A rare cause of peripheral neuropathy masquerading as periodic paralysis in a young child: A case report

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INTRODUCTION

Peripheral nervous system dysfunction complicates various systemic diseases, commonly seen in the adult population than children.The prevalence of peripheral neuropathies in children from resource-poor countries is not known.[1]

Children are exposed to multiple types of systemic dysfunction, including inflammation, secondary infections and toxins which impact the peripheral nervous system.

Systemic involvement may be the presenting feature of an underlying neuropathy which may not be detected unless screened for by targeted examination and neurophysiological studies.

Children who have an acute presentation with peripheral neuropathy should be assessed for AIDP, critical illness polyneuropathy, toxin exposure, diphtheria, postvaccination neuropathy, acute porphyria and tyrosinemia.[2]

CASE DESCRIPTION

A 2.5-year-old developmentally normal female child born out of non consanguineous marriage, completely immunized and well built for age presented with recurrent episodes of progressive, ascending weakness involving both appendicular and axial systems.

These episodes were not characterized by severe respiratory muscle involvement.

Examination revealed hypotonia, hyporeflexia and absent Babinski reflex. Autonomic signs were noted in subsequent episodes.

No history of similar neurological illness in family

No neuropathic crises episodes have occurred after initiation of NTBC therapy with improvement in foot drop noted subsequently.

Fig 1: Timeline depicting clinical course

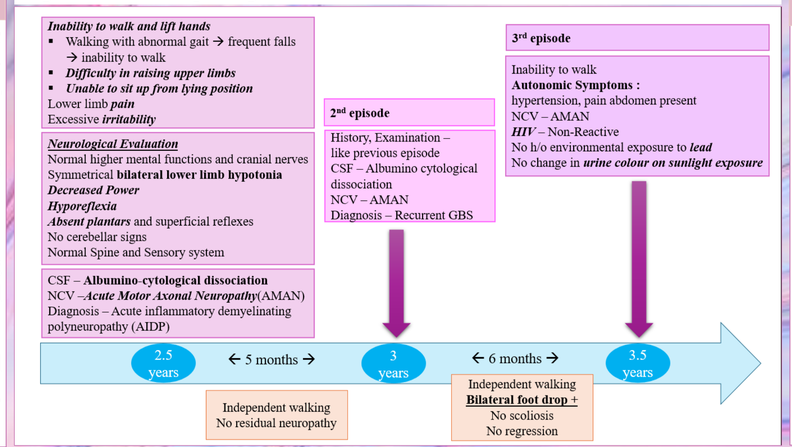


Fig 2: Episode based diagnostic and therapeutic flowchart

SUCCINYLACETONE (URINE)
Method - GC - MS

Compound	Result	Ref. Range in %	Elevation Factor
Succinylacetone	117.94	0	117.94
4-Hydroxyphenyllactic Acid	2448.00	1.8	1360.00
4-Hydroxyphenylpyruvic Acid	0	0.2	0
N-Acetyltyrosine	0	0	0

Impression:- Organic acid profile suggestive of Tyrosinemia Type-1

WHOLE EXOME SEQUENCING

CLINICAL INDICATIONS

Clinical suspicion: Chronic Axonal neuropathy/ polyneuropathy
Family history : Not significant

RESULTS AND INTERPRETATION

HOMOZYGOUS PATHOGENIC VARIANT DETECTED IN THE *FAH* GENE

HETEROZYGOUS VARIANT OF UNCERTAIN SIGNIFICANCE DETECTED IN THE *MFN2* GENE

PROBABLE COMPOUND HETEROZYGOUS VARIANTS OF UNCERTAIN SIGNIFICANCE DETECTED IN THE *FIG4* GENE

CLINICAL CORRELATION RECOMMENDED

KEY FINDINGS

Gene [Transcript]	Exon/Intron	Variant	Zygosity	Disease	Inheritance	Clinical Significance
FAH (NM_000137.4)	Exon 9	c.709C>T p.Arg237Ter	Homozygous	Tyrosinemia, type 1	Autosomal recessive	Pathogenic

DISCUSSION

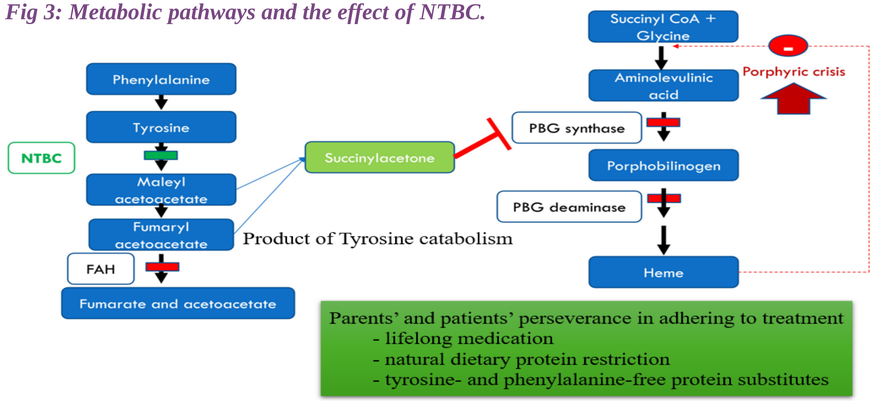
Illustrate the complexity and presentation of peripheral neuropathy and the challenges encountered in elucidating its etiology → emphasizing the need for clinicians to be aware of this life threatening but preventable and treatable neurologic crises associated with Tyrosinemia Type 1.

Diverse clinical presentation - Diarrhoea, vomiting, jaundice, liver failure, kidney failure, neurological crisis, rickets, failure to thrive, and hepatocellular carcinoma.[3]

Spectrum of neurological status – Normal / PNS (peripheral axons involvement with secondary demyelination) / CNS (neuronal/synaptic dysfunction → low IQ, cognitive decline, attention deficits, memory and processing problems, and psychomotor and behavioural impairment.[3]

Neuropathic crises - Seizures, confusion, painful paraesthesia, autonomic signs, hyponatremia, self-mutilation, respiratory muscle and/or progressive ascending paralysis and death.[4] No available biochemical marker available for the diagnosis or severity correlation → clinical diagnosis and management

Fig 3: Metabolic pathways and the effect of NTBC.



CONCLUSION

- Underscore the significance of recognizing Hereditary Tyrosinemia I as a crucial and treatable condition with a diverse clinical presentation
- include tyrosinemia in the differential diagnosis for children with recurrent peripheral neuropathy, as signs of liver disease and renal tubular dysfunction might be inconspicuous.
- The neurogenic crises in tyrosinemia shares a physiological basis akin to those observed in porphyria and lead poisoning, thereby presenting with similar clinical manifestations.
- Acute exacerbations of neurogenic crises in tyrosinemia can pose life-threatening risks; however, specific treatment modalities (Nitisinone/NTBC) are available, highlighting the importance of early detection and intervention.

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