

# Neurosyphilis presenting with myelitis-Case series and literature review

Yali Wu

Capital Medical University Affiliated Beijing Ditan Hospital <https://orcid.org/0000-0002-9737-6439>

Wenqing Wu (✉ [wwqdtty@163.com](mailto:wwqdtty@163.com))

<https://orcid.org/0000-0001-7428-5529>

---

## Case report

**Keywords:** Syphilis, Neurosyphilis, Spinal cord, Magnetic resonance imaging

**Posted Date:** April 5th, 2019

**DOI:** <https://doi.org/10.21203/rs.2.1849/v1>

**License:**  This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

---

**Version of Record:** A version of this preprint was published at Journal of Infection and Chemotherapy on February 1st, 2020. See the published version at <https://doi.org/10.1016/j.jiac.2019.09.007>.

# Abstract

Background Neurosyphilis is a great imitator because of its various clinical symptoms. Syphilitic myelitis is extremely rare manifestation of neurosyphilis and often misdiagnosed. However, a small amount of literature in the past described its clinical manifestations and imaging features, and there was no relevant data on the prognosis, especially the long-term prognosis. In this paper, 4 syphilis myelitis patients admitted to our hospital between July 2012 and July 2017 were retrospectively reviewed. In the 4 patients, 2 were females, and 2 were males. We present our experiences with syphilitic myelitis, discuss the characteristics, treatment and prognosis. Case presentation The diagnosis criteria were applied: (1) diagnosis of myelitis established by two experienced neurologist based on symptoms and longitudinally extensive transverse myelitis (LETM) at the cervical and thoracic levels mimicked neuromyelitis optica (NMO) on magnetic resonance imaging (MRI) ; (2) Neurosyphilis (NS) was diagnosed by positive treponema pallidum particle assay (TPPA) and toluidine red untreated serum test (TRUST) in the serum and CSF; (3) negative human immunodeficiency virus (HIV). Likewise, all patients were negative for serum anti-aquaporin 4 (AQP-4), as well as negative bacterial, fungal, virus, or mycobacterium tuberculosis in the CSF. Treatment included intravenous penicillin G, with 24 million units of penicillin G per day administered intravenously for 14 days, and three patients were also treated with systemic corticosteroids. Neurological examination, serologic syphilis diagnostic tests (TPPA, TRUST) and cerebrospinal fluid tests (TPPA, TRUST) were examined approximately every 12~24 weeks after treatment. The follow-up time ranged from 12 to 70 months, with an average of 36.6 months. The prognosis was well in 3 cases who received early anti-syphilis treatment, but 1 case who received delayed treatment due to misdiagnose had no improvement. Conclusions Neurosyphilis should be considered when there are long hyperintensity lesions in the MRI spinal cord. Prompt diagnosis and combined antibiotics-corticosteroid therapy may improve neurological prognosis.

## Background

Neurosyphilis (NS) is a chronic sexually transmitted disease and caused by treponema pallidum infection[1, 2]. Neurosyphilis can affect any part of the central nervous system (CNS) at any stage[3, 4]. Neurosyphilis is classified asymptomatic NS and symptomatic NS, the symptomatic NS includes meningeal, meningovascular, paralytic dementia, tabes dorsals and gumma[2]. However, its typical forms have often been replaced by atypical ones because of widespread use of antibiotics, so this induced diagnostic problems. Owing to the unusual rarity, the diagnosis, treatment, and prognosis have not been well elaborated. In this study, we report 4 syphilitic myelitis patients, discuss the characteristics, treatment and prognosis. As we know, CSF venereal disease research laboratory (VDRL) test is the reference test for the laboratory diagnosis of NS. However, there are no commercial VDRL reagents approved by the State Food and Drug Administration for VDRL examination in China. There are research suggesting that TRUST can be considered as an alternative test for NS diagnosis when the VDRL is not available[5]. In this study, CSF TRUST is used to diagnose NS, given that the specificity and sensitivity of TRUST are similar to

VDRL and rapid plasma reagin (RPR), but they are easier and less expensive to perform[6]. We used the modified Rankin Scale (mRS) to assess the neurological improvement.

