CASE REPORT

A complex neurological presentation of syphilis

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SUMMARY

Syphilis is a contagious sexually transmitted infection notable for its complex array of systemic presentations. It is caused by the spirochaete *Treponema pallidum* and although once considered to be a largely historical condition in the UK, the recent rise in incidence makes syphilis increasingly relevant when considering unusual presentations in at-risk patients. The disease has three stages: primary, secondary and tertiary. The tertiary stage is associated with a plethora of neurological features ranging from psychosis to seizure caused by direct invasion of the spirochaete into the central nervous system. Here we describe the case of a 45-year-old man presenting with tonic clonic seizures on a background of balance and visual problems. Following normal examination and routine investigations further serology confirmed a diagnosis of neurosyphilis. The patient was started on appropriate treatment and made an excellent clinical recovery.

BACKGROUND

With over 3000 new cases annually,¹ syphilis remains a relatively rare disease. However, its resurgence in recent years (especially in men who have sex with men and in the presence of HIV coinfection)¹ combined with its highly variable manifestations make syphilis an important consideration when investigating complex presentations with a wide differential diagnosis. About 30–40% of untreated syphilis cases will go on to develop symptomatic late disease,² and although neurological features can occur early in the disease process, they typically develop many years after initial infection (with up to a 25-year incubation period).³

This complex presentation of syphilis in a previously undiagnosed patient highlights how syphilis is still a relevant disease deserving consideration even in complex neurological patients.

CASE PRESENTATION

History

A left handed 45-year-old man presented to the Accident and Emergency with a tonic-clonic seizure lasting 1–2 min and underwent a further similar seizure while in hospital. The initial seizure was preceded by paraesthesiae with mild weakness in all limbs and post-ictally the patient experienced weakness in his right arm lasting 20 min. He had not experienced a seizure before, was not a known epileptic and had no family history of seizures.

On questioning, the patient described intermittent clumsiness and numbness in his left hand with mild and fluctuating balance problems in the 6 months preceding his admission. In addition, he reported gradual reduction in visual acuity in his

left eye which had been identified on routine testing at work. He was otherwise well and had not experienced any other visual, sensory, motor or bowel/bladder disturbance. Some years prior he had contracted gonorrhoea which was treated with a single dose of intramuscular ceftriaxone. He was not screened for syphilis at this time but had undergone regular negative HIV testing.

The patient took no medications and drank alcohol very occasionally. He did not smoke or take illicit drugs. He worked as a roadside mechanic and for 6 years had been in a monogamous relationship with a single male partner.

Examination

Neurological examination revealed normal tone and power throughout with normal cranial nerves. There was mild impairment of coordination in his left hand and his gait appeared slightly unsteady.

Ophthalmology testing revealed slight refractive error in the left eye but normal optic discs.

INVESTIGATIONS

Blood tests were unremarkable except for a raised white cell count of $11.9 \times 10^9/L$ (neutrophils 10.2). Vasculitis serology (including antinuclear antibody, anti-ds-DNA and complement) was normal and HIV testing was negative.

Cerebrospinal fluid (CSF) analysis showed a reactive picture with raised protein and white cell count ($55/mm^3$ and $1.16 g/L$ respectively). Viral PCR (including enterovirus and herpes simplex virus) was negative and there was no bacterial growth. Cryptococcal and tuberculosis tests were also negative.

CT and MRI brain imaging showed no focal abnormalities.

Further serological testing was syphilis enzyme immunoassay positive with a high rapid plasma reagin (RPR) titre of 1:128.

DIFFERENTIAL DIAGNOSIS

- Epilepsy
- Infection: encephalitis, meningitis, neurosyphilis
- Demyelinating disease
- Cerebral vasculitis

TREATMENT

Immediate management included empirical treatment for encephalitis with intravenous aciclovir and cefotaxime while CSF and serological results were pending. He was also started on Levetiracetam as seizure prophylaxis due to the unusual nature of his presentation with no clear provoking cause for his seizures.

