Neurosyphilis

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Neurosyphilis is a rare complication of syphilis, a sexually transmitted disease caused by the bacterium Treponema pallidum. While syphilis can affect various organs and systems in the body, neurosyphilis specifically involves the central nervous system (brain and spinal cord).

Neurosyphilis can occur at any stage of syphilis infection, but it's more common in the later stages, particularly if the infection has not been treated or if it has been inadequately treated.

Clinical features

Symptoms of neurosyphilis can vary widely and may include:

Mental disorders: Such as dementia, confusion, and personality changes. Motor abnormalities: Including weakness, tremors, and difficulty with muscle coordination. Sensory deficits: Such as numbness, tingling, or pain. Visual problems: Such as vision loss or changes in vision. Problems with gait and balance: Difficulty walking or maintaining balance. Headaches: Often severe and persistent.

Diagnosis

Diagnosis typically involves a combination of clinical evaluation, blood tests for syphilis antibodies, and cerebrospinal fluid (CSF) analysis.

Cerebrospinal fluid analysis

Cerebrospinal fluid analysis is a crucial component in the diagnosis of neurosyphilis. It helps detect specific abnormalities indicative of central nervous system (CNS) involvement by Treponema pallidum, the bacterium that causes syphilis. Here's what you might expect to find in CSF analysis for neurosyphilis:

Elevated White Blood Cell (WBC) Count: Neurosyphilis can cause inflammation of the meninges and the CNS, leading to an increase in white blood cells in the CSF. Lymphocytic pleocytosis, characterized by an elevated lymphocyte count, is commonly observed. Elevated Protein Levels: The protein concentration in the CSF may be elevated due to inflammation and breakdown of the blood-brain

barrier. This elevation in protein levels is often observed in neurosyphilis. Positive Venereal Disease Research Laboratory (VDRL) Test: The VDRL test is a nonspecific test used to detect antibodies in the blood or CSF that are produced in response to syphilis infection. A positive VDRL test in the CSF indicates the presence of syphilis antibodies within the CNS and suggests neurosyphilis. Positive Treponemal Test: Treponemal tests, such as the fluorescent treponemal antibody absorption (FTA-ABS) test or the Treponema pallidum particle agglutination assay (TP-PA), detect antibodies specifically directed against Treponema pallidum. While these tests are typically used to confirm syphilis infection, a positive treponemal test in the CSF further supports the diagnosis of neurosyphilis. Positive Polymerase Chain Reaction (PCR) Test: PCR testing of CSF can directly detect the presence of Treponema pallidum DNA, providing a rapid and specific diagnosis of neurosyphilis. However, PCR testing may not always be readily available in all healthcare settings. Absence of Other Pathogens: CSF analysis may also include tests to rule out other infectious agents that can cause similar neurological symptoms, such as viral, bacterial, or fungal pathogens. It's important to note that the interpretation of CSF findings in the diagnosis of neurosyphilis should be done in conjunction with clinical evaluation and other laboratory tests. Additionally, the absence of abnormalities in CSF analysis does not completely rule out neurosyphilis, as the disease can sometimes present with normal CSF findings, particularly in early stages or in cases of asymptomatic neurosyphilis. Therefore, clinical judgment and comprehensive assessment are essential for accurate diagnosis and appropriate management of neurosyphilis.

Differential diagnosis

Multiple Sclerosis (MS): MS is a chronic autoimmune disorder that affects the central nervous system. It can cause symptoms similar to those of neurosyphilis, such as cognitive impairment, visual disturbances, and motor dysfunction. Imaging studies such as MRI can help differentiate between MS and neurosyphilis.

HIV-Associated Neurocognitive Disorders (HAND): HIV infection can also affect the central nervous system, leading to various neurological symptoms collectively known as HIV-associated neurocognitive disorders. Since neurosyphilis and HIV can coexist, patients with neurosyphilis may also have HIV infection, making the diagnosis more complex.

Lyme Disease: Lyme disease, caused by the bacterium Borrelia burgdorferi, can sometimes present with neurological symptoms resembling those of neurosyphilis, including cognitive impairment and neuropathy. A history of tick exposure and serological tests for Lyme disease may help differentiate it from neurosyphilis.

Guillain-Barré Syndrome (GBS): GBS is an autoimmune disorder characterized by acute inflammation of the peripheral nerves. It can lead to symptoms such as muscle weakness, sensory disturbances, and paralysis, which can overlap with those of neurosyphilis. Electrophysiological studies and cerebrospinal fluid analysis can aid in the diagnosis of GBS.

Viral Meningitis or Encephalitis: Infections such as viral meningitis or encephalitis can cause neurological symptoms similar to those of neurosyphilis. However, these conditions are caused by viruses rather than bacteria. Lumbar puncture and analysis of cerebrospinal fluid can help distinguish between viral and bacterial causes of neurological symptoms.

Brain Tumors or Mass Lesions: In some cases, neurological symptoms may be caused by structural abnormalities in the brain, such as tumors or mass lesions. Imaging studies such as MRI can help identify these abnormalities and differentiate them from neurosyphilis.

Other Infectious Diseases: Other bacterial, viral, or parasitic infections affecting the central nervous system, such as tuberculosis, cryptococcosis, or toxoplasmosis, may also present with neurological symptoms similar to those of neurosyphilis. Laboratory tests and imaging studies are essential for differential diagnosis.

