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## Neurosyphilis presenting with normal pressure hydrocephalus in a 76 year old man

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### Summary

**Background:**

Normal pressure hydrocephalus (NPH) is composed of gait abnormalities, urinary incontinence and decline in mentation. It is uncommonly induced by syphilitic infection.

**Case Report:**

A 76 year-old male present with gait disturbances, urinary incontinence, declining vision and cognition, with a known diagnosis of NPH. He underwent therapeutic lumbar puncture (LP), which demonstrated leukocytosis and elevated protein. Venereal disease research laboratory testing (VDRL) was reactive in a 1:64 dilution with positive fluorescent Treponemal Antibody (FTA-Abs). The subject was treated with 14 days of Intravenous (IV) Penicillin 3 million units for 3 weeks and intramuscular benzathine PCN for 2 shots, with marked clinical improvement.

**Conclusions:**

The incidence of Tabes Dorsalis is limited in the age of penicillin, especially in subjects without HIV. Subjects are diagnosed with either LP RPR or VDRL, confirmed with FTA-Abs. Common treatment is IV PCN 1.4–3 mU for 10–14 days.

**key words:**

**neurosyphilis • tabes dorsalis • normal pressure hydrocephalus**

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## BACKGROUND

Normal Pressure Hydrocephalus (NPH) is a known clinical entity first defined in 1965 by Hakim and Adams as an intracranial pressure of 150–200 centimeters of water (cm H<sub>2</sub>O) [1]. The most common clinical manifestations of this condition included the triad of gait abnormalities, urinary incontinence and a decline in mentation. The source of this clinical triad stems from the communicating and nonobstructive nature of NPH, and is a result of arachnoid villi blockage [2]. Several etiologies have been associated with initiating occlusion of the arachnoid villi (Table 1) [3]. In the setting of meningitis induced NPH, lymphocytic proliferation releases cytokines, causing inflammation of meningeal tissue [4]. The advancement of the inflammatory process causes tissues fibrosis and hence occlusion of the arachnoid villi. Syphilis is a less common etiology of meningitis, which also causes tissue inflammation in the meninges, arachnoid villi occlusion and subsequently NPH. The first described case of neurosyphilis induced NPH was in 1979 by Amaducci, et al. [5]. Other than Amaducci et al, to our knowledge there are 3 known case reports depicting NPH in the setting of neurosyphilis [6–8]. In this article we describe the first case of NPH from neurosyphilis in the American Literature, a 76 year-old HIV negative male who presented with frequent falls and gait instability from known NPH caused by undiagnosed neurosyphilis.

## CASE REPORT

A 76 year-old Caucasian male was in his usual state of health, until presented with gait disturbances and frequent falls. The falls were continuous from previous visit and worsening 4 days prior to admission. He described this gait disturbance as “wobbly on my (his) feet,” constant, lasting each time ambulation was initiated until his “legs gave out” or he sat down, aggravated with ambulation and alleviated with lying flat, rest. Associated symptoms included; mild cognitive decline (per family), decreasing visual acuity, urinary incontinence and dysuria. The patient denied trauma, loss of consciousness, tongue biting, seizure like activity, headache, fever, chills, photophobia.

The patient was previously admitted for this issue four months prior to his presentation and at that time was diagnosed with NPH via computer tomography (CT) scan showing “ventriculomegaly.” The subject reported having seen physicians at multiple institutions with no change in the severity of his symptoms. His past medical history is positive for diabetes, hypertension, ischemic stroke, coronary artery disease, myocardial infarction, diverticulosis and prostate cancer, treated with prostatectomy. Past surgical history was positive for coronary artery bypass graft, bilateral total hip arthroplastys and right total knee arthroplasty. He does not use illegal substances, tobacco nor alcohol. He has been divorced for 15 years, does not report any new sexual partners and denied any history of sexually transmitted infections. Family history is non-contributory and he has no allergies to medications.