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On obtaining positive syphilis serology the patient was immediately reviewed by the infectious diseases team and treatment for neurosyphilis was started. As per UK guidelines this entailed 17 days of intramuscular procaine penicillin and oral probenecid (to reduce renal excretion of penicillin).⁴ He also received three days of oral prednisolone as prophylaxis for the Jarisch-Herxheimer reaction.

OUTCOME AND FOLLOW-UP

The patient was discharged home following the initial three days of treatment in which he was monitored for the Jarisch-Herxheimer reaction. He was informed that he was obliged to stop driving and to alert the Driver and Vehicle Licensing Agency (DVLA) that he had experienced seizures. This was of extra significance given that the patient's occupation entailed the driving of heavy goods vehicles.

He received genitourinary and neurology follow-up for review of symptoms and RPR monitoring to ensure eradication of the disease.

His symptoms greatly improved and the RPR titre fell dramatically within three months so it was decided he did not require a repeat lumbar puncture to obtain a gold standard diagnosis.

Neuropsychometry was arranged for formal memory assessment as it was later found he had been experiencing a degree of cognitive impairment. Six months later the patient had made a complete recovery.

DISCUSSION

Seizure is a relatively uncommon feature of neurosyphilis, present in roughly 7% to 25% of cases.^{5–7} The more common presentations are neuropsychiatric, consisting of psychosis, delirium and dementia.⁸ Other presentations include cerebrovascular accidents (14.9%), ocular symptoms (11.9%) and myelopathies (9.3%).⁵ Recently Omer *et al*⁹ reported neurosyphilis presenting as acute collapse with MRI brain changes, whereas Hajjaj *et al*¹⁰ highlighted the case of a 49-year-old man with a longstanding chancre presenting as status epilepticus. In this instance a CT head demonstrated ventricular collapse and loss of sulci. This is in contrast to our case in which imaging was normal despite the patient experiencing significant symptoms. Neurosyphilis has even been reported to mimic a Jacksonian epilepsy-related hemiparesis.¹¹ As well as a wide variety of neurological presentations, these cases highlight that neurosyphilis even has a wide variety of seizure presentations and is to be considered in patients presenting with seizures of unclear cause.

Although HIV testing was performed when the patient was treated for gonorrhoea, syphilis was not screened for at that time. White *et al*¹² found that less than a third of patients tested for gonorrhoea and chlamydia were also screened for syphilis. This is disappointing considering how readily syphilis can be treated with prevention of progression to late disease.

This patient received a single dose of intramuscular ceftriaxone (500 mg) as treatment for gonorrhoea (as per national guidelines).¹³ Although courses of ceftriaxone at a higher dose for durations in excess of two weeks have been shown to effectively treat neurosyphilis,¹⁴ high failure rates (up to 23%)¹⁵ combined with limited trial data mean it is not considered first line.¹⁶ A 17-day course of intramuscular procaine penicillin with probenecid remains the recommended treatment for neurosyphilis,^{4 17} and it is unlikely that the single 500 mg dose of ceftriaxone would have been sufficient to eradicate syphilis infection in this case.

Syphilis was not tested for on initial CSF examination even though a positive CSF result is required to make a gold standard

diagnosis. While this case highlights the importance of thorough CSF examination (especially in neurological disease in men who have sex with men), syphilis CSF screening may not be as reliable as previously thought with up to 50% of neurosyphilis cases having negative CSF testing.¹⁸ This brings into question whether a negative CSF result can reliably exclude neurosyphilis in cases with high clinical suspicion.

Learning points

- Syphilis is still a significant and potentially debilitating sexually transmitted infection (STI) which can be easily treated. It is important to screen for syphilis when treating more common STIs.
- Syphilis has a wide variety of neurological presentations, not just memory and cognitive problems (serological testing forms an important part of the 'dementia screen').
- HIV-negative status does not negate the need to screen for other STIs which may be asymptomatic at that time.
- Take an adequate volume of cerebrospinal fluid, it is difficult to predict how many tests may be required.
- Brain imaging may be normal even in patients with significant symptoms of neurosyphilis.

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