

Neurosyphilis

Santosh Kadel MS MLS (ASCP)^{CM}

Objectives

By the end of the presentation the audience will be able to:

1. explain the neurological manifestations of neurosyphilis.
2. list lab tests that are helpful in the diagnosis of neurosyphilis
3. explain pathogenesis of neurosyphilis
4. discuss the treatment for neurosyphilis

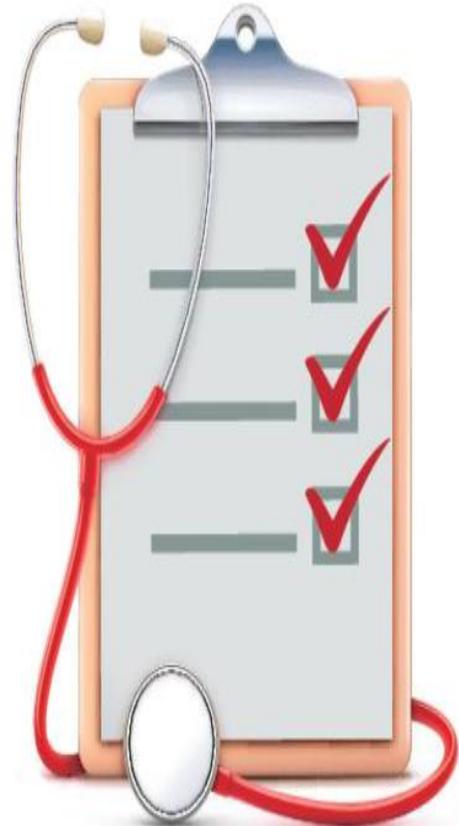


History of Present Illness (HPI)

- A 64-year-old man presented to the Emergency Department with chief complaint of fever. Onset of fever was 8 hours prior to the visit noted at PCP clinic. Spouse reported that for the past day, patient has been less interactive than baseline. Patient was quiet, non-verbal. Decreased oral intake. New onset drooling. Not following routine commands well. Had rhinorrhea. Wore adult diapers.

Physical Exam

- BP 116/63
- Pulse 93
- Temp 37.3 °C (99.2 °F) (Oral)
- Resp 18
- Ht 1.778 m (5' 10")
- Wt 82.6 kg (182 lb)
- SpO₂ 95%
- BMI 26.11 kg/m²



Review of Systems

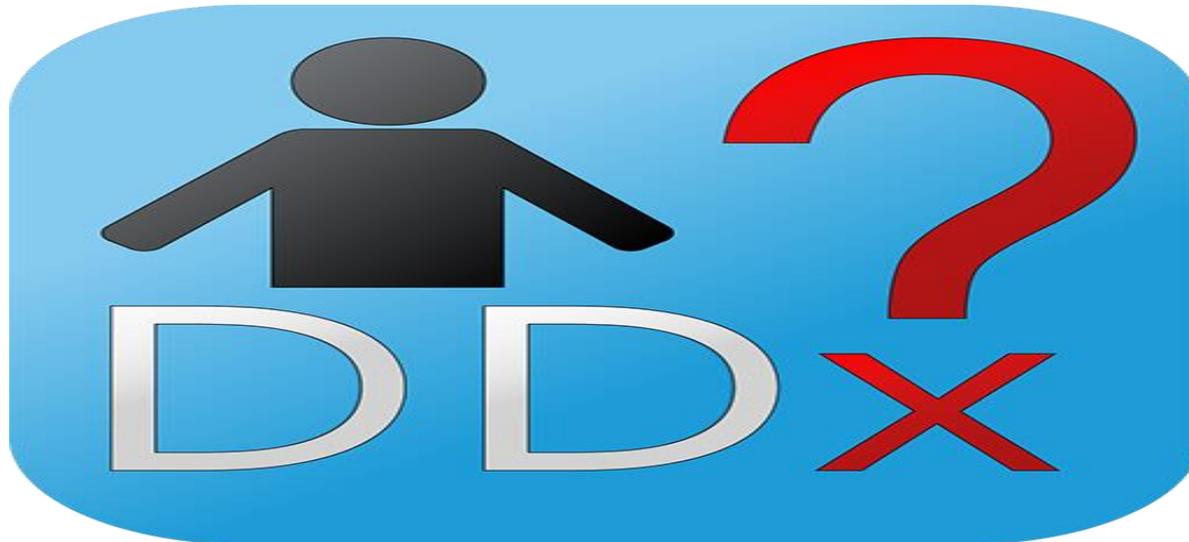
- Head: no swelling and no obvious injury
- Neck: supple and trachea midline
- Eyes: extraocular movements intact
- ENT: normal on external inspection
- Cardiovascular: regular rate and rhythm
- Respiratory: chest non-tender, no respiratory distress and breath sounds normal
- Abdomen: soft, non-tender
- Back: non-tender
- Skin: intact and warm, dry
- Extremities: atraumatic, normal range of motion and no pedal edema
- Neuro/Psych: awake, alert, moves upper extremities; spouse reported bilateral lower extremity weakness and tremors requiring wheelchair, dependency was at baseline.

