

# INFECTIOUS MYELOPATHIES

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## OVERVIEW

Infectious myelopathies may result as a consequence of direct viral invasion or as a para-infectious immune-mediated process. The microorganisms associated with myelopathy are many, and include a variety of bacterial, viral, fungal, and parasitic pathogens. Epidemiological risk factors, clinical characteristics, CSF profiles, and imaging features may assist in the approach to the differential diagnosis of infectious myelopathies.

## DIAGNOSTICS

Detailed history should include identification of patient-specific epidemiological risk factors including environmental contact with animals or insects, occupational and recreational exposures, season, and travel history/geographical areas, as well as immunological status, e.g. use of immunosuppressant medications and/or co-morbid disorders of cell-mediated or humoral immunodeficiency. Constitutional symptoms, recent gastrointestinal or pulmonary symptoms, and presence of rash may also help in formulating the differential. Detailed neurological examination should be performed and should include identification of possible sensory level for localization. Laboratory investigations should include complete blood count with differential, peripheral blood smear, chemistry profile, blood cultures and HIV antibody screening. Both acute and convalescent serological testing in the serum should be obtained with specific studies depending on geographical location/exposures and may include specific arboviral studies (i.e. West Nile IgM and IgG), RPR, Lyme testing, Ehrlichia/Anaplasma, Rickettsial antibody panel, interferon-gamma release assay for TB, Coccidioidomycosis/ Histoplasmosis/ Blastomycosis testing, and urine Histoplasmosis antigen testing. Assuming no contraindications to lumbar puncture, cerebrospinal fluid (CSF) should be obtained with studies to include opening pressure, cell count with differential, protein, glucose, gram stain and culture, acid fast smear and AFB culture, fungal stain and culture, serological testing (e.g. specific arboviral IgM and IgG), and pathogen-specific PCRs (e.g. herpesviruses, enterovirus). Imaging studies should include MRI of the total spine with contrast, and potentially also MRI brain. Select MRI patterns of transverse spinal abnormality may help to narrow the differential.

## BACTERIAL INFECTIONS

Bacterial causes of infectious myelitis include pyogenic infections, e.g. paraspinal infections or spondylitis/discitis, and may be associated with epidural abscess formation (Staph aureus is putative pathogen in >50% of cases). Specific other bacterial pathogens associated with myelitis include:

- 1- **Mycobacterial/tuberculosis:** Tuberculous myelitis may be associated with spondylodiscitis (Pott's disease) and frequently involves the thoracic and lumbar spine. It is often accompanied by a radiculitis (i.e. a radiculomyelitis) with MRI demonstrating thickening of lumbosacral nerve roots with pathological enhancement. Intramedullary tuberculomas may also occur less commonly (may be solitary, or multiple lesions).
- 2- **Neuroborreliosis:** Lyme disease is caused by *Borrelia burgdorferi* which is transmitted by an infected tick. Neurological manifestations are many and include cranial nerve palsies, radiculitis, peripheral neuropathy, meningitis, and encephalitis, in addition to myelitis (there may be overlap in phenotypic features). MRI may show longitudinally extensive centromedullary lesions (especially involving mid-thoracic and lumbar regions).
- 3- **Neurosyphilis:** Neurosyphilis encompasses a myriad of neurological manifestations caused by the spirochete *Treponema pallidum*, and while less common in the post-antibiotic era, syphilitic myelitis should be considered within the differential for myelitis, particularly given findings are non-specific. More specific MRI findings may include "candle gutting appearance" and "flip-flop" signs. Myelitis may present as cord swelling involving central cord parenchyma and extending over multiple levels longitudinally as seen in meningomyelitis, though may also include meningovascular cord disease (secondary to ischemia), cord atrophy (as seen in tabes dorsalis), as well as osteitis and gummae, which may present as intramedullary lesions and can cause cord compression. CSF typically shows lymphocytic predominant pleocytosis with elevated protein.

- 4- **Neurobrucellosis:** Brucella is a zoonotic gram-negative coccobacillus; animals with potential for infection include cattle, goats and pigs. Clinically patients may have undulant fever in association with transverse myelitis.
- 5- **Mycoplasma pneumoniae:** *M. pneumoniae* is a common cause of respiratory infections though may also be associated with transverse myelitis.
- 6- **Rickettsial/Ehrlichiae/Anaplasma:** These are tick-borne infections; Rickettsiae and Ehrlichiae are frequently associated with rashes; Anaplasma may be associated with other laboratory abnormalities including leukopenia, thrombocytopenia, and/or transaminitis.

