# The great imitator: neurosyphilis presenting as subacute confusion

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## Introduction

Neurosyphilis often presents with non-specific symptoms and is challenging to diagnose. As a result, it is not routinely considered in the differential diagnosis for confusion and is easily missed.

This article presents a case of a 69-year-old man who presented to his GP with worsening confusion and an unsteady gait. A confusion screen, including syphilis serology, was performed in primary care. His syphilis serology was positive, so he was admitted to hospital for further investigations. CSF syphilis serology confirmed the diagnosis of neurosyphilis. This case highlights important learning points regarding the diagnosis, workup and management of neurosyphilis, and serves as a reminder to consider syphilis serology in patients presenting with confusion.

## Case report

A 69-year-old Caucasian man presented to his GP with worsening confusion and unsteadiness. He had a background of previous ischaemic stroke, aortic stenosis (bicuspid aortic valve), Barrett's oesophagus and benign prostatic hyperplasia. He was independent in all activities of daily living, was an ex-smoker and drank two glasses of wine a day.

A confusion screen revealed normal calcium and folate levels, normal thyroid function, and mild vitamin $B_{12}$ deficiency which was replaced accordingly. Computed tomography of the head revealed an old infarct in the right frontal corona radiata and mild small vessel disease changes. Of note, syphilis serology was positive for Treponema pallidum particle agglutination assay (TPPA) and syphilis rapid plasmin reagin titre (1:16), which was confirmed at the reference laboratory.

He was admitted to hospital for further investigations, as the possibility of neurosyphilis was considered. The patient reported having had many casual male and female sexual partners, and denied being treated for syphilis previously. His wife reported unusual behaviour over the last 3 months, including driving on the pedestrian lane and forgetting his way around the house. Systems review was unremarkable apart from occasional urinary incontinence.

The patient was haemodynamically stable on examination. He had a slow rising pulse and an ejection systolic murmur radiating to the carotids, in keeping with aortic stenosis. His Glasgow Coma Scale was 15/15 and abbreviated mental test score was 5/5. Apart from an ataxic gait and a positive Romberg's test, neurological examination was otherwise normal. Mini mental state examination performed revealed a score of 26/30. He lost 3 points on counting backwards from 100 by sevens and 1 point on copying a diagram of two intersecting pentagons.

The initial differential diagnosis included neurosyphilis with probable tabes dorsalis, Wernicke's encephalopathy and vascular dementia.

Initial baseline blood tests were unremarkable and a sexually transmitted infection screen for HIV, chlamydia and gonorrhoea was negative. Electrocardiogram showed sinus rhythm with left axis deviation, and an echocardiogram revealed severe aortic stenosis, with normal left ventricular size and function. Magnetic resonance imaging of the brain showed evidence of chronic small vessel disease.

Repeat syphilis serology was positive for syphilis IgM, TPPA and the Venereal Disease Research Laboratory (VDRL) test. CSF microscopy revealed raised levels of polymorphs ($72 \times 10^6$/litre), lymphocytes ($112 \times 10^6$/litre) and red blood cells of $8 \times 10^6$/litre. Even in the absence of plasma glucose at the time of sampling, the CSF glucose was significantly low at 1.5 mmol/litre. Gram stain and viral polymerase chain reaction were negative. Reference laboratory CSF syphilis serology was positive for treponema IgM, IgG, TPPA and VDRL, confirming the diagnosis of neurosyphilis.

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**Case report (continued)**

He was commenced on ceftriaxone for 14 days and prednisolone for 3 days, as per British Association for Sexual Health and HIV guidelines. Contact tracing was also undertaken.

On review 1 month after discharge, the patient reported an improvement in memory, with an objective improvement in his mini mental state examination score to 30/30. Serological testing revealed improvement in rapid plasmin reagin titre to 1:4. He was due to have repeat CSF at 3, 6 and 12 months but died from decompensated cardiac failure. Interestingly, postmortem examination of the brain and aorta did not show evidence of syphilis-related disease. Specifically, there were no pathological changes in the leptomeninges or cerebral cortex, and preparations for spirochaetes were negative.

## Discussion

Syphilis is caused by a spirochaete bacterium, *Treponema pallidum*, and is transmitted sexually, or vertically via the placenta. Stages of infection can be classified into primary, secondary, latent and tertiary syphilis. There are three manifestations of tertiary syphilis: neurosyphilis, gummatous and cardiovascular syphilis (Kingston et al, 2016).

