Multiple Sclerosis

Definition of Disease

A chronic inflammatory disease involving degeneration of central nervous system (CNS) myelin, scarring/formation of plaques, and loss of axons is present (Mccance et al., 2014). 0.1% of the population affected, 2.1 million worldwide, higher in whites, and the etiology is unknown (Mccance et al., 2014). MS is the most prevalent CNS demyelinating disorder (Mccance et al., 2014).

Pathphysiology

MS is described as occurring when a previous infectious insult to the nervous system has occurred in a genetically susceptible individual with an abnormal CNS immune (Mccance et al., 2014). Auto-reactive T and B cells recognize myelin autoantigens and trigger inflammation in the CNS, leading to irreversible tissue damage: ogliodendrocyte injury, demyelination, and axonal degeneration (Mccance et al., 2014). MS degeneration process begins early and continues to progress throughout life.

Immunopathology

Derived from the experimental autoimmune encephalomyelitis animal model (EAE) (Constantinescu et al., 2011). Following environmental triggers and genetic susceptibility, activation of myelin specific auto-reactive CD 4+ and CD8+ T cells cross blood-brain barrier and enter the CNS and attack myelin (Mccance et al., 2014). Process is driven by the expression of cell surface integrins (VLA-4) on inflammatory cells that mediate their binding to the vascular cell adhesion molecule (VCAM-1) expressed on endothelial cells(Gold et al., 2011). VCAM-1 expression is induced by TNF-α and in IFN-γ during inflammation. Matrix metalloproteases (MMPS) are released by the Tcells to facilitate passage through the extracellular matrix(Gold et al., 2011).

After entry into the CNS, T cells are reactivated on encountering CNS-related auto-antigentic peptides within class 2 molecules of the MHC expressed by antigen/dendritic cells(Gold et al., 2011). Production of IL-17 by Th17 cells play an important role within this process (Mccance et al., 2011). Myelin disruption occurs, leading to additional inflammation and activation of complement and specific B lymphocytes to site of tissue injury(Gold et al., 2011). As the inflammatory changes in the CNS increase, loss of brain volume progresses. Demyelination disrupts Na+, Ca++, and K+ ion channels: calcium influx is proinflammatory and neurotoxic(Mccance et al., 2014). The immune cells also produce glutamate, a neurotoxin (Mccance et al., 2014).

Genetics

Not inherited in a Mendelian fashion, first degree relatives have a 1-5 times increased risk of MS, while the concordance rate in monozygotic twins is 35% (Gold & Wolinsky, 2011).

HLA

A genetic link exist in the human leukocyte antigen (HLA) complex: a large cluster of genes responsible for many immune functions (Mccance et al., 2014). Patients carrying the class 2 major histocompitability complex (MHC) HLA-DR2 genes are susceptible to MS (Gold et al., 2011). Several risk loci beyond the MHC have been identified, including the interleukin-7 (IL-7) receptor, interleukin-2 receptor alpha chain (IL2RA) and CD58 (Gold et al., 2011).

Epidemiology

The cause of MS is unknown, however, along with several genetic polymorphisms involved, Vitamin D deficiency, cigarette smoking, and viral infections are know to be associated with MS.

Viral infections Strong correlation that suggests influenza A and Epstein Barr Virus (EBV) viral infections are associated with a high occurrence of exacerbation in MS patients (Oikonen et al., 2011). Also, studies have correlated an association of varicella zoster virus with MS (Kang et al., 2011)

Geographic Factors MS is relatively common in Europe, U.S., Canada, New Zealand (Wingerchuk, 2011). However, rare in tropical regions: this geographical distribution of MS supports an association between latitude and regional disease prevalence (Wingerchuk, 2011).

Sunlight/Vit. D Correlates or contributes to the latitude gradient of MS prevalence (Wingerchuck, 2011). Most people with established MS have relatively low Vitamin D levels and the level appears to decline over time (Wingerchuk, 2011).

