Brief Report

Syphilitic meningomyelitis misdiagnosed as spinal cord tumor: Case and review

Huiqing Dong[1]*, Zheng Liu[1]*, Yunyun Duan[2], Dawei Li[1], Zhandong Qiu[1], Yaou Liu[2], Jing Huang[3], Chaodong Wang[1]

[1]Department of Neurology, Xuanwu Hospital, Capital Medical University, Beijing, People's Republic of China, [2]Department of Radiology, Beijing Tiantan Hospital, Capital Medical University, Beijing, People's Republic of China, [3]Department of Radiology, Xuanwu Hospital, Capital Medical University, Beijing, People's Republic of China

Context: Syphilitic meningomyelitis is a rare manifestation of neurosyphilis, not well described in the literature.
Methods: We reported a rare case of a 29-year-old female with syphilitic meningomyelitis. Her clinical manifestations and imaging findings were discussed with the related literatures reviewed.
Results: The patient presented with progressive bilateral lower extremities numbness and weakness for months. Laboratory tests revealed positive serum Treponema pallidum Hemagglutinin Test (TPHA) and rapid plasma reagin test (RPR). The cerebral spinal fluid (CSF) was positive with TPHA but negative for RPR with lymphocytic pleocytosis and elevated protein. Spinal MRI showed swelling and high-signal intensity of thoracic spinal cord except T6-7 level with associated gadolinium enhancement ("flip-flop sign") and peripheral strip-like enhancement on T1WI ("candle guttering appearance"). She was initially diagnosed as spinal cord tumor due to the chronic clinical onset and cord swelling with central enhancement found on thoracic MRI. After dramatic clinical and radiographic improvement with dexamethosone and serological tests of syphilis, she was diagnosed as probable syphilitic meningomyelitis. Till now, there are 12 cases of syphilitic myelitis reported with spinal cord MR images. Thoracic cord is the predominant involved segment (10/12), "candle guttering appearance" is the most common enhancing characteristics of the lesion (7/12), "flip-flop sign" may be seen in the stage with significant inflammation (3/12).
Conclusion: Syphilitic meningomyelitis can occur at early or late stage of syphilis, the onset may be acute, subacute or chronic. The imaging findings suggested focal inflammation of the spinal cord. Prognosis is relatively good after proper treatment.

Keywords: Neurosyphilis, Myelopathy, Magnetic resonance

Introduction

Neurosyphilis (NS) is defined as Treponema pallidum infection of the central nervous system during any stage of the disease.[1] Unlike general paresis and tabes dorsalis, syphilitic meningomyelitis is considered a rare manifestation of the NS.[2] And sometimes it can cause significant diagnostic and therapeutic challenges by mimicking other acute, subacute or chronic myelopathy, or space-occupying myelopathy. Here, we report the case of a 29-year-old woman suffering from syphilitic meningomyelitis with chronic clinical course and unusual imaging findings with the related literatures reviewed.

Case presentation

A 29-year-old female was admitted to our hospital with a history of intermittent fever for 9 months, associated with numbness of two lower limbs after 6 months from the beginning of the symptoms, and later progressing to right lower limb weakness for over 2 months period on April 2015. The peak of temperature presented by the patient was 39.1°C. The fever subsided several days after antipyretic treatment without antibiotics. This situation recurred several times for 3 months. Six months prior to the admission, she felt

*The first two authors contributed equally to the article.
Correspondence to: Zheng Liu, Department of Neurology, Xuan Wu Hospital, Capital Medical University, Beijing 100053, People's Republic of China; Ph: 008613910320552; 0086-10-83198899 ext 8701. Email: lzwcy2003@aliyun.com

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numbness on both feet, which ascended gradually to upper abdomen two months later. Two and half months prior to admission, she developed proximal weakness of the right leg and needed crutches to walk. She reported no autonomic dysfunction. Due to the cord swelling with central enhancement found on thoracic MRI ordered by a neurologist in local hospital, she was initially diagnosed as spinal cord tumor and admitted to neurosurgery department and received dexamethosone 10 mg per day and mannitol 250 ml every 6 h per day for three days. She had subsequent significant clinical and radiographic improvement. She was able to walk without assistance and the cord lesion diminished significantly. Subsequently, she was referred to neurology department. Upon further questioning, the patient revealed red pimples of the perineal region 2 years prior to the beginning of the symptoms that were relieved by Ofloxacin ointment. She denied venereal disease exposure and extramarital sex. She worked as a cashier in a bath center.

Her physical examination on admission showed that she was alert and oriented. The cranial-nerve functions were normal. Argyll Robertson pupils, which fail to react to light but constrict during near vision, were not observed. Muscle tones were normal. The muscle strength of the right leg was grade 4/5 (Oxford scale), other muscles strength was normal. Pinprick sensation below T7 level was decreased. Vibration sensation below T12 level was reduced. Bilateral finger-nose tests were normal. Bilateral heel-knee-shin tests showed slight dysmetria. Romberg's sign (A sign which is swaying of the body that occurs when the eyes are closed.) was positive. She was unable to perform tandem gait well. She had brisk deep tendon reflexes in the right lower limb and right flexor plantar response.