## VIRAL INFECTIONS

Viral causes of infectious myelitis are many. CSF PCRs make up the cornerstone of diagnostic testing; serologies recommended for certain virus; also consider nasopharyngeal, respiratory, and stool viral cultures.

- 1- **Herpesviruses:** HSV-1, HSV-2, VZV, EBV, and CMV can all cause infectious myelitis; respective PCR testing can be obtained in the CSF. In the adult population, HSV-2 is more commonly associated with myelitis than HSV-1. Reactivation of herpesvirus in sacral dorsal root ganglia can result in radiculomyelitis, secondary to inflammation of the corresponding dorsal root and adjacent spinal cord. Clinically, sensory impairment preferentially involves pain and temperature modalities, and onset is subacute, i.e. on the order of days to weeks. In general, herpesviruses preferentially involve the white matter of the spinal cord. CMV should be considered particularly in immunocompromised patients; CSF may demonstrate a neutrophilic predominance and mild hypoglycorrhachia. MRI is normal approximately 50% of the time; [ventral] nerve root enhancement of the cauda equina may be seen; strong association with Guillain-Barre syndrome noted. EBV myelitis may be preceded by mononucleosis, with development of myelitis symptoms several weeks later, though can also occur concomitant with mononucleosis; corresponding serologic testing should be obtained.
- 2- **Enteroviruses:** Enteroviruses are transmitted primarily via fecal-oral transmission and are recognized as an emerging pathogen in children, as well as [immunocompromised, i.e. a/hypogammaglobulinemic] adults. Enteroviruses implicated in myelitis include EV-71, coxsackievirus, echovirus, and poliovirus (as well as association with EV-D68). Enteroviruses have a predilection for anterior horn cell involvement; correspondingly, MRI findings typically consist of abnormal signal within the anterior cord or ventral nerve roots. High fevers often occur in association with neurological symptoms.
- 3- **Flaviviruses:** These infections are mosquito-borne, and are more commonly associated with encephalitis, though can also be associated with myelitis. West Nile Virus is now considered endemic in the US, and has been associated with a polio-like illness characterized by acute flaccid paralysis. St. Louis encephalitis virus has overlapping phenotypic features. Other flaviviruses to consider globally include Japanese encephalitis virus, dengue, and tick-borne encephalitis virus. Accompanying symptoms may include fevers, rash, and fatigue. Myelitis (with MRI findings of longitudinally extensive cord edema) has been reported in association with Zika infection (and clinically distinct from the suspected Zika-associated GBS cases).
- 4- **HIV:** HIV is classically associated with a vacuolar myelopathy. Imaging may show non-enhancing abnormal cord signal of dorsal and lateral columns and spinal cord atrophy.
- 5- **HTLV I:** The vast majority of HTLV infections, i.e. greater than 95%, are asymptomatic though HAM/TSP (HTLV-associated myelopathy/tropical spastic paraparesis) may occur in some cases. MRI spine may show increased T2 signal in lateral columns +/- diffuse spinal cord atrophy.
- 6- **Rabies:** Rabies is a Lyssavirus associated with fatal encephalitis. The paralytic form (manifest as ascending paralysis) may be associated with myelitis. CSF characteristically is non-specific with low-grade lymphocytic predominant pleocytosis.

## FUNGAL INFECTIONS

- 1- **Endemic mycotic infections:** These include Coccidioidomycosis, Histoplasmosis, and Blastomycosis (each with varying geographic distributions). In extra-pulmonary infection, dissemination to the CNS may occur. In Coccidioidomycosis, myelitis with complete spinal/subarachnoid block may be seen, with accompanying leptomeningeal enhancement and nerve root thickening. Additional spinal complications may include syrinx formation, vertebral osteomyelitis, as well as granuloma formation.

- 2- **Cryptococcus:** This occurs most commonly in immunocompromised patients.

#### PARASITIC INFECTIONS

- 1- **Neurocysticercosis:** This parasitic infection is caused by the pork tapeworm known as *Taenia solium*. Spinal imaging may demonstrate the presence of intradural/extramedullary cysts with arachnoiditis, intramedullary cystic mass, and/or cauda equina clumping and enhancement.
- 2- **Schistosomiasis:** *Schistosoma mansoni* has been associated with myelitis. CSF may show elevated eosinophils. Typical MRI findings include irregular, patchy, multinodular medullary lesions with heterogeneous enhancement, most commonly from T11-L1 levels.

#### CONCLUSION

The differential diagnosis for infectious myelopathies is quite broad; identification of epidemiological risk factors, clinical features, and imaging characteristics can help tailor the differential.

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