Disease described/classifications

Along with the signs & symptoms listed below, the major classifications/descriptions of MS are based on the disease pattern: relapsing-remitting, primary progressive, secondary progressive and progressive relapsing (Mccance et al., 2014).

Sign and Symptoms

MS occurs between 20 and 40 years of age (peak at 30 years). Male to female 1:2 (Mccance et al., 2014). The signs and symptoms of MS can be categorized into established syndromes within location of damage.

Optico-Spinal (OSMS) presents with optic nerve and spinal cord axonal loss, evolves rapidly over hours to days. Symptoms include impaired central vision, optic papillitis, and *optic neuritis* (Mccance et al., 2014). Brainstem lesion common symptoms (III through XII) include *Internuclear opthalmoplegia*, nystagmus, diplopia, eye pain, and dysarthria (Mccance et al., 2014). Other brainstem lesion residuals include vomiting, tinnitus, facial weakness/sensory deficit (Mccance et al., 2014).

Spinal MS is the second most common type, involving spinal tracts and dorsal column (Mccance et al., 2014). Weakness,numbness, and stiffness in limbs along with lower limbs more affected than upper limbs. *Lhermitte phenomenon* described as an electric shock down the back and to the legs(Richman & Schub, 2013). *Spastic paraparesis* is the most common neurological finding in MS (Mccance et al., 2014). Others include\ spastic bladder, urgency, hesitancy preceding incontinence, constipation and impotence(Mccance et al., 2014).

Motor deficits/Cerebellar include deep tendon hyperreflexia, diminished cremasteric reflex, clonus, poor coordination, presence of *Babinski reflex and Hoffman's* sign, spasticity, ataxia, impaired speech/dysphagia (Richman & Schub, 2013). Other cerebellar MS symptoms include the Charcot triad: dysarthria, intention tremor, and nystagmus(Mccance et al., 2014).

Cognitive deficits include dementia and depression (Richman & Schub, 2013).

Diagnosis

Known as the McDonald criteria (Mccance et al., 2014).

Assessment onset of symptoms, duration, including pain and fatigue(Richman & Schub, 2013). Signs and symptoms indicating disease with 2 or more episodes lasting at least 24 hours and occurring at least 1 month apart (Richman & Schub, 2013).

Lab Analysis of CSF aspirated during lumbar puncture will indicate elevated immunoglobulins, myelin debris, and mildly elevated or normal protein (Richman & Schub, 2013). Immunoglubulin G index is found in 2/3 of individuals with MS and oligoclonal bands of IgG on electrophoresis in more than 90%(Mccance et al., 2014).

Diagnostic Studies MRI and CT scan may indicate plaques and/or glial scars in the brain and spinal cord. VEP test may diagnose optic nerve demyelination (Richman & Schub, 2013) (Mccance et al., 2014).

Treatment

Overall, provide symptomatic relief and reduce risk of complications: permanent neurological damage (Richman & Schub, 2013). Acute relapses treated with corticosteroids: methylprednisolone. Oral and injectable disease modifying drugs are used to decrease relapse, promote remyelination, suppress B&T cell function, prevent demyelination. Options for immunosuppression include interferons (Avonex, Rebif, Betaseron), glatiramer, natalizumab, and and fingolimod (Richman & Schub, 2013).Vitamin D for reduction of risk (Mccance et al., 2014).

Pain and fatigue Can be assisted or relieved with analgesics, ice, heat, TENS. Amanadine, modafinil as ordered to combat fatigue (Richman & Schub, 2013).

Bladder dysfunction & constipation can be relieved by avoiding bladder irritants, timed voiding, regulating fluid intake, anti-cholinergic medications (Ditropan), and constipation assisted with stool softeners/fiber (Richman & Schub, 2013).

Spasticity can be relieved with baclofen or anti-epileptics (Richman & Schub, 2013).

Referrals for physical therapy (PT), occupational therapy (OT), and speech therapist based upon disease progression (Richman & Schub, 2013).

Recommendations & Further Readings

National Multiple Sclerosis Society (http://www.nationalmssociety.org/)

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