Laboratory tests revealed normal hepatic, renal, thyroid function. She had negative angiotensin-converting enzyme, antinuclear antibodies, antineutrophil cytoplasmic antibodies, anticardiolipin antibodies and rheumatic factor. Serum immunoelectrophoresis and immunoglobulin studies showed no abnormalities. Serum lyme and brucella antibodies were negative. She had positive serum Treponema pallidum Hemagglutinin Test (TPHA) and rapid plasma reagin test (RPR, 1:4). CSF examination revealed 20×10^6 cells/l, 54 mg/dl protein, 37 mg/dl glucose and 112 mg/dl chloride. The cerebral spinal fluid (CSF) was positive with TPHA but negative for RPR. CSF revealed positive oligoband (OB), which indicated intrathecal IgG synthesis. CSF India ink stains were negative for cryptococcus. Bacterial growth was negative both on the blood and on the chocolate culture media Serum and CSF AQP-4 antibody was both negative.

Spinal MRI revealed swelling and diffuse high-signal intensity of the thoracic spinal cord parenchyma except T6-7 level with associated focal gadolinium at T6-7 level ("flip-flop sign", Figs. 1 and 2). In T10 level, peripheral strip-like enhancement at the surface the spinal cord was shown on T1WI ("candle guttering appearance", Fig. 2). Brain MRI was normal. The thoracic spinal cord lesion improved significantly after three-day dexamathosone treatment. She was diagnosed as probable syphilitic meningomyelitis based on clinical and imaging features and laboratory examinations. Patient received treatment with intravenous penicillin G 4 million units every 4 h for 14 days and dexamathosone 5 mg/d for 3 days before penicillin to prevent Jarisch-Herxheimer reaction (2015-4-29). Symptoms improved by day seven. By day 12 after treatment, her neurological examination showed normal muscle strength, right flexor plantar response and positive Romberg test. And the follow-up MRI showed limited cord lesion of T6-7 with a slight enhancement. Six months after treatment, she had complete clinical recovery.

Discussion

Syphilis is a sexually transmitted infectious disease caused by spirochete Treponema pallidum. The incidence of syphilis has decreased significantly with the discovery of penicillin. However, its prevalence has risen due to unprotected sex, mostly of men who have sex with men, and worldwide increased prevalence of acquired immune-deficiency syndrome.[3,4] The incidence of NS is estimated to be about 4–10% in untreated syphilis.[5] Syphilis can affect any part of the central nervous system at any stage of infection, and NS may be involved in the early course of the disease.[1] There are several types of syphilitic myelopathy,[2] some of them can happen in both early and late stages, including syphilitic meningomyelitis, spinal vascular syphilis, syphilitic poliomyelitis, and syphilitic spinal pachymeningitis (the last one including spinal cord gumma and syphilitic hypertrophic pachymeningitis). They can develop several weeks to several years after primary infection and affects meninges, vessels and spinal cord respectively or in different combinations. The late-stage syphilitic myelopathy mainly refers to as parenchymatous NS (tabes dorsalis/TD), the commonest type, which occurs 10–20 years after the primary infection and is the result of irreversible neuronal degeneration. The different types of syphilitic myelopathy may coexist and the pathogenesis may be diverse.