Vital signs on admission included; blood pressure of 159/94, pulse of 97, temperature of 97° Fahrenheit (36.1° Celsius), respiratory rate 18 and saturating 97% o room air. Pertinent physical examination included orientation to person, not

**Table 1.** Etiologies of normal pressure hydrocephalus.

Etiologies of normal pressure hydrocephalus	
Primary	Secondary
Idiopathic	Traumatic brain injury
	Ischemic stroke
	Hemorrhagic stroke
	Central nervous system tumor
	Meningitis

National Institute of Neurological Disorders and Stroke. (2011, April 29). NINDS Normal Pressure Hydrocephalus Information. [http://www.ninds.nih.gov/disorders/normal\\_pressure\\_hydrocephalus/normal\\_pressure\\_hydrocephalus.htm](http://www.ninds.nih.gov/disorders/normal_pressure_hydrocephalus/normal_pressure_hydrocephalus.htm).

place nor time, motor weakness in the right upper extremity of three out of five and four out of five in the left upper extremity. Motor strength in the lower extremities was recorded as three out of five bilaterally. No sensory deficits were recorded. The subject demonstrated difficulty with dysidiadokinesia and finger to nose, wide-based gait, frank lateropulsion and frank abasia, with negative Romberg testing and heel to shin. Otherwise physical examination was normal.

Laboratory studies included a normal chemistry panel and complete blood count. Urinalysis was normal, urine and blood cultures were sent and showed no growth during the course of the subjects stay. Day two of admission the subject underwent lumbar puncture with an opening pressure of 155 cm H<sub>2</sub>O, clear in color, protein was 94 mg/dL, glucose of 64 mg/dL, WBC 47/uL, 46 nucleated WBC/uL, 10 RBC, 4% polymorphonuclear WBC, 88% lymphocytes. Gram stain was negative, CSF culture was negative, Herpes simplex virus 1 and 2 were both negative.

Cerebrospinal fluid Venereal Disease Research Laboratory (VDRL) was positive in a 1: 64 dilution. Rapid Plasma Reagent (RPR) was sent and nonreactive, Fluorescent Treponemal Antibodies (FTA-Abs) were also sent and were re-recorded as reactive. The subject’s motor weakness relented slightly after large volume lumbar puncture was performed. Consultation by infectious disease department was reported as follows:

“Almost certainly this is Neurosyphilis. CSF VDRL is a highly specific test, and when false positives occur they are typically low titer... but the symptom constellation, abnormal protein and lymphocytes are all quite consistent with Neurosyphilis. Not clear how much of what has been attributed to microvascular disease in the past was all due to syphilis.

He will need treatment: Intravenous (IV) Penicillin 3 million units q 4 hours for 14 days (minimum of 10 days) after which will need Intramuscular (IM) benzathine PCN x2 doses to complete Rx for late latent syphilis. He needs an HIV test, which I discussed with him, which will impact on his follow-up management if positive. Would also consider a good ophthalmologic exam and an echocardiogram, if these have not been done recently. Since his LP was abnormal, will need a follow-up LP by 6 months to assess for

resolution of CSF abnormalities and need to retreat. Can also follow his serum RPR titers. Uncertain how much of this disease now is reversible and how much is static with regard to his CNS symptoms.

He does not want his family to know about the syphilis diagnosis. I did explain to him that because syphilis is a reportable disease, he will be contacted by the health department."

HIV testing was sent and was nonreactive. The patient was started on IV Penicillin (PCN) 3 million units (mU) for 14 days and 2 doses of benzathine PCN for 2 doses and told to follow up with our hospital's infectious disease department. Once starting the therapy, the subject's motor strength improved, urinary difficulty lessened in severity and the subject was alert and oriented times 3, with some residual cerebellar disease.

## DISCUSSION

Since 1940, limited case reports have encompassed the study of neurosyphilis in the post-penicillin era. From 1980–1997, only 92 cases were described, among which, data was available on merely 77 [9]. Three to nine percent of affected persons in the pre-penicillin generations developed *Tabes dorsalis*, making our patient a unique case in this, the post-penicillin era.

*Tabes dorsalis* was originally described by Romberg as; ataxic gait, lightening pains, paresthesia, failing vision and bladder dysfunction [10]. Indeed these symptoms coincide with NPH and because of this, the diagnosis of neurosyphilis cannot be made based upon clinical symptoms alone. These clinical findings can be explained by the pathophysiology of the disease in which *Treponema pallidum* infiltrates the lymphatic system within minutes of contraction, the posterior columns of the spinal cord within hours. It is this infiltration that explains the diagnostic testing available for syphilis.