Early neurosyphilis occurs weeks to years after primary infection, affecting the CSF, meninges and vasculature. Symptoms include headaches, emotional lability and insomnia. Late neurosyphilis occurs 10–25 years after infection, affecting the brain and spinal cord parenchyma. Forms of late neurosyphilis include general paresis and tabes dorsalis. General paresis presents with forgetfulness, personality changes and seizures. Tabes dorsalis results from dorsal column inflammation, causing ataxia, areflexia and pupillary changes (Ghanem, 2010; Wasserman et al, 2011; Kamath et al, 2013; Kingston et al, 2016; Prynn et al, 2016; Vora and French, 2018; Marra, 2020).

A thorough history, including sexual history, is important to identify the stage of infection. Clinical examination of the skin, genitalia, neurological and cardiovascular systems is important to identify potential complications. As *T. pallidum* cannot be cultured using standard methods, various serological tests are used to diagnose syphilis (Kingston et al, 2016).

Penicillin is an effective treatment, as *T. pallidum* does not have the molecular machinery to develop resistance. The British Association for Sexual Health and HIV recommended first-line treatment for neurosyphilis is procaine penicillin and probenecid for 14 days (Kingston et al, 2016). An alternative regimen is ceftriaxone for 10–14 days, which can be given in the outpatient setting given its once-daily dosing regimen (Kingston et al, 2016). A 3-day course of prednisolone should be given 24 hours before initiating antibiotics, to prevent fever associated with the Jarisch–Herxheimer reaction. It is also important to discuss partner notification and offer treatment to asymptomatic contacts.

This case highlights an important learning point that syphilis can present non-specifically and should be considered as part of a confusion screen (Barrett and Burns, 2014; National Institute for Health and Care Excellence, 2018).

## Learning points

- Consider syphilis in patients presenting with confusion or neuropsychiatric symptoms.
- Remember to take a thorough sexual history to identify the stage of infection and potential complications.
- Diagnosis is a challenge as *Treponema pallidum* cannot be cultured using standard methods, and serology is challenging to interpret.
- Penicillin is still an effective treatment as *T. pallidum* does not have the molecular machinery to develop resistance.
- Remember to discuss partner notification and offer treatment to asymptomatic contacts if appropriate.

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## References

Barrett E, Burns A. Dementia revealed: what primary care needs to know. 2014. https://www.england.nhs.uk/wp-content/uploads/2014/09/dementia-revealed-toolkit.pdf (accessed 23 April 2021)

Ghanem KG. Review: Neurosyphilis: a historical perspective and review. CNS Neurosci Ther. 2010;16(5):e157-168–e168. https:/doi.org/10.1111/j.1755-5949.2010.00183.x

Kamath M, Rizvi M, O'Nions J, Brook G. A complex neurological presentation of syphilis. BMJ Case Rep. 2013;2013:bcr2013200309. https:/doi.org/10.1136/bcr-2013-200309

Kingston M, French P, Higgins S et al. UK national guidelines on the management of syphilis 2015. Int J Std Aids. 2016;27(6):421–446. https:/doi.org/10.1177/0956462415624059

Marra CM. Neurosyphilis. 2020. https://www.uptodate.com/contents/neurosyphilis#H4 (accessed 28 May 2021)

National Institute for Health and Care Excellence. Dementia: assessment, management and support for people living with dementia and their carers. 2018. https://www.nice.org.uk/guidance/ng97/resources/dementia-assessment-management-and-support-for-people-living-with-dementia-and-their-carers-pdf-1837760199109 (accessed 2 June 2021)

Prynn J, Hussain A, Winnett A. Diagnosing neurosyphilis: a case of confusion. BMJ Case Rep. 2016;2016:bcr2016216582. https:/doi.org/10.1136/bcr-2016-216582

Vora N, French P. Don't forget about syphilis: the great pretender. Br J Hosp Med. 2018;79(4):188–189. https:/doi.org/10.12968/hmed.2018.79.4.188

Wasserman S, Vallie Y, Bryer A. The great pretender. Lancet. 2011;377(9781):1976. https:/doi.org/10.1016/S0140-6736(11)60365-6