Disorders of the spinal cord can pose diagnostic and therapeutic challenges. The advent of new diagnostic tools such as magnetic resonance imaging (MRI) have improved diagnostic accuracy. Spinal imaging is essential in suspected spinal cord disease, as compressive lesions must be detected, and surgical intervention effected where appropriate. Imaging also enables accurate identification and localisation of non-compressive lesions.

The term ‘non-compressive myelopathy’ encompasses a diverse group of diseases, traditionally lumped together under a single label to establish the distinction from compressive cord lesions that may need surgical relief. Many infective (for example viral, tuberculosis, syphilis, tropical spastic paraparesis), inflammatory (post-viral, vasculitic), vascular (infarction), demyelinating (multiple sclerosis), degenerative (motor neurone disease) and metabolic (vitamin B12 deficiency) disorders are included under this generic term. It carries a risk of being a dustbin diagnosis, as a sense of therapeutic nihilism may preclude further investigation. A diligent search to establish the underlying cause is vital, as many are eminently treatable, and supportive care, prognostication and counselling are needed even where specific treatment is not available.

Hereditary spastic paraparesis (HSP, Strümpell-Lorrain syndrome) is one such disorder. Initial case descriptions by Seeligmüller, Strümpell and Lorrain in the late 19th century led to the recognition of HSP as a distinct clinical entity among the ‘heredo-familial neuro-degenerative disorders’. Meticulous study of affected kindreds [1–3] has helped define the clinical features, the different types, and the patterns of inheritance.

Progressive spasticity of the lower limbs, as the name implies, is the clinical hallmark of HSP. Upper limb involvement is usually minimal, compared to severe spasticity of the legs. Weakness is usually mild, and difficulty in walking and the characteristic gait disturbance, sometimes leading to severe disability, are caused by spasticity. Hyper-reflexia and extensor plantar responses are cardinal features, and mild ataxia, pes cavus, loss of ankle jerks, mild sensory impairment and sphincter involvement are sometimes noted. Cranial nerve involvement and corticobulbar tract involvement are not seen [4,5].

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The main clinical features can be explained by the pathological changes in HSP. Axonal degeneration of the corticospinal tracts (producing spasticity), posterior columns (sensory impairment, absent ankle jerks) and spinocerebellar tracts (ataxia) are the main pathological findings. This degeneration is a dying-back process starting in the terminal portions of the longest tracts in the spinal cord, thereby explaining the predominant lower
limb involvement. Dorsal roots and ganglia, peripheral nerves and anterior horn cells are usually not involved [5, 6].

Over the years, many other neurological and non-neurological findings have been noted in association with HSP. This has led to the classification of HSP into ‘pure’ and ‘complicated’ HSP, depending on their absence or presence. These include optic atrophy, pigmented retinopathy, dysarthria, amyotrophy, extrapyramidal disturbance, peripheral neuropathy, dementia, mental retardation, epilepsy, deafness, adrenal insufficiency and ichthyosis [4,5].

Inheritance of HSP can be autosomal dominant, recessive, or X-linked. Autosomal dominant HSP is the commonest, accounting for over 80% of cases [4,5,7]. Pure and complicated forms are seen with all modes of inheritance [4,5]. Age of onset can vary from infancy to the eighth decade, and seems to have an impact on the disease course and severity [3]. Early onset HSP (<35 years, type I) is relatively benign with slow progression, and many patients are asymptomatic, and have only spasticity on examination. Late onset HSP (>35 years, type II) is associated with more sensory symptoms, more sphincter involvement, more severe disability, and a more rapidly progressive disease course [3,5].

There is marked variation in the age of onset, clinical manifestations, disease severity and the clinical course between affected families, and even between members of the same family. This inter-familial and intra-familial clinical heterogeneity is seen in both pure and complicated forms, and irrespective of the age of onset and mode of inheritance [5,8].

In the September issue of the journal, Beligaswatte and colleagues [9] described a patient with complicated HSP that may well add to the clinical range of HSP. Although lack of electromyographic findings and pathological confirmation on nerve biopsy are limitations, their description of a demyelinating neuropathy further widens the variety of neurological features associated with HSP. Impairment of vibration and joint position sense and loss of ankle jerks are seen in pure HSP, but these are considered to be due to pathology of the posterior columns, rather than peripheral nerve involvement. Nerve conduction studies are usually normal in pure HSP [5,8]. Neuropathy is a well-recognised association in complicated HSP, but is commonly asymptomatic, usually sensory, and is largely limited to descriptions of axonal degeneration [4,5,10]. Distal sensorimotor neuropathy and mixed demyelinating-axonal changes on neurophysiological studies have been occasionally reported with complicated HSP [11,12].

The genetic basis of HSP is being slowly unravelled, and the associated chromosome loci are being discovered on a regular basis. The current classification of HSP is based on chromosome location (SPG 1 to SPG 27, SPG = spastic paraplegia gene). Several candidate genes and the proteins coded for by them have been identified (e.g., SPG4– spastin, SPG17 – paraplegin, SPG3A– atlastin, SPG1– L1 cell adhesion molecule, SPG2– proteolipid protein, SPG20– Troyer syndrome–spartin) [4,5,7,13,14]. Many more are certain to be discovered.

The clinical heterogeneity in HSP is probably explained by the genetic heterogeneity. Autosomal dominant HSP, for example, is produced by changes in 10 different genetic loci (out of those discovered to date). Even within the same locus, inter-familial and intra-familial clinical variation is seen [5,13]. This may be due to different mutations occurring in the same locus, and a single mutation may produce a clinically homogeneous entity.

Molecular genetics may hold the key to precise diagnosis, including prenatal diagnosis, classification and treatment of HSP in the near future. Until such time, much can be done with symptomatic treatment, physical therapy, and appropriate counselling to minimise the disability and to relieve
the psychosocial problems associated with the diagnosis of a hereditary and degenerative disorder.

References


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**Disorders of appetite and eating**

*Appetite disorders are common in most fields of medicine and take a heavy toll on the health care system*

**Regulation of appetite**

Appetite is defined as an instinctive physical desire for food or drink, which is often felt as hunger, and serves to ensure adequate energy intake to maintain metabolism. Recent advances in physiological, biochemical, genetic and behavioural sciences have helped towards a better understanding of multiple inter-related factors concerned in the regulation of appetite and its abnormalities. As a result, the long established view that food intake is tightly controlled by hypothalamic centres is now replaced by the concept that appetite and eating are regulated by a complex, integrated network of neural and chemical signals [1]. Neural signals relaying on the hypothalamic nuclei are received from cortical, brainstem and limbic areas of the brain, and also from the oro-pharyngeal region, other parts of the gastrointestinal system and adipose tissue [2]. The mediators of these signals are both neurochemical and hormonal. They act from peripheral and central sites [1]. The central mediators are the orexigenic neuropeptides such as neuropeptide Y (NPY), Agouti related peptide (AGRP) and orexins, and the anorexigenic neuropeptides, melanocortins and cocaine and amphetamine related peptide (CART) [1]. The identified peripheral mediators include cholecystokinin (CCK), peptide YY, ghrelin, leptin and insulin. Additionally, appetite is further influenced by behaviours learnt through positive and negative conditioning to taste, which determine the choice of food [3]. For example, the