Initial Laboratory Findings

- WBC – 14.24 (4.20 - 10.70 $10^3/\mu\text{L}$)
- Absolute Neutrophil Count – 12.27 (1.99 - 6.95 $10^3/\text{uL}$)
- Sodium – 148 (135 - 145 mmol/L)
- Chloride – 108 (98 - 108 mmol/L)
- Carbon dioxide – 25 (23 - 31 mmol/L)
- Creatinine – 1.50 (baseline Cr <1.10 mg/dL)
- Lactic Acid – 1.59 (0.5 – 2.2 mmol/L)
- Urinalysis – positive nitrite, small leuk est, 3-5 RBC, 5-10 WBC, and moderate bacteria.

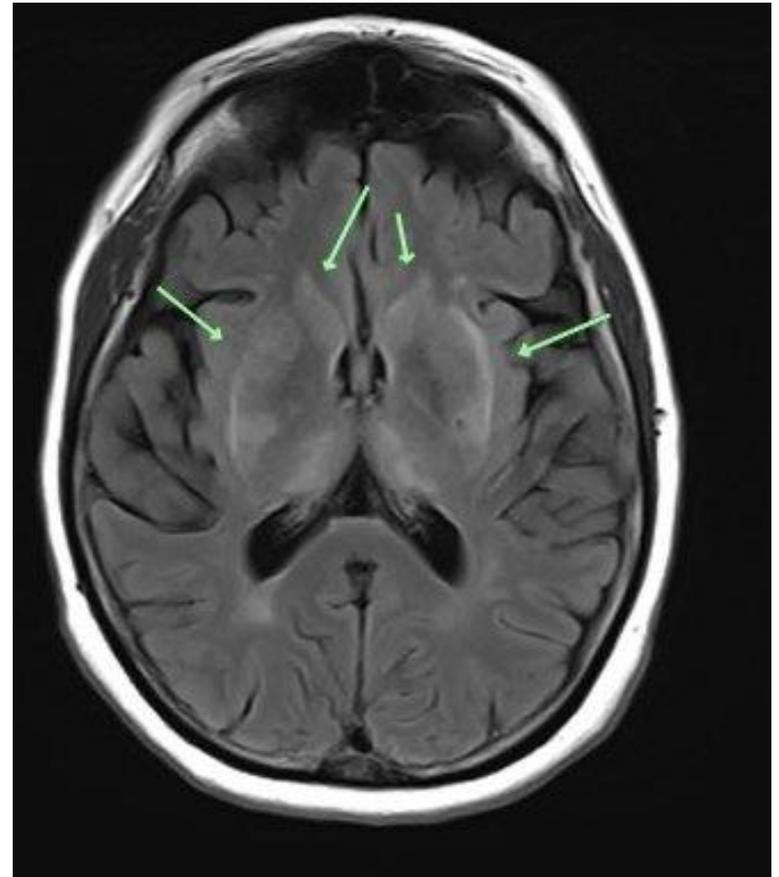
Differential Diagnosis

- Urosepsis w/hyponatremia
- URI w/hyponatremia
- Normal pressure hydrocephalus w/dehydration
- CNS infection w/dehydration



