Rapidly Progressive Dementia in a Patient with a Prior History of Yaws Disease, Could this be Neuroyaws?

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Abstract

Whether non-venereal treponematosis infection can cause neurological complications remains uncertain. We present a case of an elderly man with a childhood history of yaws infection and positive syphilis serology presenting with rapidly progressive dementia and neuropsychiatric symptoms consistent with neurosyphilis. The patient passed away one year from the onset of symptoms following a rapid downhill course. Given the effectiveness of antibiotic treatment, clinicians should be highly suspicious of the possibility of central nervous system involvement in patients with a prior history of non-venereal treponematosis.

Keywords: Neurophilis; Dementia; Neuropsychiatry; Endemic Treponematosis; Yaws; Neuroyaws

Introduction

Venereal syphilis is caused by *T. pallidum pallidum*, while non-venereal treponematoses or endemic treponematases (ET) are classified by different subspecies of *T. pallidum: yaws* by *T. p. pertenue*, bejel by *T. p. endemium*, and pinta by *T. p. carateum*. The non-venereal treponematoses are so genetically similar to *T. p. pallidum* that they are indistinguishable in commonly used serology tests for syphilis and respond equally well to penicillin treatment [1]. These spirochetes are thought to affect at least 2.5 million people worldwide [2]. Since 1980, there has been an upsurge in new ET infections in West Africa, South America, Southeast Asia, the South Pacific islands, and the Middle East [3-20], which has caused the World Health Organization to push for new eradication strategies [21]. When comparing syphilis and ETs symptoms, the familiar syphilis finding of gummatous bone and cartilage destruction is well-established in yaws and bejel; however, only syphilis has proven findings of central nervous system involvement. We present a case of an elderly patient with a history of childhood yaws infection and a late-life presentation of rapidly progressive neuropsychiatric abnormalities.

Case Report

A 79-year-old Jamaican male with a recent diagnosis of dementia and no past psychiatric history was referred to a geriatric psychiatry unit from his nursing home for management of agitation and combative paranoid behavior. Communication from the nursing home indicated that over the past few months the patient's confusion and paranoia had worsened, and he had begun to express concerns that the staff intended to hurt him. The patient's daughter was able to establish that the onset of the dementia was one year prior to the admission and appeared to have rapidly worsened with impairment in recent and remote memory. The daughter stated that the patient was legally blind, having gradually lost most of his sight over a two-year period. She recalled a few episodes of visual hallucinations in which the patient reported seeing nits and shadows. Upon admission, the patient had a positive syphilis IgG and a rapid plasmin reagin (RPR) titer of 1:8 compared to 1:4 noted three months earlier. Medical work up failed to identify any other correctable causes for the patient's confusion and agitation.

Review of past medical history found the patient had a history of yaws, as he was born in Jamaica at a time when yaws was endemic; proof of adequate antibiotic treatment could not be confirmed. In addition, whether the patient had ever developed syphilis or if his lifestyle placed him at risk for syphilis could not be established. Physical examination showed slurred speech, generalized weakness, and limited lateral eye movement. Reflexes were globally absent, sensation testing was unreliable, and Romberg's sign was positive. The patient was mostly confused and disoriented during the admission. Agitation, restlessness, and insomnia were prominent features. Detailed cognitive testing was not possible due to patient's inability to cooperate.

Three months prior to contact with the patient, he had been admitted to a medical unit with generalized weakness, slurred speech, and facial droop. The symptoms were attributed to a possible transient ischemic attack (TIA). During that admission, the patient was described as confused and agitated. He was seen by neurology and infectious disease services for a mildly elevated RPR titer at 1:4. Numerous attempts to perform lumbar puncture (LP) for a CSF-VDRL test were unsuccessful due to dry taps. Brain MRI appreciated parenchymal volume loss and noticeable atrophy compared to a brain MRI obtained 3 years earlier. EEG demonstrated diffuse slowing compatible with encephalopathy, and MRI of the lumbar spine revealed moderate to severe spino stenosis at the L3-L4 level.

