Hereditary Motor and Sensory Neuropathies

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The hereditary motor neuropathies comprise a heterogeneous group which, apart from the inherited recurrent focal neuropathies, is characterized by its symmetrical nature, insidious onset, and slow progression. Until the primary genetic and biochemical bases of these disorders are known, they will remain classified according to clinical, genetic, and pathologic features (Table 1). There also exists a rare group of neuropathies characterized by selective involvement of peripheral sensory and autonomic neurons (Table 2). These disorders, which are usually autosomal recessive, are manifest by varying degrees of autonomic dysfunction or insensitivity to pain and temperature, occasionally with striking self-mutilation. The spinal muscular atrophies and those diseases which clinically involve different parts of the nervous system, such as Refsum’s disease, the leukodystrophies, and Friedreich’s ataxia, will not be considered here.

Congenital disorders have their onset in the neonatal period or early infancy; affected infants are weak, hypotonic, and areflexic.

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**Table 1**

**Some Hereditary Motor Neuropathies**

<table>
<thead>
<tr>
<th>Hereditary Motor and Sensory Neuropathy (HMSN)</th>
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<tbody>
<tr>
<td>HMSN Type I (Charcot-Marie-Tooth)</td>
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<tr>
<td>Autosomal dominant hypertrophic neuropathy</td>
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<tr>
<td>HMSN Type II</td>
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<tr>
<td>Neuronal type of Charcot-Marie-Tooth</td>
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<tr>
<td>HMSN Type III (Dejerine-Sottas)</td>
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<tr>
<td>Autosomal recessive hypertrophic neuropathy</td>
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<tr>
<td>Inherited Recurrent Focal Neuropathy</td>
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<td>Inherited brachial plexus neuropathy</td>
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<tr>
<td>Hereditary neuropathy with liability to pressure palsies</td>
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</tbody>
</table>

continued from page 428

biopsy shows partial hypomyelination with atypical onion-bulb formation. Some of the latter group may represent early presentations of the hypertrophic form of Charcot-Marie-Tooth or Dejerine-Sottas disease or be due to decreased myelin production by abnormal Schwann’s cells.

**HEREDITARY MOTOR AND SENSORY NEUROPATHY (HMSN)**

**HMSN Type I (Hypertrophic Form of Charcot-Marie-Tooth Disease)**

This autosomal dominant disorder shows great variability in clinical expression. Presentation is usually in late childhood but may present earlier. Conversely, some individuals remain asymptomatic well into adulthood; diagnosis in these individuals can be established only by nerve conduction studies. In symptomatic children, initial signs consist of motor delay and clumsy gait. Weakness begins in the distal leg muscles, particularly the intrinsic foot muscles, the peroneal and the anterior tibial muscles, which leads to pes cavus, hammer toes, and foot drop. Muscle wasting occurs in a distal distribution. Progression is slow and only after many years do the distal upper limbs become involved. Some individuals eventually show wasting and clawing of the hands and palpable superficial nerves of the head and neck. Sensory changes are usually slight. Postural tremor and ataxia are frequent.
features. Diminution of the Achilles tendon reflexes is usual, but decreased deep tendon reflexes at other sites are variable. Diagnosis is suspected from the clinical picture and confirmed by the presence of slow motor nerve conduction velocities (<50% of normal) in the patient and one parent. Elevated cerebrospinal fluid protein is characteristic of older patients. Sural nerve biopsy shows onion-bulb formation which increases with age.

HMSN Type II (Neuronal Form of Charcot-Marie-Tooth Disease)

This disorder is also autosomal dominant. An autosomal recessive type with early onset has also been described. The clinical features are similar to HMSN type I but are milder and deformity, if it occurs, does so later. Slow progression and variable distal sensory loss are features. Motor nerve conduction velocities are usually normal or only slightly decreased but occasionally are difficult to obtain, particularly in the lower extremities.

HMSN Type III (Dejerine-Sottas Disease)

This is an autosomal recessive or sporadic disorder, which characteristically presents in early childhood with hypotonia, weakness, and delayed motor milestones. As in HMSN type I, the lower extremities are predominantly affected and eventually show distal wasting. Lower facial weakness also occurs and leads to a characteristic facial affect with prominent pouting lips (lèvres de tapir). The greater auricular and cervical nerves are usually palpable. Ataxia is a prominent feature and may be more disabling than the decreased muscle power. Sensory loss can be found, particularly involving vibration and position sense and, to a lesser degree, touch and superficial pain sensation. Loss of deep tendon reflexes is more likely than in HMSN type I, and motor nerve conduction velocities are extremely slow. Findings on sural nerve biopsy are similar to but more marked than those seen in HMSN type I.

INHERITED RECURRENT FOCAL NEUROPATHY

As opposed to the hereditary motor and sensory neuropathies—which produce symmetrical weakness, are of insidious onset, and are slowly progressive—these disorders are focal in distribution and acute in onset. They may be recurrent with variable degrees of resolution.

Inherited Brachial Plexus Neuropathy

Although onset is usually in the second or third decade, this autosomal dominant disorder may occur in late childhood. Weakness is preceded by upper extremity pain of one-week duration. Characteristically, the limb is immobile as shoulder movement exacerbates the pain. Pain may mask the muscle weakness which appears after a few days and progresses thereafter. The weakness can be present for weeks to months and sometimes affects all of the brachial plexus innervated muscles, although there is a predilection for the proximal groups. The lumbosacral plexus and cranial nerves can be involved but not at the same time as the upper extremity. Recovery is slow but usually complete. However, some motor deficit can remain after repeated episodes. Precipitating factors have been described, including exercise, pregnancy, and delivery.

Hereditary Neuropathy with Liability to Pressure Palsies (Tomaculous Neuropathy)

This is an autosomal dominant disorder which is characterized by recurrent painless focal neuropathies. The neuropathies are often associated with relatively minor episodes of trauma or compression, such as sleeping on a limb, and the associated weakness can last for weeks. Nerves most likely to be compressed include the radial, ulnar, and peroneal nerves. Although asymptomatic, careful examination may reveal signs of a more diffuse peripheral neuropathy, particularly in older patients. On nerve conduction study, generalized, moderate slowing of the nerve conduction velocities is found along with a reduction and dispersion of the action potential amplitude. Sural nerve biopsy shows focal thickening (tomaculous) of the myelin sheath.

REFERENCES