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Sequential Bilateral Facial Nerve Palsy– A Rare Presentation Of Neurosyphilis

Case Report

ABSTRACT:

A middle-aged gentleman presented with sequential bilateral facial nerve palsy and ataxia. Diagnostic work-up revealed positive blood serology for an active syphilis infection. Interestingly, his cerebrospinal fluid was negative for syphilis. The patient responded to treatment with benzylpenicillin and made a complete recovery. Unfortunately, the diagnosis of neurosyphilis 'still' poses a challenge to clinicians due to the deficiency of 'sensitive' testing modalities and diagnostic criteria available.

We highlight the need for a low threshold to test for syphilis in patients presenting with neurological sequelae where the diagnosis is not clear.

KEYWORDS

Neurology, Syphilis, Sexual transmitted infections, Facial Palsy

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BACKGROUND:

Bilateral facial palsies are remarkably rare, representing only 0.3%-2% of facial palsy presentations globally. They often indicate serious underlying systemic disease necessitating urgent medical intervention [1] and prompt management. Although facial palsies are largely known to be idiopathic; inflammatory, infiltrative, and infectious causes including syphilis and Lyme disease - should be excluded. [2]

The incidence of syphilis has increased over the last two decades, with neurosyphilis being a relatively common complication that can occur at any stage of the disease.[3] Neurosyphilis can present with an array of neurological symptoms including peripheral neuropathies, ataxias, and cranial nerve palsies [4], but bilateral facial palsies have seldom been noted in literature to date.[5] Unfortunately, the diagnosis of neurosyphilis 'still' poses a challenge to clinicians due to the relatively low incidence of neurosyphilis and lack of diagnostic criteria available.[6]

Here, we report an unusual case of neurosyphilis presenting with a bilateral facial palsy and ataxia. This study demonstrates the importance of having a low threshold for testing for syphilis in patients with unusual neurological presentations.

CASE PRESENTATION:

A middle-aged gentleman with a background of dyslipidaemia presented with a 3-week history of right-sided facial droop and difficulty whistling. He was initially treated for a Bell's palsy 3 weeks prior to review and was subsequently managed with a course of high dose steroids. Unfortunately, this did not improve his clinical picture and he returned with drooling, headache, and difficulty walking. Social aspects of his history revealed that he engaged with male sexual partners and was a current smoker, smoking 3-4 cigarettes per day for over 30 years.

There was no history of genital ulceration or discharge, and no rashes on the palms and soles. The patient denied a history of inflammatory or maculopapular dermatoses, and he did not experience weight loss, fatigue, fevers or upper respiratory tract symptoms.

On neurological examination, he was noted to have bifacial weakness, increased tone in the left lower limb, left sided dysdiadochokinesia and gait ataxia. On ophthalmic examination there was evidence of reduced corneal reflexes bilaterally, accompanied by multidirectional nystagmus. The rest of his physical examination was unremarkable.

INVESTIGATIONS AND DIAGNOSES:

The causative diagnosis for a facial nerve palsy can be subcategorized into autoimmune, idiopathic, traumatic, vascular, neoplastic, and infectious. [3] Given the extensive possible differential diagnoses, a thorough work-up was initiated to identify the cause in our patient.

His blood serology revealed he had an active primary/secondary syphilis infection, given his positive treponemal EIA (enzyme immunoassays), TPPA (Treponema pallidum particle agglutination assay) and RPR (Rapid plasma regain) tests (table 1). His HIV serology was negative upon initial investigation. Although his lumbar puncture revealed lymphocytosis and mildly elevated protein levels, which are both in keeping with the diagnosis of neurosyphilis [7,8], his cerebrospinal fluid (CSF) VDRL (Venereal Disease Research Laboratory) test was negative (table 1).

A magnetic resonance imaging (MRI) of his brain excluded other potential differential diagnoses for his presentation. An incidental lymph node prominence was noted on his CT whole body scans (table 2) which were initially performed to rule out potential malignant causes for his presentation. Subsequent biopsies and fine needle aspiration (FNA) cytology of these lymph nodes did not provide a definitive correlation but did rule out malignancy (within its limitations). A diagnosis of neurosyphilis was further suggested by a definitive response to treatment with benzylpenicillin.