Additional Diagnostic Tests

- Chest X-ray - The heart size and mediastinal silhouette were normal. No pleural effusion or pneumothorax was seen.
- MRI - The lateral ventricles were dilated out of proportion to the degree of sulcal dilatation with periventricular T2/FLAIR. Hyperintensity may represent transependymal edema/flow.
- Electroencephalogram (EEG) - mild diffuse slowing, suggestive of a mild diffuse disturbance in cerebral function and intermittent focal slowing in the right hemisphere, suggestive of a focal disturbance in the that region.



Additional Laboratory Tests

- Urine cultures - No aerobic growth (< 1000 CFU/mL)
- Blood cultures – negative
- Vitamin B1(Thiamine) level - 188 (70 - 180 nmol/L)
- Vitamin B12 level – 630 (240 - 930 pg/mL)
- Vitamin E level – 7.7 (5.5 - 18.0 mg/L)
- Copper level – 110 (70 - 140 ug/dL)

Breakthrough

Patient's PCP revealed that patient was recently found to be positive for Fluorescent Treponemal Antibody Absorption (FTA-Abs) test

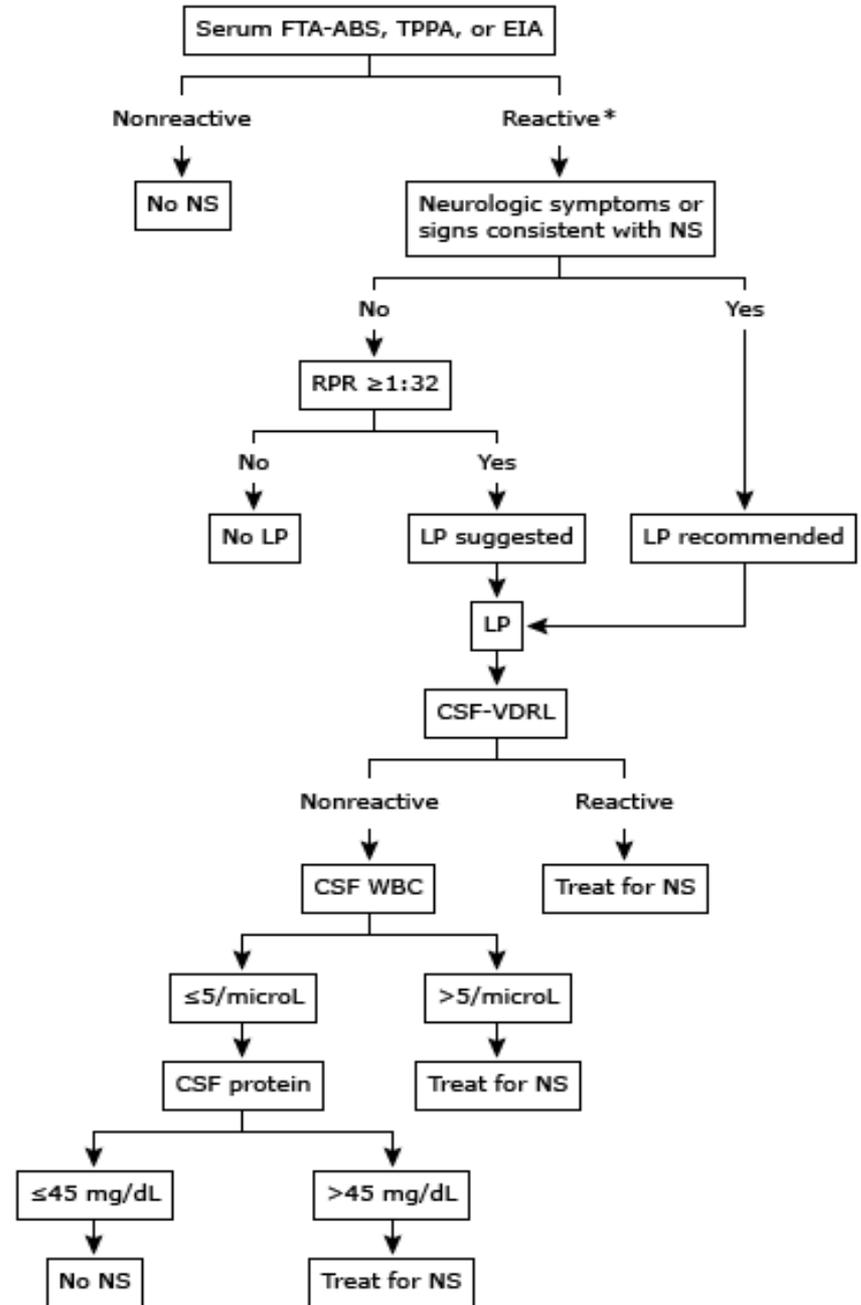
- Serum VDRL— reactive

Patient had lumbar puncture immediately after the VDRL results came back.

CSF Findings

CSF studies:

- Culture – negative
- Glucose – 46 (50 - 80 mg/dL)
- Protein – 123 (15 – 45 mg/dL)
- WBC – 34 (0-5/ μ L)
 - 96% lymphocytes
- Meningitis panel by PCR – negative
- CSF VDRL – reactive
- CSF FTA-ABS - reactive



Neurosyphilis

- Infection of the central nervous system (CNS) by *Treponema pallidum*, subspecies *pallidum*.
- Can occur at any time after initial infection.
- Early in the course of syphilis, the most common forms of neurosyphilis involve the cerebrospinal fluid, meninges, and vasculature (asymptomatic meningitis, symptomatic meningitis, and meningovascular disease).
- Late in disease, the most common forms involve the brain and spinal cord parenchyma (general paralysis of the insane and tabes dorsalis).
- syphilis is transmitted through contact with a chancre on an infected person, usually during sexual contact