Given the complexity of diagnosing neurosyphilis and the potential overlap with other conditions, healthcare providers must consider a broad differential diagnosis and use a combination of clinical evaluation, laboratory tests, and imaging studies to reach an accurate diagnosis.

In cases of Granulomatous hypophysitis-Lymphocytic hypophysitis

Treatment

Neurosyphilis treatment

Case reports

A 27-year-old immunocompetent Caucasian male who presented with uveitis and tinnitus. Physical exam was consistent with uveitis and audiometric testing revealed bilateral sensorineural hearing loss. Serum rapid plasma reagin (RPR) was reactive at 1:512 with a follow-up cerebrospinal fluid (CSF) venereal disease research laboratory (VDRL) test likewise reactive at 1:2, confirming neurosyphilis. The patient was treated with intravenous penicillin G with improvement of symptoms and with subsequent improvement of serum and CSF RPR. However, he ultimately represented with recurrent symptoms and fluctuating serum RPR levels, necessitating repeat treatment and ongoing clinical monitoring. Neurosyphilis can occur at any point during the course of a syphilis infection and may present with a variety of nonspecific findings. This case documents a particularly uncommon instance of simultaneous ocular and otosyphilis, a presentation of neurosyphilis that has only been described a handful of times [1)].

A male in his 60s with stroke risk factors presented with confusion and word-finding difficulties. He was diagnosed with acute ischemic stroke in the right basal ganglia. He was started on secondary stroke prevention measures including dual antiplatelet therapy and a high-dose statin. A highly reactive rapid plasma reagin (RPR) was performed as part of the workup and found to be positive. Follow-up fluorescent treponemal antibody absorption (TPA) test was also positive, confirming a diagnosis of syphilis. He was discharged home with a scheduled course of antibiotic treatment for tertiary syphilis but returned due to a new episode of transient facial paralysis. Further workup and physical exam findings revealed the patient had neurosyphilis. He was started on the appropriate antibiotic therapy, which significantly improved his confusion and prevented new episodes of stroke [2].

A 60-year-old man who presented with headaches for 1 year and mild confusion for 3 weeks and was initially diagnosed as having a cerebral tumor on the basis of finding a round lesion in the right lenticular nucleus with ring enhancement on gadolinium-enhanced T1-weighted brain magnetic resonance imaging. However, the discovery of positive serology for Treponema pallidum infection on routine tests on admission prompted analysis of cerebrospinal fluid, which was also positive on Treponema pallidum hemagglutination (TPHA), rapid plasma reagin (RPR), and treponemal antibody absorption (FTA-ABS) tests. Thus, he was diagnosed as having an intracranial syphilitic gumma. After commencing treatment with penicillin G, the lesion temporarily increased in size, but subsequently resolved completely with continuing antibiotic treatment. In the present era of increasing prevalence of syphilitic infection and because they are eminently treatable, syphilitic gummas should be included in the differential diagnosis of apparent brain tumors. Additionally, temporary enlargement of a probable gumma after instituting antibiotic treatment should not prompt cessation or change of the antibiotics [3]

Case reports from the HGUA

Q11869

A 34-year-old woman presented at home with a cluster of three generalized tonic-clonic seizures, characterized by loss of consciousness with limb stiffness and 1-2 minutes of head deviation, followed by postictal confusion. She experienced amnesia regarding the events until her arrival at the hospital. There were no reports of tongue biting or sphincter relaxation. Additionally, she had been experiencing a cold-like illness with cough but no fever for the past week. The patient is a regular cannabis user.

Physical Examination: Neurological examination revealed intact cognition and language. Mild superficial hypoesthesia was noted in the left brachio-crural region, with no dysmetria observed. Muscle strength was preserved, with bilateral flexor reflexes.

Investigations:

Brain magnetic resonance imaging with contrast:

Partially defined lesion measuring 3.2 x 3 x 2.2 cm in the anterior pole of the right frontal lobe, involving cortical and subcortical white matter. The lesion exhibited hyperintensity on T2 and FLAIR sequences, hypointensity on T1, and focal cortical enhancement of 3 mm. Additionally, there was mild meningeal thickening and enhancement adjacent to the lesion. No significant alterations were observed in cerebral perfusion. Thoracoabdominopelvic CT with contrast: Showed no evidence of metastasis. Brain MRI with spectroscopy: Demonstrated a decrease in NAA peak with a slight increase in Cho, without lipid/lactate peak elevation. No evident increase in myo-inositol compared to the healthy side. Cytological diagnosis of cerebrospinal fluid (CSF): Moderate pleocytosis of round cells observed. Microbiology of CSF: Negative for pathogens.

Other laboratory findings: Glucose 65 mg/dL, Protein 43.2 mg/dL, Leukocytes 6/mm^3, Red blood cells absent. Diagnosis: Based on clinical context, the lesion in the right frontal lobe is suspicious for early neurosyphilis (syphilitic gumma with associated edema and pachymeningitis). The differential diagnosis includes low-grade diffuse glioma or neuronal/glioneuronal tumor with focal meningeal involvement.

Treatment: Pending results for Rapid Plasma Reagin, AMA, ASMA, LKM, ANA, serum anti-neuronal antibodies, and CSF anti-neuronal antibodies. Follow-up: Awaiting results and planning for further investigations and treatment as indicated.

Note: The patient's history of cannabis use, along with her medical history of pernicious anemia and anxiety, should also be considered in the overall management plan.

1)
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