TREATMENT

He was treated with intravenous Benzylpenicillin 2.4g every four hours for fourteen days. He was also provided with eye care, as he was at risk of exposure keratitis secondary to his facial palsy. He was regularly reviewed by the physiotherapists both as an inpatient and outpatient for the initiation of facial exercises.

OUTCOME AND FOLLOW-UP:

The patient continued to improve with physiotherapy even after discharge. At a follow-up consultation 6-weeks later, his symptoms of ataxia had improved, and he was discharged from further review.

DISCUSSION

The incidence of primary and secondary syphilis, also known as the sexually transmissible stages of the infection, has been increasing over the last two decades. In June 2019, Public Health England initiated an ‘urgent action plan’ addressing this sudden surge.[9] Neurosyphilis remains a common complication that can occur at any stage of the disease.[3] Prompt investigation and treatment is quintessential, given the risk of developing tertiary disease, which can often be life threatening and difficult to manage. [10]

Interestingly, the epidemiology of neurosyphilis has largely paralleled that of syphilis in general. Infection by *Treponema pallidum* (the causative agent) can affect the meninges, brain, brainstem, spinal cord, nerve roots and cerebral vasculature. As a result, the disease often presents in a diverse, diagnostically challenging fashion.[11]

Neurosyphilis can present with cranial nerve palsies, although this is uncommon in comparison to other neurological phenomena such as gait ataxia, peripheral neuropathies and reflex abnormalities.[4] Many case reports [12,13] describe the presentation of unilateral facial palsies with *Treponema pallidum* infection, which are more commonly seen in those with HIV infection. The rare presentation of a bilateral facial palsy [14] as seen in our patient, especially in a HIV-negative individual is not frequently seen.[5] His

HIV serology was negative upon initial investigation; however, this was not repeated thereafter. Although he did not confirm symptoms of seroconversion; we consider this a limitation to our case study.

Bilaterality makes facial neuropathy a more worrying sign with widely varying causes that requires prompt investigation. Interestingly, an analysis of 43 cases of bilateral facial palsy revealed syphilis as a cause for only 5% of presentations.[15] Nevertheless, Given the increasing prevalence of such atypical presentations, syphilis screening should be considered in such patient cohorts.

Another diagnosis to consider in this instance would be that of sarcoidosis, which can also present with unusual neurological sequalae. However, given that his symptomologies did not settle with initial steroid treatment (given for a preliminary diagnosis of Bell's palsy), coupled with the absence of thoracic adenopathy (seen in 85-90% of patients with sarcoidosis), and granulomata on FNAC, makes this diagnosis unlikely. [16] We could have proceeded to specific sonographic imaging but felt this was not necessary in the context of a likely diagnosis of syphilis in this case.

Laboratory diagnosis of neurosyphilis remains challenging, because to date, no single lab test is both sufficiently sensitive and specific in diagnosing neurosyphilis, and a negative CSF result does not rule out the diagnosis entirely. [8] According to existing evidence, the diagnosis is largely based on abnormal serum and CSF testing. A positive CSF VDRL test is highly specific for neurosyphilis [3] and remains the 'gold standard' [11], however, its sensitivity ranges from 30-70%[7], making it unreliable at times. Some authors advocate against its use, claiming that patients having neurosyphilis may not necessarily have VDRL-reactive CSF or any CSF abnormalities altogether (4).

A systematic review of 18 studies established that a positive CSF treponema test has a weak association with the diagnosis of neurosyphilis, demonstrating that a negative test cannot exclude the diagnosis entirely[.[8] Similarly, a retrospective cohort study conducted on 27 patients (with syphilis and neurological deficit) in 1997 found that, of the seven, thought to have a diagnosis of neurosyphilis (and underwent CSF examination), only 'two' patients had a reactive CSF-FTA. [17] Nevertheless, all of these 'suspected' patients were treated with penicillin as per guidance [11] and recovered well.

Although our patient had a negative CSF VDRL test, we could have considered a CSF FTA-ABS test. However, some authors advocate that, while a positive CSF-VDRL often 'rules in' neurosyphilis, a negative CSF FTA-ABS would not necessarily 'rule out' the diagnosis, therefore, in retrospect, this would not have been a useful investigation for us to pursue.[18]

Contrary to serological testing, imaging is often neglected in the diagnostic work-up of neurosyphilis due to the wide range of potential radiological features that are often abnormal but non-specific, with the most common findings being frontal and temporoparietal atrophy. A retrospective study suggested that in fact some patients (9%) had a normal MRI in the setting of positive CSF studies. [19] Although our patient's serum EIA and TPPA were positive for syphilis, it is not part of the diagnostic criteria for neurological involvement. His CSF protein was normal, but his WBCs were elevated above five, and he did have clinical signs

(although not common to syphilis) without an alternate known cause.

