



**NEUROSYPHILIS
(GENERAL PARESIS)**

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CASE REPORT

62 year old Vietnam veteran with the history of schizophrenia diagnosed since the last 7 years was consulted by neurology because of progressive decline in mental status since the last 4-5 months worsened since the last few days prior to admission, showing character changes, trivial mood changes like sudden crying, and anger bursts all of which progressed with time. He started to forget the names of his close relatives, could not remember where he put the things, even the way to his home sometimes. He displayed anger, aggression and non sense behavior. His history revealed that he was not even able to form a meaningful sentence, he started to talk to himself, act through visual hallucinations. In the last few days before hospitalization he was reported to be much more agitated, had sleep disorder and had significant increase in his memory dysfunction, paranoia, grandiose delusions, hallucinations, and combativeness not responding to medications and high doses of haldol, there was also question of seizures since brother noticed abnormal jerking movements once lasting for less than a minute.

CASE REPORT

- History taken from brother revealed that patient has always been weird since he came back from war, but was able to keep a job but since last 7 years living with his mom , unemployed but his condition was controlled on medications. He has no drug allergies. On risperdol and haldol. Past medical history was remarkable of some illness per brother for which he never sought any treatment. Brother recalls he suffered from rashes. Family history unremarkable for seizures and psychiatric disorders.

CASE REPORT

- Physical examination was within normal limits. Neither the patient nor any of his relatives had any kind of skin lesions, before or at the time of hospitalization. In his neurological examination, he was found to be confused and was not able to establish any cooperation with the staff. His remote and recent memories were totally impaired. He was bending down his head and constantly licking his hands. There was increase in deep tendon reflexes and bilateral positive Hoffman and palmomentary reflexes. Apart from these findings, neurological examination was normal. Speech was slurred, pupils were irregular and small not reactive to light but to accommodation, rest of the cranial nerves were intact. Gait was within normal limits and toes were downgoing. No labs or imaging data was available at the time of initial consultation.

DIFFERENTIAL DIAGNOSIS

- Schizophrenia
- Acute psychosis
- seizure disorder
- Alzheimer dementia
- Bipolar disorder
- Other dementias associated with infectious diseases
 - HIV Dementia
 - Herpes encephalitis
 - PML
 - Neurosyphilis
 - CNS Borreliosis
 - Neurobrucellosis
 - CNS Tuberculosis
 - Neurocysticercosis

FINAL DIAGNOSIS

- A tentative diagnosis of neurosyphilis and other infectious causes of dementia was investigated.
- In laboratory tests; complete blood count, sedimentation, biochemical investigations of blood including serum electrolytes, renal and liver function tests were found to be normal. The serologic investigations have shown that in blood serum VDRL and TPHA are positive . In cerebrospinal fluid (CSF) examination VDRL was positive with a 1/64 titer whereas TPHA titer was 1/5120. Microscopic examination of CSF revealed 10 lymphocyte cell. In biochemical assessment of CSF; protein: 72mg/dL, glucose: 59 mg/dL, IL. CSF and serum investigations did not reveal any sign of specific infections or viral diseases including human immunodeficiency virus (HIV)

FINAL DIAGNOSIS

- Magnetic resonance imaging (MRI) of the patient was consistent with cortical atrophy. Electroencephalography (EEG) showed diffuse slowing in bilateral background activity, most significant in temporal areas. Thyroid function tests, serum apolipoprotein A1 and B, serum protein electrophoresis, immunoglobulin G, M and A levels both in CSF and serum were all within normal limits. VDRL and TPHA tests done in his wife were negative.
- Patient was diagnosed as neurosyphilis (general paresis) depending on laboratory tests and symptoms and treatment with penicillin was initiated.

GENERAL PARESIS

- About 5% of patients experience general paresis. Seen 20- 30 years after untreated infection . Symptoms: Personality changes: neurosis, euphoria, depression, over activity, paranoia Affect: Reaction to a problem is inappropriate to the problem. Often act in an "all-out" type of reaction much like a child. Reflexes: Hyperactive Eyes: Argyll Robertson pupils Sensorium: Delusions, illusions, hallucinations, and paranoid ideas Intellect: Reduction in mental capacity, orientation, retention and recall, calculations, judgment, and insight Speech: Slurred speech, S & L pronounced slowly, tremors of lips and tongue, repeats last few words, face often smooth and mask like . Several forms of general paresis :, Early stage, Simple dementia , Euphoric or expansive paretic ,Agitated paretic ,Depressed paretic . General paresis has only one highly suggestive sign, the Argyll Robertson pupil. The AR pupil is small and irregular; it accomodates to near vision but not to light. The other symptoms are nonspecific and may suggest other neurologic diagnoses, e.g. Alzheimer's disease in an elderly patient. The presence of a peripheral serology specific for syphilis (e.g., FTA-ABS) and a reactive CSF VDRL, with or without neurologic findings, should prompt treatment for neurosyphilis.

OUTCOME

- Treatment of general paresis may improve the cognitive or psychiatric disease in relatively early cases . Studies have shown that arrest of disease progression has occurred in one half of advanced cases . For the treatment of the disease in the above treatment , aqueous penicillin G with a dose of 24 million unit/day were given in divided doses for 14 days. No significant change in clinical and mental status of the patient was observed during and after the administration of penicillin regimen. Patient was discharged with the recommendations of repeating penicillin therapy regimen and performing serologic tests for syphilis in both CSF and serum three months later.
- Burke JM, Schaberg DR. Neurosyphilis in the antibiotic era. *Neurology* 1985;35:1368-1371
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CLINICAL QUESTION

The question is posed whether syphilis serology screening in the elderly mentally ill should be confined to those patients with obvious clinical manifestation of syphilis or with obscure psychiatric presentations.