## Case Presentation

Patient 1, a 43-year-old female, who had rash of legs in August 2011, presented with numbness and weakness of the bilateral feet, and constipation in July 2012, numbness of the inferior limbs extending the legs, as well as MRI showed long lesions in the cervical and thoracic central cord. She was diagnosed acute myelitis, and received prednisolone 500 mg for 5 days, then prednisone 60mg/day. However, the symptoms got deteriorated, she felt that her legs became weaker, headache, and he could not walk as good as before. The numbness extended to the chest and she had urinary dysfunction. In March 2013, she was admitted to our hospital, and lumbar puncture was performed. She was diagnosed neurosyphilis according to CSF TRUST 1:4, serum TRUST 1:32, high CSF leukocyte counts (7/uL) and CSF protein(111g/L), as well as OB and AQP-4 antibodies were negative. Physical examination showed left limb weakness with a grade of 4, and positive bilateral babinsk's sign. mRS=4. T2 MRI showed high intensity in T1-3 cord (Figure A). She was diagnosed syphilitic myelitis and started intravenous aqueous crystalline penicillin G, 4 million units intravenously every 4 hours for 14 days, followed by intramuscular injection of benzathine penicillin once a week at a dose of 2.4 million units for 3 consecutive sessions therapy. Follow-up 6 years after treatment, CSF TRUST was negative and serum TRUST was 1:2. The CSF leukocyte counts and CSF protein were normal. The numbness was disappeared, only leaving slight weakness in the left limb. mRS=1. The cervical MRI was normal, and the thoracic cord atrophy (Figure B).

Patient 2, a 69-year-old male, who had genital ulcer and syphilis 9 years ago, presented with backache and chest tightness. There were lesions in the thoracic central cord (T5-8) and received oral steroid hormone 30~60mg therapy multiple times, however, the symptoms were deteriorated, and he had difficulty in walking and had urinary incontinence. MRI showed lesions in T6-7 thoracic cord, medullary cone and cauda equina (Figure C). Physical examination showed left limb weakness with a grade of 4-5, right limb weakness with a grade of 4, and positive right babinsk's sign. Impairment of superficial and deep sensation below the level of T6. mRS=4. Positive TPPA in serum and CSF, CSF TRUST was 1:1 and serum TRUST was 1:16. The CSF showed high leukocyte (8/uL) and protein (138g/L). He was diagnosed syphilitic myelitis and was treatment of intravenous aqueous crystalline penicillin G, 4 million units intravenously every 4 hours for 14 days, followed by intramuscular injection of benzathine penicillin once a week at a dose of 2.4 million units for 3 consecutive sessions, prednisolone 500mg for 5 days, which failed to relieve his symptoms. After 1 year, he suffered significant neurological deficit despite improvement in the MRI. mRS=4. Serum TRUST was 1:8, and CSF TRUST and TPPA were negative. The CSF showed normal leukocyte counts (1/uL) and high protein(104g/L). The thoracic cord of MRI was normal, leaving lesion in the cauda equina .

Patient 3, a 42-year-old female, who had rash and diagnosed syphilis 8 months ago, presented with chest and back pain, feet numbness. Then the numbness gradually extended to her legs and saddle. At the same time, she had legs weakness, thorax and back hyperalgesia. Physical examination showed

hyperalgesia above T6, feet vibratory diminished. mRS=2. Positive TPPA in the serum and CSF, CSF TRUST was 1:1, serum TRUST was 1:32. Serum SS-A, Ro-52 and SS-B were positive. The CSF showed high leukocyte counts (88/uL) and normal protein. T2-weighted MRI showed hyperintensity lesions in cervical and thoracic central spinal cord, and enhancement in T1 central spinal cord (Figure D, E). She was diagnosed syphilitic myelitis and started therapy, including aqueous crystalline penicillin G, 4 million units intravenously every 4 hours for 14 days, oral prednisolone 60mg for 7 days, and decreased 10mg per week. After 1 year ago, her symptoms were improved, only leaving numbness in the left legs. mRS=1. The serum TRUST was 1:8, the CSF TRUST was negative, and the CSF leukocyte counts (4/uL) and protein were normal. There was no hyperintensity in the cervical and thoracic cord on T2-weighted and no enhancement in thoracic cord (Figure F).