According to the guidelines proposed by Centres for Disease Control in Europe and America,[20] the diagnostic criteria for neurosyphilis includes having a reactive VDRL in CSF or a negative CSF VDRL with either elevated CSF protein (>450mg/L) or a CSF WBC count (>5 cells/μL). This coupled with clinical symptoms or signs consistent with neurosyphilis without alternate known causes for these, should be confirmatory. Although our patient's clinical presentation fits this criterion; the rare presentation of a sequential bilateral facial palsy [4] as seen in our patient, especially in a HIV-negative individual, has seldom been reported [6], which makes our case unique.

CONCLUSION

Ultimately, our case demonstrates the need for a low threshold to test for syphilis in patients presenting with unusual neurological symptoms. Thus highlighting the challenges clinicians caring for patients with syphilis continue to face due to imperfect tests for neurosyphilis that are neither very sensitive nor specific. Therefore, serological tests should be used as a 'diagnostic aide', and not supersede clinical acumen. Antibiotic treatment should be initiated promptly if a diagnosis of neurosyphilis is possible based on serological testing, CSF examination, and elimination of other diagnoses.

LEARNING POINTS/TAKE HOME MESSAGES

- Neurosyphilis may rarely present with bifacial paresis or paralysis
- No single lab test is both sensitive and specific enough to diagnose neurosyphilis
- Clinicians should exercise clinical judgment to avoid missing atypical presentations

PATIENT'S PERSPECTIVE

When I first had the symptoms of imbalance and facial weakness, I felt worried and unhappy. In fact, I thought I was going to die. I didn't know what was going on. After being reviewed by the medical team and was told the diagnosis, I was placed on antibiotic treatment. My hospital experience was good overall. I can't complain. I feel the treatment has worked. I only have about 10% of the symptoms remaining, in comparison to when I first presented to the hospital. My face has now gone back to normal, and I am over the moon to be driving again. I've even stopped doing the facial physiotherapy exercises. I recently had a repeat screening, and everything is clear. I am reassured and happy to be moving on with my life with a positive attitude.

Table -1 Serology

Test	Result
WBC	14
CRP	14
CK	31
HBA1C	39
ESR	25
Serum Electrophoresis	Normal
ANCA	Negative
ENA	Negative
Complement	Normal
HIV	Negative
Hepatitis B&C	Negative
Syphilis	DETECTED EIA detected TPPA detected RPR positive at 1:128
Lyme	Negative
EBV	IgG detected (suggesting past infection)
CMV	IgG detected (suggesting past infection)
Mycoplasma	Negative
ACE	37 N
SARS COVID-19	Negative
CSF	Raised WBC 32 – Lymphocytic Glucose 3.7 Protein 0.9 Syphilis VDRL negative Syphilis RPR negative TB culture negative
Cytospin	Some cellular debris present but unable to assess morphology. No B cells detected. The few leukocytes correspond to mature T cells.

Table 2 Imaging and Histology

Test	Result
CT Head	Normal
MRI Head	The appearances of the brain are within normal limits for age. An incidental right frontal DVA is noted which is normal variant. There is faint enhancement of the facial nerve distal to the geniculate ganglion that is slightly greater on the right side, but this is not felt to be pathological. There are no focal lesions in the posterior fossa.
CT Thorax, Abdomen, Pelvis	There are prominent lymph nodes seen within the Axilla bilaterally and the inguinal regions. Indeterminate appearances.
Left inguinal Lymph node (Fine needle aspiration)	The biopsy displays fibrous tissue and mature adipose tissue in a minority of which is a population of small lymphocytes; the population is of modest density. No granulomas are observed. Immunohistochemistry reveals that the lymphocytes are a mixture of B cells (CD20 and CD79a) and T cells (CD3 and CD5). The lymphocytes are negative for cyclin D1. No malignancy identified. However, the etiology of the lymphadenopathy is not apparent. The causes of lymphadenopathy may sometimes be focal and not sampled by a core biopsy. This process can extend to neoplastic phenomena which would require further biopsies.