### Diagnosis of neurosyphilis

The Center for Disease Control (CDC) defined neurosyphilis as either confirmed; 1) any syphilis stage and 2) positive CSF VDRL, or presumed; any neurosyphilis stage, a non-reactive CSF-VDRL, elevated CSF protein or WBC count, clinical symptoms consistent with neurosyphilis without other known causes for these clinical abnormalities [11]. In our patient, the lumbar puncture was a vital component to the diagnosis. Though originally intended to serve as treatment for his NPH, initial CSF findings, in both our patient and in neurosyphilis, included; lymphocytic pleocytosis, high protein and a normal glucose level. Studies examining CSF findings in neurosyphilis have shown defined cut-offs for CSF pleocytosis as  $>5$  cells/mL in HIV-negative individuals and 10 cells/mL in HIV-positive individuals [12]. Majority of patient with neurosyphilis are HIV positive, therefore CSF findings are commonly obscured by opportunistic infections. With this in mind, our patient's CSF findings, though typical for patients with syphilitic meningitis, have been demonstrated in only 10% of cases of *Tabes Dorsalis* [12].

Other modalities for diagnosing this condition include the RPR and VDRL testing. A recent study demonstrated the diagnostic utility of various serologic and CSF analysis

in neurosyphilis. The results of this study demonstrated a sensitivity and specificity of the RPR testing to be 75% and 99.3%, respectively. Similarly, the sensitivity and specificity of the CSF VDRL testing was found to be 70.8% and 93%, respectively. In the case of our patient, he only had a positive CSF VDRL, however negative serum RPR [13]. These findings are common, as VDRL and RPR are specific, not sensitive tests.

The confirmatory testing in the case of HIV negative neurosyphilis is that of the Fluorescent Treponemal Antibody Testing (FTA-Abs). Hooshmand, et al. described a sample of patients in which a mere 57% was VDRL positive in the CSF, who had clinical symptoms consistent with neurosyphilis. The results of his study compared confirmatory FTA-Abs testing when compared with microhemagglutination *Treponema pallidum* (MHA-TP) testing. Among the sample population, the MHA-TP test was positive even when *T. pallidum* was not present, as confirmed by dark field microscopy and CSF DNA. In contrast, the FTA-Abs was positive in 100% of the sample population who had *T. pallidum* present in the CSF. With a negative RPR, positive VDRL, the FTA-Abs is the final and conclusive test in neurosyphilis testing, as was positive in our patient.

Studies have also examined neuroimaging to diagnose neurosyphilis. A study of 20 HIV-negative persons, with known *T. pallidum* infection, demonstrated a total of 13 subjects with MRI "enhancement." However this clinical area is less explored in the literature [12]. Another less defined area is the utilization of the CXCL13 test. This marker defined the host's innate immune response from the TLR2 on macrophages/dendritic cells when exposed to *T. pallidum* [13]. A study by Marra, et al. demonstrated a sensitivity and specificity of 90% and 37% respectively when CXCL12 levels were low, and 41% and 79% sensitivity and specificity when CXCL13 levels were elevated [13]. Tumors, autoimmune disease and other infections have been known to also cause elevations in the CXCL13 levels. Indeed the CXCL13 level showed promise, yet more investigation must occur prior to defining its true clinical utility.

### Approach to treatment

The gold standard of treatment in patients such as this was and always is Penicillin. Recommended regimens have included 18–24 million units (mU) of IV aqueous penicillin G daily either via continuous or every 4 hours. Other regimens include 2.4 mU of intramuscular procaine penicillin plus 500 mg of oral probenecid four times daily for 14 days [12]. In Penicillin allergic patients, alternative regimens of doxycycline or ceftriaxone are utilized, but data is less conclusive on their effectiveness [12]. In our patient he was treated with IV Penicillin 3 mU every 4 hours for 14 days and then 2.4 million units of intramuscular penicillin for two doses with signs of clinical improvement.

Though our patient showed evidence of clinical recovery, another area of debate is tracking the patient's response to therapy. The CDC recommend serial CSF testing every 6 months until findings have normalized or until two years from diagnosis. If at two years from diagnosis CSF findings have not normalized, the CDC recommends re-treatment [11]. Another study by Marra, et al. followed response to

therapy by normalization of CSF findings and RPR testing. Of the 110 subjects, RPR testing normalized in 57% by 4 months, 85% by 7 months and 88% by 13 months. Additionally, the odds of normalization of CSF findings and resolution of clinical findings were 28–57 times higher in the RPR negative group than the RPR positive group. Finally, response to treatment of the RPR testing was less defined in the HIV-positive subgroup [14]. Our patient was to follow up in 6 months from treatment for CSF analysis excluding CSF-RPR, as original RPR testing was negative.

## CONCLUSIONS

In the post-penicillin era, it is rare to see HIV-negative subjects with *Tabes Dorsalis*. Our literature search concluded few cases of normal pressure hydrocephalus precipitated by late latent syphilitic infection, making our subject a rare entity.

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