Patient 4, a 30-year-old male, presented systemic syphilis as rash 6 months ago, but he did not receive treatment, presented with bilateral numbness of hips for 2 months, and the numbness gradually developed to the feet, with bilateral positive Hoffmann sign and bilateral negative babinsk's sign. The pain was impaired below T2. mRS=1. T2-weighted MRI showed hyperintensity lesions in cervical and thoracic central spinal cord, and enhanced image showing enhancement in the superficial portion of thoracic cord at C4-T1. Serum TRUST was 1:16 and he was received benzathine penicillin treatment, and there was no foot numbness. Improve lumbar puncture after 1 month, serum TRUST was 1:4, CSF TRUST was 1:1, the CSF high leukocyte counts (18/uL) and high protein(53g/L). He was diagnosed syphilitic myelitis and started aqueous crystalline penicillin G, 4 million units intravenously every 4 hours for 14 days therapy, with near complete resolution of symptoms after 6 months. mRS=1.

## Discussion And Conclusions

Up to now, only 8 of cases syphilitic myelitis were reported in the world for 30 years[7-13]. The incidence rate of neurosyphilis in the untreated syphilis was 4%-10%, and 1.5% was developed to syphilitic myelitis. It is characterized by paraplegia, numbness and loss of sphincter control. The etiology probably results from thrombosis of the spinal vessels due to syphilitic vasculitis. To the best of our knowledge, the previous published studies described neuroimaging features of syphilitic myelitis and few of them discussed the treatment and clinical prognosis. In this study, we focused on the clinical manifestations, neuroimaging, treatment, as well as clinical prognosis.

The main clinical manifestations of syphilitic myelitis are acute or sub-acute onset of lower limb paralysis, numbness, and urinary dysfunction. This is different from tabes dorsalis which involved posterior column and dorsal root with the symptoms of pain electric shock like in the limbs, loss of reflex of the lower extremity tendon, and deep sensation dysfunction. In this case series, they were acute or sub-acute onset, progressive, legs weakness, impairment of superficial and deep sensation, without weakness and/or numbness of the upper limbs, 3 cases of sensory impairment from low to up, 1 case from buttock to downward. No report has been reported sensory impairment from the hips to feet. One patient had headache, we assumed her meningeal may be involved, but when she had headache, she had not contrast brain MRI to perform my suspect.

To best of our knowledge, no study has reported the specific incubation period between syphilis infection and development of myelitis syphilis based on serology. In this case series, the median time between syphilis infection and development of myelitis symptoms was 10 months (IQR6.5,84; range 6-108). Three out of four (75%) cases developed myelitis syphilis within 2 years of syphilis infection. It suggested that myelitis syphilis should be suspected even in patients with early syphilis who present with myelitis symptoms. Moreover, routine serologic syphilis is critical for prevention of irreversible neurological deficit.

Tashiro[7] firstly described the MRI findings in syphilitic myelitis in 1987. Syphilitic myelitis is usually characterized by long cord lesions, and abnormal enhancement, predominantly in the superficial parts of the spinal cord may be observed on enhanced images. The abnormalities of the spinal cord probably result from meningeal inflammation -induced demyelinating[14]. Spinal cord lesions which have resolved following treatment has been reported[15], and the disappearance of hyperintensity lesions may indicate that these changes are reversible. In our 4 patients, hyperintensity on T2-weighted images and abnormal enhancement high signal of T1 were seen in the spine. The hyperintensity lesions involved at least three segments of spinal cord, and usually involved the cervical and thoracic spinal cord. This mimicked the imaging findings of NMOSD, but predominantly in the superficial parts of the spinal cord is the specific manifestations of syphilitic myelitis which suggest spinal meninges involvement. In patient 2, hyperintensity were observed in cauda equina and round vertebra. We have not found any report about neurosyphilis involved cauda equina. The severe pain of patient 2 might be related to abnormal signals of nerve root. In patient 1, we discovered thoracic cord atrophy. This imaging manifestation has not been reported. We assumed that the reason of spinal atrophy may be chronic inflammation and demyelination, and it suggested that some lesions were irreversible. Lesions from neurosyphilis can be irreversible in the late stage, and atrophy in the spine is considered to be indicative of poor prognosis.