References

1 Bilateral Facial Palsy: A Clinical Approach - PubMed. https://pubmed.ncbi.nlm.nih.gov/34079670/ (accessed 8 May 2023).

2 Neurosyphilis Presenting As Unilateral Facial Nerve Palsy. *Journal of Hospital Medicine Volume 12 Suppl 2*https://shmabstracts.org/abstract/neurosyphilis-presenting-as-unilateral-facial-nerve-palsy/ (accessed 8 May 2023).

3 Chow F. Neurosyphilis. *Continuum (Minneap Minn)* 2021;**27**:1018–39. doi:10.1212/CON.0000000000000982

4 Smikle MF, James OB, Prabhakar P. Diagnosis of neurosyphilis: a critical assessment of current methods. *South Med J* 1988;**81**:452–4. doi:10.1097/00007611-198804000-00010

5 Ting C-H, Wang C-W, Lee J-T, *et al*. Bilateral facial nerve palsy as the sole initial symptom of syphilis: a case report. *CJEM* 2015;**17**:576–81. doi:10.1017/cem.2015.83

6 Njiru E, Abdulkadir J, Kamuren Z, *et al*. Early neurosyphilis presenting with facial palsy and an oral ulcer in a patient who is human immunodeficiency virus positive: a case report. *J Med Case Rep* 2017;**11**:134. doi:10.1186/s13256-017-1297-0

7 Ropper AH. Neurosyphilis. *N Engl J Med* 2019;**381**:1358–63. doi:10.1056/NEJMra1906228

8 Harding AS, Ghanem KG. The performance of cerebrospinal fluid treponemal-specific antibody tests in neurosyphilis: a systematic review. *Sex Transm Dis* 2012;**39**:291–7. doi:10.1097/OLQ.0b013e31824c0e62

9 Addressing the increase in syphilis in England: PHE action plan.

10 O'Byrne P, MacPherson P. Syphilis. *BMJ* 2019;**365**:l4159. doi:10.1136/bmj.l4159

11 Berger JR, Dean D. Neurosyphilis. *Handb Clin Neurol* 2014;**121**:1461–72. doi:10.1016/B978-0-7020-4088-7.00098-5

12 Abkur TM, Ahmed GS, Alfaki NO, *et al*. Neurosyphilis presenting with a stroke-like syndrome. *BMJ Case Rep* 2015;**2015**:bcr2014206988. doi:10.1136/bcr-2014-206988

13 Singh S, Puranik P, Lin E, *et al*. Neurosyphilis in AIDS patient presenting as isolated cranial nerve 6 palsy. *Clin Case Rep* 2020;**8**:1877–9. doi:10.1002/ccr3.3018

14 Yu Y, Wei M, Huang Y, *et al*. Clinical presentation and imaging of general paresis due to neurosyphilis in patients negative for human immunodeficiency virus. *J Clin Neurosci* 2010;**17**:308–10. doi:10.1016/j.jocn.2009.07.092

15 Keane JR. Bilateral seventh nerve palsy: analysis of 43 cases and review of the literature. *Neurology* 1994;**44**:1198–202. doi:10.1212/wnl.44.7.1198

16 Ozgul MA, Cetinkaya E, Kirkil G, *et al*. Lymph node characteristics of sarcoidosis with endobronchial ultrasound. *Endosc Ultrasound* 2014;**3**:232–7. doi:10.4103/2303-9027.144541

17 Rodgers CA, Murphy S. Diagnosis of neurosyphilis: appraisal of clinical caseload. *Genitourin Med* 1997;**73**:528–32. doi:10.1136/sti.73.6.528

18 Ho EL, Marra CM. Treponemal tests for neurosyphilis--less accurate than what we thought? *Sex Transm Dis* 2012;**39**:298–9. doi:10.1097/OLQ.0b013e31824ee574

19 Nagappa M, Sinha S, Taly AB, *et al*. Neurosyphilis: MRI features and their phenotypic correlation in a cohort of 35 patients from a tertiary care university hospital. *Neuroradiology* 2013;**55**:379–88. doi:10.1007/s00234-012-1017-9

20 Janier M, Hegyi V, Dupin N, *et al*. 2014 European guideline on the management of syphilis. *J Eur Acad Dermatol Venereol* 2014;**28**:1581–93. doi:10.1111/jdv.12734