- Christina MM. Neurosyphilis. *Current Neurology and Neuroscience Reports* 2004, 4:435-440.
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- Duffy JD: General paralysis of the insane: neuropsychiatry's first challenge. *J Neuropsychiatry Clin Neurosci* 1995; 7(2): 243-9

DIAGNOSTIC CRITERIA

- 1. Serum MHA-TP or FTA-ABS positive. RPR, VDRL may be negative in late stage.
- 2. CSF pleocytosis with a mild elevation of CSF protein.
- 3. CSF VDRL: low sensitivity (22-69%), but if positive is highly specific for Neurosyphilis.
- 4. CSF FTA-ABS or MHA-TP if negative, exclude diagnosis. If positive, does not confirm diagnosis.

Traditional Criteria (CDC)

- Confirmed case: CSF-VDRL test positive
- Compatible case : pleiocytosis (CSF WBC count $>10/\text{mm}^3$) and CSF protein elevated
- ($> 0.50 \text{ g/l}$)
- Netherlands STD Guidelines 1997
- Prerequisite: Positive CSF-TPHA
- Confirmed case: CSF-VDRL test positive
- Compatible case: CSF-IgG index > 0.70 and WBC count $> 10/\text{mm}^3$

THERAPEUTIC OPTIONS

- Penicillin remains the mainstay of treatment for neurosyphilis. The CDC recommends that neurosyphilis be treated with intravenous aqueous crystalline penicillin G, 18 to 24 million units, divided into six doses daily or as a continuous infusion, for 10 to 14 days. An alternative regimen is intramuscular procaine penicillin G, 2.4 million units once daily with oral probenecid, 500 mg four times daily, both for 10 to 14 days. For penicillin-allergic patients, intramuscular or intravenous ceftriaxone, 2 g once daily is recommended as an alternative. Penicillin skin testing and desensitization are reserved for those individuals in whom the safety of ceftriaxone is of concern . There are few data supporting the efficacy of ceftriaxone for treatment of neurosyphilis; this is especially true for late neurosyphilis.
- Azithromycin has been used to treat early syphilis and incubating syphilis . Because of its excellent CNS penetration, azithromycin could potentially be used to treat neurosyphilis.
- Follow up monitoring:
 - If CSF pleocytosis, repeat CSF every month until cell count is normal
 - If CSF cell count has not decreased after 6 months , or if CSF is not normal after 2 years, consider retreatment.

BOARD TYPE QUESTIONS

1. Which infection has strong epidemiological association with neurosyphilis?

- Lyme borreliosis
- HIV
- Sarcoidosis
- Herpes encephalitis
- Tuberculosis
- Correct answer: B. HIV

BOARD TYPE QUESTIONS

Explanation:

Evidence is shown that syphilis has become a major public health problem again. From 1988 to 1995 the permanently growing number of new cases of syphilis in the world was observed. The majority of the syphilitic cases in the patients are difficult for curing. The central nervous system is often involved in early syphilis. Previously the neurosyphilis was very rare. The reason for development of this stage of syphilis, may be an inadequate treatment as well as a weakening of the immunological responses. The latter one very often is caused by additional non-symptomatic infection including human immunodeficiency virus (HIV). Syphilitic ulcers act as a portal of entry for HIV. Analysis of cases with double infection with *Treponema pallidum* and HIV indicate that HIV infection may accelerate the course of syphilis and the presence of syphilis may also have influence on progression of the chronic HIV infection to AIDS. Taking into account that HIV infection alters the response to the treatment also, one can suggest that all of the patients with syphilis should be examined for the presence of HIV infection.

- Podwinska J, et al .Syphilis and AIDS.Arch Immunol Ther Exp (Warsz). 1996;44(5-6):329-33.
- Holtom PD, Larsen RA, Leal ME, et al: Prevalence of neurosyphilis in human immunodeficiency virus–infected patients with latent syphilis. Am J Med 1992; 93:9–12

BOARD TYPE QUESTIONS

2. What percentage of patients with untreated syphilis develop symptomatic neurosyphilis?

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- a. < 1 %
- b. 1-2 %
- c. 3- 7 %
- d. 4- 9%
- e. 8- 10%

■ Correct answer: D.

An estimated 4- 9 % of patients with untreated syphilis develop symptomatic neurosyphilis, with meningovascular syphilis in 2-3 %, general paresis in 2-5%, and Tabes dorsalis in 1- 5%.

BOARD TYPE QUESTIONS

3. Which of the statement about Jarisch-Herxheimer reaction is correct.
- a. Occurs 2 to 6 hours after starting Syphilis treatment
 - b. Symptoms last for 24 hours
 - c. Occurs in 25 % cases of latent syphilis
 - d. Characterized by fever, rigors, adenopathy and arthralgias.
 - e. All the above are true.

Correct answer: E

The Jarisch-Herxheimer reaction describes the release of endotoxin when large numbers of organisms are killed by antibiotics. It is seen in 50% of patients with primary syphilis and about 90% of patients with secondary syphilis. It is not a dose related phenomenon; thus giving a smaller dose is of no value.

PATIENT RESOURCES

The following sites are useful if more information on syphilis is sought:

- www.cdc.gov Centres for Disease Control
- www.who.int World Health Organization
- www.ashastd.org American Social Hygiene Association
- www.vnh.org Virtual Naval Hospital

COMMENTS

Neurosyphilis among elderly patients remains an important public health problem. New cases are not adequately detected, and delay in diagnosis is common: often clinical presentation does not follow the traditional course; mental changes may imitate other types of dementia and psychiatric disorders; and stroke is often attributed to age and associated risk factors. All elderly patients with neurological or psychiatric disorders of doubtful etiology should have syphilis serology checked routinely.

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