The diagnosis of syphilitic myelitis mainly depends on clinical manifestations, neuroimaging, as well as laboratory tests. Syphilitic myelitis has to be distinguished from other causes of myelitis, e.g. immune-mediated spinal cord diseases, such as acute transverse myelitis, optic neuromyelitis spectrum disease, multiple sclerosis, spinal tumor, such as glioma, metastasis and lymphoma, abscess, HIV induced myelopathy and other specific infections, such as tuberculous myelopathy, cryptococcal myelopathy. Serologic and CSF tests are the key to diagnosis[16]. All patients were negative for antibodies against AQP-4, and hyperintensity in the spine on T2-weighted MRI were diminished or improved after antibiotic treatment, it can exclude NMOSD.

Serologic SS-A, Ro-52 and SS-B were positive in patient 3, but her symptom was improved and the MRI lesions were disappeared after penicillin treatment. There is no report of autoimmune diseases caused by treponema pallidum. We should pay attention to the relationship between syphilis and autoimmune bodies, and follow up those biomarkers.

Early diagnosis of neurosyphilis and appropriate antibiotic treatment can result in clinical improvement. The diagnostic challenges illustrate the importance of comprehensive evaluation, including laboratory and neuroimaging examinations should be emphasized. Neurosyphilis is considered to be a treatable

disease with early diagnosis and treatment. According to existing literature, the first-choice treatment for neurosyphilis is intravenous penicillin[17]. Patient 2 was originally misdiagnosed with demyelination for 7 years before receiving anti-syphilis treatment. Symptoms showed no obvious improvement after treatment for neurosyphilis. The remaining 3 patients received anti-syphilis treatment timely and their symptoms did improve to varying degrees upon follow-up. As we know, this is the first paper to discuss the treatment and long follow-up time.

It was common corticosteroid was given before and during antibiotic therapy in order to prevent the Jarish - Herxheimer reaction. However, as we know, there have been no clinical studies regarding the usefulness of corticosteroid therapy for syphilitic myelitis. However, our case series suggested that corticosteroids may be useful as an adjunctive treatment. Previous study revealed that treatment of systemic corticosteroids may be an important adjunctive therapy for early neurosyphilis presenting with multiple cranial nerve palsies[18]. Moreover, there have been a few reports of gumma treated by corticosteroids without antibiotics[19]. Therefore, corticosteroid treatment could be effective in some clinical forms of neurosyphilis, such as cranial neuropathy, syphilitic myelitis, and gumma. In my study, Patient 1 and patient 3 received combined antibiotics-corticosteroid treatment and the effectiveness of corticosteroid therapy as an adjunctive treatment to improve neurological functions was well. We speculate the reason may be related to corticosteroid can reduce spinal cord edema and inhibit inflammation. Patient 2 only received corticosteroid therapy before penicillin therapy, suggesting that corticosteroid therapy was only adjuvant therapy, penicillin should be given as soon as possible.

In conclusion, syphilitic myelitis is rare, and clinical and imaging are not specific, hence high misdiagnosis was observed, which prevents patients receiving appropriate and early treatment, and often results in more severe neurologic damage. When encountering long-segment hyperintensity spinal cord lesions, we should think of syphilis and undergo related biomarker test, and all patients should undergo CSF examination as soon as possible when TRUST are positive in serum. Prompt diagnosis and combined antibiotics-corticosteroid therapy may improve neurological prognosis.

Limitations of this study include the small single center nature of our study. Secondly, the number of patients enrolled is low, which may result in the selection bias. Further studies with multi-center randomized findings are needed.

## Abbreviations

AQP4=Anti-aquaporin 4, CSF=Cerebrospinal fluid, MRI=Magnetic resonance imaging, NMOSD=Neuromyelitis optic spectrum disorder, OB= Oligoclonal bands, TRUST=toluidine red untreated serum test, TPPA=Treponema pallidum particle assay, HIV=human immunodeficiency virus, VDRL= venereal disease research laboratory, RPR= rapid plasma regain, CNS =central nervous system, LETM= longitudinally extensive transverse myelitis, mRS=modified Rankin Scale

## Declarations

## Ethics approval and consent to participate

The study protocol was approved by the Ethics Committee of Beijing Ditan Hospital, Capital Medical University. Written informed consent was obtained from all the participants.

## Consent to publish

Written informed consents were obtained from the patients for publication of this case report.