Discussion

Over the course of one year, the patient went from a new diagnosis of dementia to rapidly progressive symptoms that resulted in his death. While rapidly progressive dementia occurs rarely in patients suffering from neurodegenerative disorders, it is far more commonly associated with infectious diseases of the central nervous system (CNS). The patient presented with rapidly progressive dementia associated with neuropsychiatric symptoms, which is the most common form of presentation of general paresis. Symptoms of general paresis include personality changes, amnesia, delirium, delusions, and hallucinations with less frequent presentation of stroke, cranial nerve, and brainstem dysfunction. The patient presented with hypotonia, loss of reflexes, rapid
impairment of vision, urinary incontinence, generalized weakness, and positive Romberg’s sign. Such a clinical presentation is commonly seen in patients with tubas dorsalis [22,23]. Taboparesis describes the simultaneous occurrence of both tubas dorsalis and general paresis and suggests widespread parenchymal damage that occurs in patients with parenchymatous neurosyphilis. Furthermore, patients with neurosyphilis can present with stroke or TIA symptoms, as a result of meningovascular involvement. Although meningovascular disease more commonly precedes general paresis and tubas dorsalis, overlap is not unheard of in the literature [23,24].

Literature has described neurologic and ophthalmologic abnormalities possibly caused by yaws and bejel but without firm evidence of a causal relationship [1,25-27]. It is generally believed that non-venereal treponematoses do not affect the CNS; however, case reports of optic atrophy [1] and cerebrospinal fluid abnormalities [28] suggest otherwise. Roman and Roman looked at associations between myelopathies and late yaws and proposed that all potential complications of veneral syphilis are possible including neurologic pathology [29].

In the case of this patient, if the patient did suffer from a CNS infection, the patient’s positive serology did not allow the clinician to decipher between yaws and syphilis [30]. Nevertheless, the treatment is similar [1,31] and it would be incumbent on clinicians to treat the patient to prevent further disease progression. Moreover, given the difficulties of performing a LP in this patient due to spinal stenosis, we believe a risk-benefit analysis might well have concluded that proceeding with antibiotic treatment on an empirical basis was warranted. The literature shows that patients who have dementia due to neurosyphilis often have only a partial recovery after antibiotic treatment [32]. Psychosis and behavioral manifestations show a particularly variable response with some authors reporting an improvement of psychotic symptoms with penicillin treatment; however, the overall benefit of antibiotics therapy is limited in advanced neuronal damage [33,34]. While treatment of late stage neurosyphilis is not likely to eliminate all associated symptoms [22,32], the treatment has a reasonable chance of improving the patient’s quality of life.

Of special note, low or negative serum RPR titers can occur in patients with symptoms consistent with neurosyphilis [35] and should not discourage clinicians from pursuing diagnosis and treatment. As per CDC guidelines, LP is indicated in patients with syphilis who have not discourage clinicians from pursuing diagnosis and treatment. As per CDC guidelines, LP is indicated in patients with symptoms consistent with neurosyphilis [22,32], the treatment has a reasonable chance of improving the patient’s quality of life.

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Conflict of Interest

The authors declare no conflict of interests.

