Medical Conditions That Mimic Multiple Sclerosis

Disease	What It Is	How It Mimics MS	How to Tell It From MS
Adrenoleukodystrophy and adrenomyeloneuropathy	An X-linked genetic defect of a transporter protein, causing peroxisome dysfunction and an excess of very-long-chain fatty acids.	Adult forms commonly cause progressive paraparesis and ataxia, usually with confluent posterior white-matter changes on MRI. Female carriers may present with mild disease also.	Serum testing will show high levels of very-long-chain fatty acids. The ACTH stimulation test usually shows impaired adrenal function.
Behçet disease	An autoimmune syndrome of oral and genital ulcers, uveitis, and arthritis affecting predominantly Mediterranean and Middle East patients.	Rare reports of focal weakness and myelopathy, along with visual (uveitis/iritis) symptoms. MRI may show white-matter changes.	Rare in North America. CSF shows pleocytosis without characteristic IgG abnormalities. Biopsy of mucocutaneous ulcers is definitive.
Clinically isolated syndrome or monosymptomatic demyelination	A single attack of optic neuritis, transverse myelitis, or other lesion confined to 1 anatomic localization at 1 point in time. This sometimes represents the first attack of MS.	Same symptoms. More than half have an abnormal MRI, with subclinical lesions elsewhere in the brain.	Time. Another attack disseminated in time and space will confirm MS. Another lesion on MRI done 1 month later implies MS.
CNS lymphoma	Lymphoma of the central nervous system, usually in immunocompromised patients.	Focal neurologic deficits with multifocal enhancing MRI lesions.	CSF does not have IgG abnormalities but will often show positive cytology. Lesions are highly steroid responsive. Brain biopsy may be necessary.
Devic disease, or neuromyelitis optica (NMO)	Acute inflammatory demyelination predominantly affecting the optic nerves and spinal cord, associated with an NMO-IgG antibody against the aquaporin-4 channel.	Optic neuritis and transverse myelitis characterize NMO and are also common symptoms of MS. As many as 15% of NMO patients have lesions in areas other than the optic nerves and spinal cord, both clinically and on MRI.	Diagnostic criteria for NMO include lesions affecting the optic nerve and spinal cord, but with myelitis extending continuously over 3 or more contiguous segments of the cord. Patients should also be seropositive for the NMO-IgG antibody.
HIV/AIDS	Retroviral infection with HIV-1 that can involve the nervous system, most commonly in gay males or intravenous drug users.	May cause optic neuritis, myelopathy, mental status changes, and focal deficits with white-matter changes on MRI scan and abnormal CSF.	Occurs in high-risk populations who may have diminished CD4 cell counts and positive HIV serology.
Lyme disease (neuroborreliosis)	Infection by tick-borne spirochete *Borrelia burgdorferi*.	It can cause persistent focal neurologic findings and signal abnormalities on MRI scan of the brain.	History of erythema migrans rash. Western blot is the most definitive serology, and CSF will show positive PCR.
Progressive multifocal leukoencephalopathy (PML)	CNS infection by JC virus in an immunosuppressed patient, causing progressive (and sometimes relapsing) deficits leading to death within weeks or months.	Can have multifocal CNS deficits, which sometimes relapse. The MRI is abnormal, showing white-matter lesions.	It occurs in immune-compromised patients, the deficits are usually progressive rather than relapsing, the time course is short, and MRI lesions are generally larger and more confluent. CSF PCR may be positive for JC virus, but brain biopsy may be necessary for the diagnosis.
Sarcoidosis	A granulomatous multisystem disease of unknown etiology.	May involve optic nerve or spinal cord. MRI may show white-matter lesions. Rare patients have oligoclonal bands in their CSF.	Often systemic symptoms, especially in the lungs. Serum and CSF ACE levels may be elevated. MRI often shows meningeal enhancement. Biopsy (of skin, lymph node or lung) is definitive.
Sjögren syndrome	An autoimmune disease of dry eyes and mouth with arthritis and vasculitis.	Occasional reports of neurologic symptoms, especially progressive myelopathy. MRI may show white-matter lesions and spinal fluid may show oligoclonal bands with increased IgG.	Positive serology for SS-A (Ro) and SS-B (La) autoantibodies. Prominent dry eyes and mouth. Salivary gland biopsy can be definitive.
Syphilis	Chronic CNS infection by the spirochete *Treponema pallidum*.	Can cause optic neuritis, myelopathy, and other focal neurologic findings.	MRI is usually normal. Negative serology (FTA-ABS) rules out syphilis. Infection now rare except in HIV-positive or immunocompromised patients.
Systemic lupus erythematosus (SLE)	An autoimmune multisystem disease, including vasculitis that commonly affects the central nervous system.	Common in young women and may affect the nervous system, especially optic nerve and spinal cord. MRI white-matter changes are common, and up to 60% have oligoclonal bands and IgG abnormalities in CSF.	Positive serology with ANA and double-stranded DNA autoantibodies. Systemic involvement especially includes kidneys and skin and hematologic changes. Can be very difficult to distinguish from MS.
Vitamin B12 deficiency	CNS damage due to deficiency of vitamin B12, commonly caused by pernicious anemia.	May cause CNS deficits, especially a progressive myelopathy, rarely with MRI signal abnormalities.	CBC is often abnormal and serum B12 levels are low. Methylmalonic acid and homocysteine are often abnormal.

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Abbreviations: ACE = angiotensin-converting enzyme, ACTH = adrenocorticotropic hormone, AIDS = acquired immune deficiency syndrome, ANA = antinuclear antibodies, CBC = complete blood count, CD4 = cluster of differentiation 4, CNS = central nervous system, CSF = cerebrospinal fluid, DNA = deoxyribonucleic acid, FTA-ABS = fluorescent treponemal antibody-absorption, HIV = human immunodeficiency virus, IgG = immunoglobulin G, JC virus = John Cunningham virus, MRI = magnetic resonance imaging, MS = multiple sclerosis, PCR = polymerase chain reaction.