxin gene returned negative, while serum vitamin E levels were significantly diminished, even unmeasurable according to laboratory reference ranges.

Both siblings were diagnosed with ataxia due to vitamin E deficiency. They commenced treatment with 1000 mg/day of liposoluble vitamin E capsules, resulting in remarkable improvement within three months, particularly in their tendon reflexes. Genetic testing for the tocopherol transfer protein (TTPA) gene could not be performed.

3. Discussions:

The broad array of hereditary ataxias encompasses various causes, including autosomal recessive types. Only a few etiologies benefit from dietary or biochemical therapies, such as cerebrotendinous xanthomatosis, Refsum disease, abetalipoproteinemia, Niemann-Pick C disease, coenzyme Q10 deficiency, and ataxia with vitamin E deficiency (AVED) [1,2].

AVED is very peculiar: it typically manifests in late childhood or early adolescence with symptoms such as dysarthria, poor balance (especially in low-light conditions), and progressive clumsiness. Although phenotypically similar to Friedreich's ataxia, AVED is more commonly associated with head titubation or dystonia and less frequently with cardiomyopathy [1,3].

Our 2 siblings had early manifestations that might be related to a profound gentic imprint. Intersestingly, the clinical phenotype of AVED displays significant variability in severity among siblings while maintaining a relatively uniform course within the same family [4].

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Genetically, AVED is caused by mutations in the TTPA gene located on chromosome 8q13. This protein binds alpha-tocopherol (a form of vitamin E) and very-low-density lipoproteins (VLDLs) in the liver. Mutations in TTPA hinder the incorporation of vitamin E into VLDLs, preventing its distribution into systemic circulation [5].

Epidemiologically, most reported cases have originated from the Mediterranean region, with the 744delA mutation being most prevalent among 22 known variants associated with early-onset forms of AVED [6].

In practice, every child presenting with ataxia should be screened for AVED to facilitate early diagnosis and prompt initiation of vitamin E treatment to prevent neurological impairment [7].

Diagnosis is confirmed through a simple blood test revealing normal lipid levels but significantly low vitamin E concentrations while excluding Friedreich's ataxia as a differential diagnosis [8].

The table 1 provides a comprehensive comparison between AVED and Friedreich Ataxia, outlining their distinct clinical features, genetic backgrounds, and treatment approaches. Understanding these differences is crucial for accurate diagnosis and management in clinical practice.

Table 1 : Comparative table of AVED and Friedreich Ataxia

Feature	Ataxia with Vitamin E Deficiency (AVED)	Friedreich Ataxia
Etiology	Caused by mutations in the TTPA gene (tocopherol transfer protein) leading to vitamin E deficiency.	Caused by GAA repeat expansions in the FXN gene, leading to frataxin deficiency
Inheritance Pattern	Autosomal recessive	Autosomal recessive
Onset of Symptoms	Late childhood to early adolescence	Typically between ages 5 and 15
Clinical Symptoms	Dysarthria, ataxia, poor balance (especially in low light), progressive clumsiness, head titubation, dystonia	Gait and limb ataxia, dysarthria, loss of deep tendon reflexes, scoliosis, diabetes mellitus, and hypertrophic cardiomyopathy.
Neurological Findings	Hyporeflexia/areflexia; cerebellar signs predominant	Loss of proprioception and vibratory sense; sensory ataxia; lower limb weakness.
Cardiomyopathy	Rarely associated	Commonly associated with hypertrophic cardiomyopathy
Genetic Testing	Negative frataxin gene sequencing; TTPA gene testing may confirm diagnosis	Genetic testing for FXN gene mutations confirms diagnosis.
Biochemical Findings	Low serum vitamin E levels with normal lipid levels	Normal vitamin levels; abnormal frataxin levels not typically assessed.
Treatment	High-dose vitamin E supplementation (800-1500 mg/day); regular monitoring of vitamin E levels	Supportive care; no specific treatment to reverse disease progression; physical therapy and management of complications.
Prognosis	Generally good with treatment; symptoms can improve significantly with vitamin E supplementation.	Progressive decline in motor function; life expectancy may be reduced due to complications.
Geographic Prevalence	More frequently reported in Mediterranean populations	More common in individuals of European descent; worldwide distribution.

Treatment involves continuous daily supplementation of vitamin E at doses ranging from 800 to 1500 mg/day. During supplementation, plasma vitamin E levels should be monitored regularly (e.g., every six months) to maintain them within the high-normal range [9].

Acquired non-constitutional vitamin E deficiency may occur in children with chronic diseases that impair fat-soluble vitamin absorption, including cystic fibrosis, inflammatory bowel diseases, celiac disease, cholestatic liver disease, or short bowel syndrome [10-13]. Symptoms may be similar; however, supplementation doses are typically lower than those prescribed for AVED [14].

4. Conclusion

Recognizing Ataxia with Vitamin E Deficiency (AVED) is crucial for any child presenting with ataxia, as this condition is a specific and treatable cause of neurological impairment, particularly prevalent in Mediterranean populations.
Early identification through vitamin E level screening facilitates timely intervention, significantly improving patient outcomes.
Additionally, distinguishing AVED from other hereditary ataxias, such as Friedreich's ataxia, is vital for appropriate care, with genetic testing playing a key role in confirming the diagnosis

Declaration of interests

The authors have nothing to disclose.

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