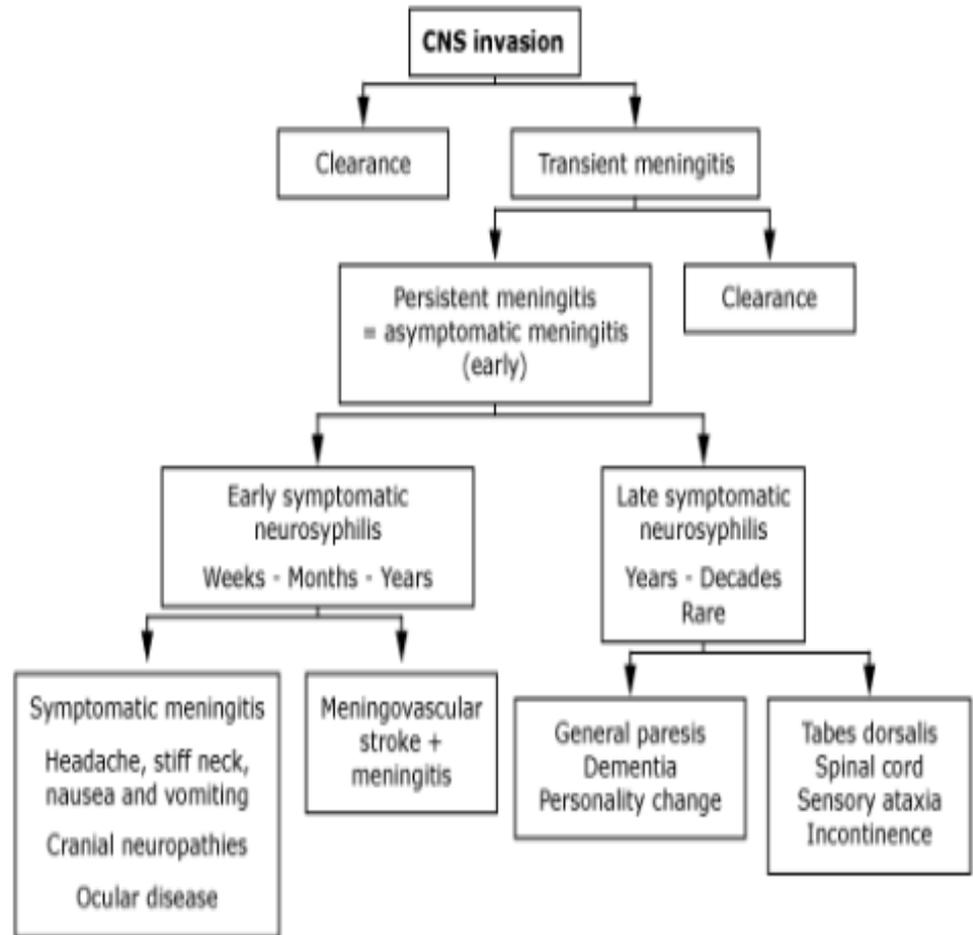
Epidemiology

- Common in the pre-antibiotic era, occurring in 25 to 35 percent of patients with syphilis
- In modern era, most frequently seen in persons with HIV.
- In the United States, the rates of syphilis have been increasing since 2000. The majority of new cases first occurred in men, but in recent years, an increasing number of cases have been reported in women and infants born to infected mothers.

Pathogenesis

- Begins with invasion of the cerebrospinal fluid (CSF)
- *T. pallidum* infection can be identified in the CSF from approximately one-quarter of untreated patients with early syphilis.
- Spontaneous resolution may occur in some cases without an inflammatory response or after a transient meningitis
- Number of CSF CD4+ T cells and the amount of gamma-interferon produced by CSF lymphocytes increases throughout the period of bacterial clearance, consistent with a "Th-1-type" cellular immune response

Natural history of neurosyphilis



Diagnostic Criteria

- According to the Centers for Disease Control and Prevention (CDC), there are two categories:
 - Confirmed neurosyphilis defined as:
 1. any stage of syphilis and
 2. a reactive CSF VDRL.
 - Presumptive neurosyphilis defined as:
 1. any stage of syphilis,
 2. a nonreactive CSF VDRL,
 3. CSF pleocytosis or elevated protein, and
 4. clinical signs or symptoms consistent with syphilis without an alternate diagnosis to account for these.

Diagnosis

- Serologic Testing
 - Screening tests:
 - Venereal disease research laboratory (VDRL)
 - Rapid plasma reagin (RPR)
 - confirmatory test: Serum treponemal tests
 - Fluorescent treponemal antibody absorption (FTA-ABS)
 - *T. pallidum* particle agglutination assay (TPPA)
- Cerebrospinal fluid (CSF) Examination
 - CSF-VDRL (reactive test establishes the diagnosis of neurosyphilis)
 - CSF-RPR
 - CSF FTA-ABS (non-reactive test excludes the diagnosis of neurosyphilis)
 - CSF cell count
 - CSF protein

Treatment

- Aqueous crystalline penicillin G (18 to 24 million units per day, administered as 3 to 4 million units intravenous [IV] every four hours, or 24 million units daily as a continuous infusion) for 10 to 14 days

OR

- Procaine penicillin G (2.4 million units intramuscular [IM] once daily) plus probenecid (500 mg orally four times a day), both for 10 to 14 days

Follow-up

- CDC recommends follow-up CSF examinations every 6 months until CSF abnormalities have resolved. If by the end of 2 years, CSF abnormalities have not resolved, retreatment for neurosyphilis is recommended.
- Marra et al. found that a 4-fold decline in serologic RPR titers correlated with resolution of CSF parameters in persons with neurosyphilis who were not HIV-infected.

References

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THANK
YOU!



Questions?

