NEUROLOGIST **SPECIALIST GUIDE**

The neurological impact of Hunter syndrome varies widely across the disease spectrum.[1] By definition, patients with the severe phenotype have profound central nervous system (CNS) involvement and patients with the attenuated phenotype exhibit little neurological involvement.[1]

Evaluation

Neurological involvement is initially suspected by globally delayed developmental milestones (e.g. the ability to sit unsupported, to walk, and to speak).[2] Cognitive status should be evaluated with neurodevelopmental assessments rather than through CNS morphology and physiology, as structural abnormalities are not well-correlated with cognitive impairment in MPS II patients.[1] It is necessary to evaluate multiple domains of function with age-appropriate instruments and to repeat testing at yearly intervals.[1]

Management of Clinical Consequences

Depending on the disease severity, neurological manifestations may include developmental delay, cognitive impairment, behavioral problems, seizures, spinal cord compression, carpal tunnel syndrome (CTS), and communicating hydrocephalus.[3]

Behavioral problems in MPS II can include hyperactivity, obstinacy, and aggression; these problems appear to be limited to patients with the severe phenotype.[1] Behavioral problems typically begin in the second year of life and continue until age 8 or 9 when neurodegeneration limits this behavior.[1] Behavioral therapy or the use of behavior-modifying medical therapy can be used for behavioral problems, although both are generally not very successful.[1,3]

Seizures are reported to occur in more than half of MPS II patients with the severe phenotype before they reach the age of 10 years.[2] Parents may not initially recognize seizures, as absence seizures, which are common in MPS II, are characterized by "staring" episodes.[1] Absence seizures may not require medication, whereas generalized tonic–clonic seizures can normally be controlled with anticonvulsant therapy.[1] Progressive compression of the spinal cord can lead to reduced activity, paresis and spasticity, abnormal gait, muscle weakness, clumsiness with fine motor skills, pain or loss of sensation in the upper and lower body, and bladder and bowel dysfunction.[1,3]

Screening MPS II patients for clinical and radiological evidence of **spinal cord compression** may be useful, because if left untreated cord compression can lead to irreversible neurological dysfunction.[1] Decompression surgery should be considered as soon as symptoms of cord compression occur.[3]

CTS is commonly seen in MPS II patients aged 5–10.[1] Standard electrophysiological testing will identify median nerve compression before symptoms appear. MPS II patients can be screened for CTS by initiating testing in patients aged 4–5 and repeating at 1–2-year intervals.[1] For CTS, decompression of the median nerve should be considered in patients with loss of hand sensation, hand function, or abnormal conduction studies.[3]

Signs of hydrocephalus can include **behavioral changes, headache, and vision disturbances**.[1] Communicating hydrocephalus or evidence of progressive ventricular enlargement can be treated with the placement of a ventriculoperitoneal shunt in order to relieve intracranial pressure.[3]

1. Muenzer J *et al. Pediatrics 2009*; 124(6): e1228–1239. 2. Martin R *et al. Pediatrics 2008*; 121(2): e377-386. 3. Scarpa M *et al. Orphanet J Rare Dis 2011*; 6(72): 1–18.

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