References

1. Farnsworth N, Rosen T (2006) Endemic treponematoses: review and update. Clin Dermatol 24: 181-190.
2. Antal GM, Lukehart SA, Meheus AZ (2002) The endemic treponematoses. Microbes Infect 4: 83-84.
3. Hopkins DR, Flórez D (1977) Pinta, yaws, and venereal syphilis in Colombia. Int J Epidemiol 6: 349-355.
4. Organization WH (1981) Endemic Treponematoses. Wkly Epidemiol Rec 1: 241-244.
5. Pace JL, Csonka GW (1984) Endemic non-venereal syphilis (bejel) in Saudi Arabia. Br J Vener Dis 60: 293-297.
6. [No authors listed] (1985) International Symposium on Yaws and Other Endemic Treponematoses. Washington, D.C., April 16-18, 1984. Rev Infect Dis 7 Suppl 2: S217-S351.
7. Csonka G, Pace J (1985) Endemic nonvenereal treponematoses (bejel) in Saudi Arabia. Rev Infect Dis 7 Suppl 2: S260-S265.
8. Widy-Wirek R (1985) Surveillance and control of resurgent yaws in the African region. Rev Infect Dis 7 Suppl 2: S227-232.
9. Fohn MJ, Wignall S, Baker-Zander SA, Lukehart SA (1988) Specificity of antibodies from patients with pinta for antigens of Treponema pallidum subspecies paliidum. J Infect Dis 157: 32-37.
10. Gazin P, Meynard D (1988) [A clinical and serologic survey of bejel in north Burkina Faso]. Bull Soc Pathol Exot Filiales 81: 827-831.
11. Pecher SA, Croce J (1988) [Immunology of tularaemia]. Med Cutan Ibero Latino 16: 111-114.
12. Autier P, Delcambe JF, Sangaré D, Lamine D, Kessler W, et al. (1989) [Serological and clinical studies of endemic treponematoses in the Republic of Mali]. Ann Soc Belg Med Trop 69: 319-329.
13. Yakinci C, Ozcan A, Aslan T, Demirhan B (1995) Bejel in Malatya, Turkey. J Trop Pediatr 41: 117-120.
14. Julvez J, Michault A, Kerdelhue V (1998) [Serologic studies of non-venereal treponematoses in infants in Niafey, Niger]. Med Trop (Mars) 58: 36-40.
15. Manning LA, Ogle GD (2002) Yaws in the periurban settlements of Port Moresby, Papua New Guinea. P N G Med J 45: 206-212.
16. Giuliani M, Latini A, Palamara G, Maini A, Di Carlo A (2005) The clinical appearance of pinta mimics secondary syphilis: another trap of treponematosis? Clin Infect Dis 40: 1548.
17. Toure B, Koffi NM, Assi PK, Ake O, Konan DJ (2007) [Yaws in Côte d'Ivoire: health problem forgotten and neglected]. Bull Soc Pathol Exot Filiales 100: 130-132.
18. Capuano C, Ozaki M (2011) Yaws in the Western pacific region: a review of the literature. J Trop Med 2011: 642832.
19. [No authors listed] (2012) Eradication of yaws—the Morges strategy. Wkly Epidemiol Rec 87: 189-194.
20. Abdolrasouli A, Croucher A, Hemmati Y, Mabey D (2013) A case of endemic syphilis, Iran. Emerg Infect Dis 19: 162-163.
21. World Health O (2012) Summary report of a consultation on the eradication of yaws, 5-7 March 201, Morges, Switzerland.
22. Stefani A, Riello M, Rossini F, Mariotto S, Freni F, et al. (2013) Neurosyphilis manifesting with rapidly progressive dementia: report of three cases. Neurol Sci 34: 2027-2030.
23. Mehrabian S, Raycheva MR, Petrova EP, Tsvankov NK, Traykov LD (2009) Neurosyphilis presenting with dementia, chronic chorioretinitis and adverse reactions to treatment: a case report. Cases J 2: 8334.
24. Miklossy J1 (2008) Biology and neuropathology of dementia in syphilis and Lyme disease. Handb Clin Neurol 89: 825-844.
25. MiğA O, A majs D, Bassat Q (2013) Advances in the diagnosis of endemic treponematoses: yaws, bejel, and pinta. PLoS Negl Trop Dis 7: e2283.
26. Hoff H, J Shaby (1940) Nervous manifestations of bejel. Transactions of the Royal Society of Tropical Medicine and Hygiene 33: 549-551.
27. Smith JL (1971) Neuro-ophthalmological study of late yaws. J. Neuroophthalmology 1: 80-89.
28. Hewer TF (1934) Some observations on yaws and syphilis in the Southern Sudan. Transactions of The Royal Society of Tropical Medicine and Hygiene 27: 593-608.

29. Roman GC, Roman LN (1986) Occurrence of congenital, cardiovascular, visceral, neurologic, and neuro-ophthalmologic complications in late yaws: a theme for future research. Rev Infect Dis 8: 760-70.

30. de Capraris PJ, Della-Latta P (2013) Serologic cross-reactivity of syphilis, yaws, and pinta. Am Fam Physician 87: 80.

31. Marks M, Lebari D, Solomon AW, Higgins SP2 (2014) Yaws. Int J STD AIDS .

32. Takada LT, Caramelli P, Radanovic M, Anghinah R, Hartmann AP, et al. (2003) Prevalence of potentially reversible dementias in a dementia outpatient clinic of a tertiary university-affiliated hospital in Brazil. Arq Neuropsiquiatr 61: 925-929.

33. Wahab S, Md Rani SA, Sharis Othman S (2013) Neurosyphilis and psychosis. Asia Pac Psychiatry 5 Suppl 1: 90-94.

34. Friedrich F, Geusau A, Friedrich ME, Vyssoki B, Pfleger T, et al. (2012) [The chameleon of psychiatry - psychiatric manifestations of neurosyphilis]. Psychiatr Prax 39: 7-13.

35. Nitrini R (2010) Did you rule out neurosyphilis. Dementia & Neuropsychologia 4: 338-345.

36. Pastuszczak M, Wojas-Pelc A (2013) Current standards for diagnosis and treatment of syphilis: selection of some practical issues, based on the European (IUSTI) and U.S. (CDC) guidelines. Postepy Dermatol Alergol 30: 203-210.