## Availability of data and materials

The datasets supporting the conclusions of this article are included within the article.

## Competing interests

The authors declare that they have no competing interests.

## Funding

There's no funding available.

## Authors' contributions

WY was involved in the direct care of patients; she examined and assessed patients on admission, reviewed the literature, and wrote the case and the final draft. WW helped in the design, made significant modifications in the manuscript and approved the final draft. All authors read and approved the final manuscript.

## Acknowledgements

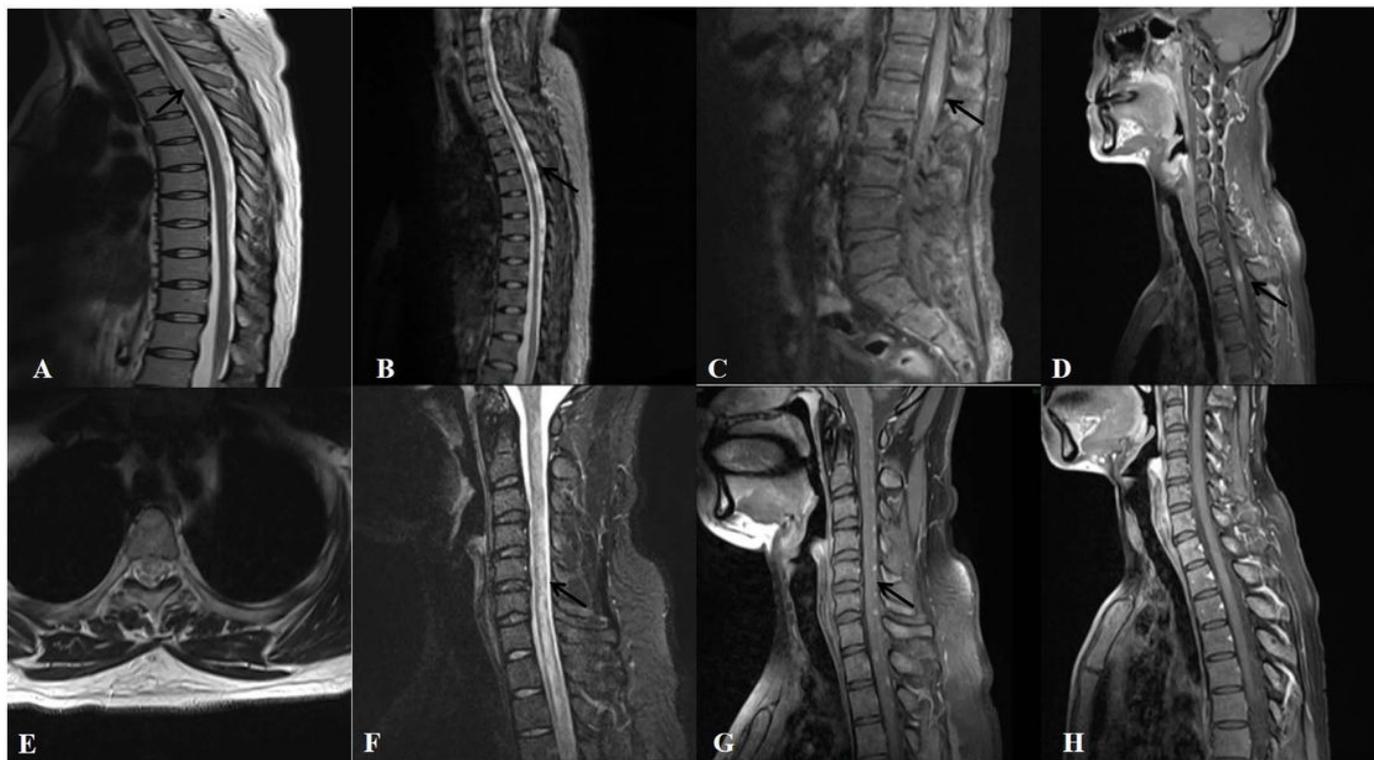
We thank doctor Jingjing Li who gave us instruction in neuroimage of neurosyphilis and other colleagues for the excellent care the patient received, and that made this report possible.

