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Childhood mitochondrial neuropathies: Clinical, electrophysiological and histopathological characteristics

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While mitochondrial diseases in children are often associated and occasionally present with peripheral neuropathies, their presence is under-recognised because of the overwhelming central nervous system involvement. The availability of rehabilitative measures and increasingly, disease modifying or curative therapy, increases the need for early diagnosis and the specification of the nature of the peripheral neuropathy may aid this effort. We describe the clinical, electrophysiological and histopathological characteristics of 11 children with peripheral neuropathy associated with mitochondrial disease due to identified mutations of the nuclear genome (*POLG*-4, *SURF1*-3, *MVP17*-1) or respiratory chain defects ($n = 4$). In patients with *POLG* mutations the neuropathy was clinically evident only in the second decade, between 10 and 16 years age, caused mild disability. Nerve conduction studies, in addition to the prominent sensory involvement also reported in adults, showed significant slowing of motor conduction velocity, which was seen in one patient as early as 18 days of age. In contrast, neuropathy associated with *SURF1* mutations had an early onset (10–18 months of age), and often presented with a sensory ataxia. These children had foot drop, prominent distal weakness and progressive distal contractures. Nerve conduction studies showed low amplitude or absent sensory potentials and slowed motor conduction velocities. The neuropathies associated with mitochondrial disease are heterogeneous in their clinical, electrophysiological and histopathological characteristics and their accurate characterization may help identification of the underlying syndrome.

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Baseline neurologic function in symptomatic patients in the Transthyretin Amyloidosis Outcomes Survey (THAOS)

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To describe baseline neurologic function of symptomatic patients in an international registry for transthyretin amyloidosis (ATTR). The Transthyretin Amyloidosis Outcomes Survey (THAOS) characterizes the natural history of ATTR, regional differences in disease expression, and genotypic-phenotypic relationships. Eligible patients have confirmed genotyped TTR mutations with or without symptomatic disease, or wild-type ATTR. Recommended minimal neurologic evaluations include pinprick, touch, and vibration of the great toe; ankle and patellar reflexes; muscle strength of toes and ankles. Data are shown for symptomatic patients with five sensory assessments (pinprick, cold, touch, vibration and position sense) performed up to the thigh. Of 592 patients enrolled (38 sites/17 countries), data are available for 364 symptomatic patients with TTR mutations (median age 47 years [range 21–89], 75% Caucasian, 73% V30M). Most (82%) had sensory symptoms, mainly neuropathic pain/paresthesia (64%), numbness (56%), temperature/pain insensitivity (49%) and tingling (49%). In patients with all sensory assessments ($n = 99$), more had decreased/absent small fiber function (pinprick–toe: 85%, mid-foot: 76%, mid-calf: 48%, knee: 38%, thigh: 23%; cold–toe: 88%, mid-foot: 83%, mid-calf: 68%, knee: 50%, thigh: 31%) than impairments of large fiber function (vibration–toe: 73%, ankle: 44%, knee: 34%, hip: 20%; position sense–toe: 28%, ankle: 21%; touch–toe: 72%, mid-foot: 65%, mid-calf: 36%, knee: 25%, thigh: 16%). Results confirm the prevalence of small fiber symptoms. Sensory dysfunction and muscle strength (not shown) demonstrated a distal to proximal pattern. In symptomatic patients enrolled in THAOS, sensory small fiber impairment is more common than large fiber impairment, with distal abnormalities more common than proximal.

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Pediatric chronic inflammatory demyelinantig polyneuropathy and reversible posterior leukoencephalopathy – case report

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Chronic inflammatory demyelinanting polyneuropathy (CIDP) is a rare condition in the pediatric population, with an estimated prevalence of 0.48 per 100.000 children. Available data comes from small pediatric series and extrapolation from adult. There is a male preponderance, as in adults, and clinical subacute onset of weakness is more frequently described, but there are also descriptions of initial presentation mimicking Guillain-Barré syndrome. There is only one case reported with central nervous system involvement. We present a case of CIDP with Reversible Posterior Leukoencephalopathy. Six year old boy was admitted to Hospital with 48 h of prostration, headache and anorexia. Brain computed tomography scan and liquor analysis were unremarkable. He was kept under observation. In the following 48 h he developed ascending muscular weakness, with respiratory muscles involvement, requiring assisted ventilation. He also presented high blood pressure, coetaneous flushing and bradycardia. At neurologic examination a tetraparesis with reflexes abolition was evident. Lombar tap was repeated reveling albuminic-citologic dissociation. Brain magnetic resonance imaging (MRI) was performed showing lesions sugestive of reversible posterior encephalopathy. Neurophysiologic study was according to acquired demyelinanting polyneuropathy. Therapy with corticosteroids and Intravenous immunoglobulin was started with good clinical evolution. Brain MRI was repeated with complete resolution of the lesions. By the 7th week there was a discrete clinical relapse. At four months of follow up he presents independent gait with discrete ataxia. We describe a patient that full fields criteria for CIDP with an atypical presentation, with central nervous system involvement. Clinical suspicion and recognition of this disease is needed when observing children with muscular weakness.

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