Neurosyphilis
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Key Points:
• Symptomatic neurosyphilis may be acute (acute syphilitic meningitis) or late/chronic, which includes both meningo-vascular syphilis and parenchymal neurosyphilis (general paresis and/or tabes dorsalis)
• To make things even more confusing, there may be overlap between syndromes of meningo-vascular and parenchymal neurosyphilis
• Most forms of CNS syphilis should generate CSF with a lymphocytosis and elevated protein
• HIV+ patients with syphilis may have discordance between their clinical illness and syphilis serologies

I. Asymptomatic neurosyphilis: 15-40% of patients with syphilis will have some CSF abnormalities
   • Diagnosed by positive CSF VDRL; serum treponemal and non-treponemal tests usually positive as well
   • LP: 10-100 WBC (lymphocyte predominance), protein 50-100
   • Rarely CSF VDRL will be negative with positive serum tests; in that case, if the patient has a CSF consistent with syphilis, many people will treat for neurosyphilis

II. Acute syphilitic meningitis: 6% of syphilis patients
   • Typically the earliest manifestation of neurosyphilis
   • Often associated with cranial nerve palsies, fever, HA, meningismus, and may have signs of cortical involvement
   • CSF may be much like asymptomatic neurosyphilis or may demonstrate higher cell counts/protein and lower glucose
   • Serum and CSF VDRL almost always positive

III. Meningovascular syphilis: 10-12% of patients
   • Syphilitic endarteritis causes infarction clinically similar to stroke, although may have a prodrome
   • CSF: lymphocytosis, elevated protein; CSF VDRL usually positive

IV. General paresis: Relatively rare; occurs 15-20 years after initial infection
   • Syphilitic infection of the meninges and cortex causes personality changes, paranoia, emotional lability, eventually progressing to memory loss and dementia
   • CSF: elevated lymphs and/or protein; VDRL usually positive in pre-HIV era but current data suggests sensitivity of 27-92%. Treponemal tests may be more sensitive but often are not standardized for use on CSF. A PCR has been developed but data on utility not known.

V. Tabes dorsalis: Now rare; disease of posterior columns of spinal cord that occurs 18-25 years after infection. Often coexists with general paresis.
   • Manifestations: abnormal gait, paresthesias, lightning pains of extremities, loss of proprioception on exam, positive Romberg; Argyll-Robertson pupils may be seen with this and/or general paresis
   • Abnormal CSF is less common in this setting, and CSF VDRL was normal in up to 1/3 of cases in pre-HIV era

VI. Pearls about neurosyphilis:
• Any inflammatory disease of the eye can be mimicked by neurosyphilis
• The cranial nerves most commonly involved in neurosyphilis are VII and VIII
• Syphilitic otitis causes tinnitus and may be the only symptom at presentation
• In non-HIV+ patients, those with neurosyphilis should have a positive serum treponemal test (MHATP/FTA)
• In non-HIV+ patients, a positive CSF VDRL always indicates neurosyphilis, whereas a positive CSF PCR for syphilis simply indicates that CSF invasion has occurred
• HIV+ patients may have titers discordant from their true disease state and therefore probably warrant more aggressive treatment; they may also progress more quickly than pts in the pre-HIV era