## References

- [1]. Fenton, K.A., et al., Infectious syphilis in high-income settings in the 21st century. *Lancet Infect Dis.* 2008; 8(4): 244-53.
- [2]. Berger, J.R., Neurosyphilis and the spinal cord: then and now. *J Nerv Ment Dis.* 2011; 199(12): 912-3.
- [3]. Bhai, S. and J.L. Lyons, Neurosyphilis Update: Atypical is the New Typical. *Curr Infect Dis Rep.* 2015; 17(5): 481.
- [4]. Lewis, D.A. and H. Young, Syphilis. *Sex Transm Infect.* 2006; 82 Suppl 4: 13-5.

- [5]. Gu, W., et al., Comparing the performance characteristics of CSF-TRUST and CSF-VDRL for syphilis: a cross-sectional study. *BMJ Open*, 2013. 3(2). pii: e002204.
- [6]. Zhu, L., et al., Comparison of the cerebrospinal fluid (CSF) toluidine red unheated serum test and the CSF rapid plasma reagin test with the CSF venereal disease research laboratory test for diagnosis of neurosyphilis among HIV-negative syphilis patients in China. *J Clin Microbiol*. 2014; 52(3): 736-40.
- [7]. Tashiro, K., et al., Syphilitic myelitis with its magnetic resonance imaging (MRI) verification and successful treatment. *Jpn J Psychiatry Neurol*. 1987; 41(2): 269-71.
- [8]. Nabatame, H., et al., MRI of syphilitic myelitis. *Neuroradiology*.1992; 34(2): 105-6.
- [9]. Kikuchi, S., et al., Subacute syphilitic meningomyelitis with characteristic spinal MRI findings. *J Neurol*, 2003. 250(1): p. 106-7.
- [10]. Janier, M., Acute syphilitic myelitis in a young man. *Genitourin Med*, 1988. 64(3): p. 206.
- [11]. He, D. and B. Jiang, Syphilitic myelitis: magnetic resonance imaging features. *Neurol India*. 2014; 62(1): 89-91.
- [12]. Chilver-Stainer, L., et al., Syphilitic myelitis: rare, nonspecific, but treatable. *Neurology*. 2009; 72(7): 673-5.
- [13]. Bulundwe, K.K., C.J. Myburgh and R.F. Gledhill, Syringomyelia complicating syphilitic spinal meningitis: a case report. *Eur J Neurol*. 2000; 7(2): 231-6.
- [14]. Kararizou, E., et al., Chronic inflammatory demyelinating polyneuropathy associated with neurosyphilis. *Am J Med Sci*. 2015; 349(1): 90-1.
- [15]. Marra, C.M., Syphilis Screening in Neurology. *JAMA Neurol*. 2016; 73(8): 926-7.
- [16]. Workowski, K.A., Centers for Disease Control and Prevention Sexually Transmitted Diseases Treatment Guidelines. *Clin Infect Dis*. 2015; 61 Suppl 8: S759-62.
- [17]. Ali, L. and K.L. Roos, Antibacterial therapy of neurosyphilis: lack of impact of new therapies. *CNS Drugs*. 2002; 16(12): 799-802.
- [18]. Komamura, H., et al., Early neurosyphilis presenting with multiple cranial nerve palsies: A case report of management by combined penicillin-corticosteroid treatment. *J Infect Chemother*, 2018; Dec 8. pii: S1341-321X(18)30459-8.
- [19]. Herrold, J.M., A syphilitic cerebral gumma manifesting as a brain-stem mass lesion that responded to corticosteroid monotherapy. *Mayo Clin Proc*. 1994; 69(10): 960-1.

## Figures



**Figure 1**

Fig.A T2-weighted MRI showing hyperintensity areas in the T1-T3 in Patient1 Fig.B T2-weighted MRI showing atrophy in thoracic spinal cord in patient 1 Fig.C enhanced image showing enhancement in cauda equina in patient 2 Fig.D enhancement in thoracic cord at T1 in Patient 3 Fig.E axial showed high intensity areas in the T2 in Patient 1 Fig.F T2-weighted MRI showing high intensity areas in the C4-T2 in Patient 4 Fig.G enhancement in the superficial portion of C4-T2 in Patient 4 Fig.H T2-weighted MRI showing high intensity areas disappeared

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [supplement1.docx](#)