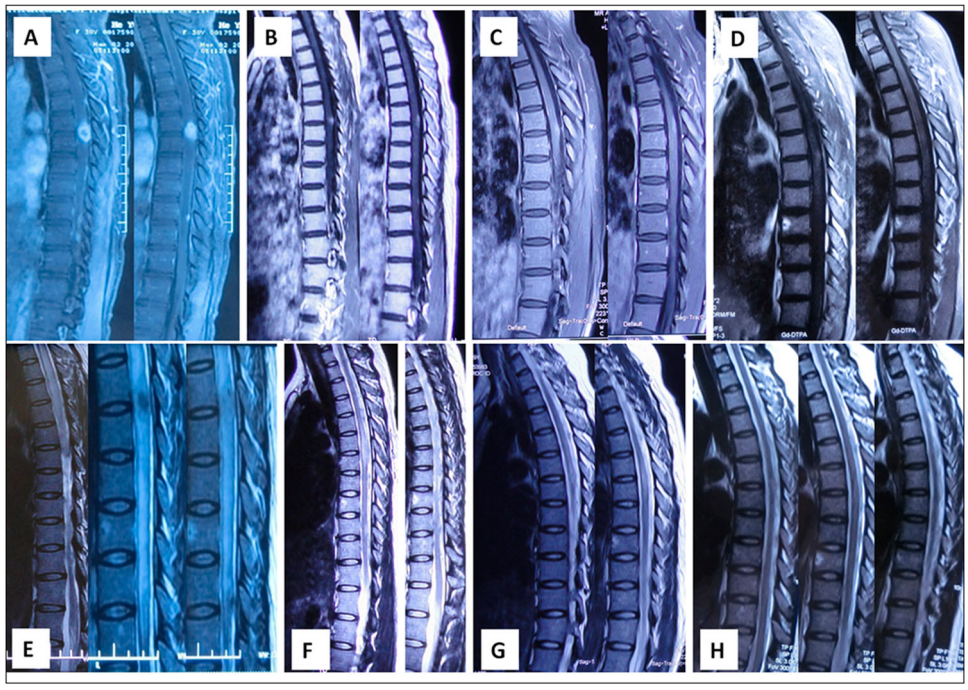

Figure 1 The spinal cord MRI evolution of syphilic meningomyelitis. Spinal MRI revealed swelling and diffuse high-signal intensity of the whole thoracic spinal cord parenchyma except T6-7 level (E), and focal gadolinium enhancement at this T2WI-low-signal area (A) ("flip-flop sign"). The thoracic spinal cord lesion subsided after three-day dexamathosone treatment (B, F). Gadolinium-enhanced TIWI and T2WI before treatment (C, G, about one month after BF) and 12 days after treatment (D, H) showed further diminished lesion in spinal cord.

Our patient was misdiagnosed initially as a spinal cord tumor due to its chronic onset and MR findings of cord swelling with significant associated enhancement and edema. However, symptoms improved clinically and radiographically with dexamathosone. The diagnosis of syphilis requires use of two serological tests: a nontreponemal test (*i.e.* Venereal Disease Research Laboratory [VDRL] or Rapid Plasma Reagin [RPR]) and a treponemal test (*i.e.* fluorescent treponemal antibody absorbed [FTA-ABS] tests, the T. pallidum passive particle agglutination [TPPA] assay or the T. pallidum hemagglutination assay [TPHA]). In our patient, serum TPHA and RPR tests were positive, but CSF PRP test was negative. Patient's CSF showed mononuclear pleocytosis and elevated protein, in combination with a positive response to penicillin treatment. Based on those findings, the patient was diagnosed as probable NS following the diagnostic criteria.[6] The subtype of NS could be syphilitic meningomyelitis based on her symptoms, perineal pimples prior history, spinal cord imaging characteristics and response to steroid and antibiotic.

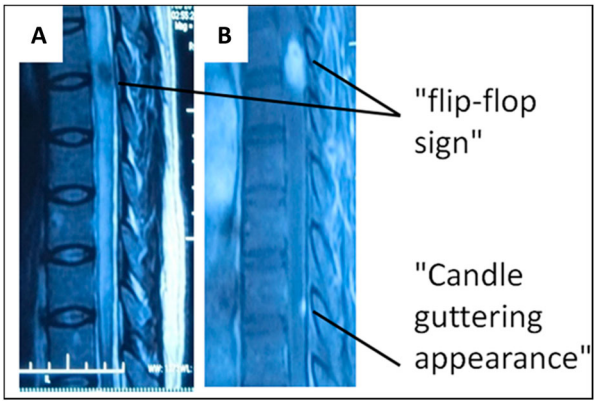

Figure 2 "Flip-flop sign" and "Candle guttering appearance" of syphilic meningomyelitis "Flip-flop sign": high-signal intensity of the thoracic spinal cord parenchyma except T6-7 level (A), and abnormally enhanced parenchyma were observed at this T2WI-low-signal area (B). "Candle guttering appearance": peripheral strip-like enhancement from the surface of the spinal cord in T10 level.

Syphilitic meningomyelitis is an extremely rare manifestation of syphilis in the modern antibiotic era. It was first reported in 1944.[7] Meningomyelitis develops 6 years (1–30) on average after initial infection.[2] Thoracic spinal cord is the most commonly affected anatomical location. Patients presented with variable degrees of sensory levels, limb weakness, pyramidal signs, bladder and bowel dysfunction. Onset may be subacute or chronic, and occasionally it can be acute. The pathogenesis of meningomyelitis is diverse. It may

be caused by direct involvement of the spinal cord parenchyma by the spirochetes infection, or may be the indirect result of inflammation effect on the meninges and blood vessels, or post-infectious immune-mediated demyelination on the spinal cord. Immune-mediated course may have a subacute duration, while meningovascular involvement usually leads to acute onset, versus gummatous NS often has subacute or chronic onset. In our patient, chronic progressive clinical presentation, spinal cord swelling, and the rapid recovery of symptoms and dramatic improvement of image findings after three days dexamathosone suggested meningomyelitis, which mainly resulted from immune-mediated process, rather than ischemia (spinal meningo-vascular syphilis). The diagnosis of NS is based on a CSF WBC count greater than or equal to 20×10^6 cells/l and/or a reactive CSF VDRL results. Without serological studies, the diagnosis of syphilitic meningomyelitis is difficult as it can mimic idiopathic transverse myelitis, acute disseminated encephalomyelitis (ADEM), spinal cord infarction, spinal arteriovenous malformation, spinal cord tumors, other subacute or chronic infectious myelopathy (such as tuberculosis or cryptococcosis).[8–10]

Tashiro *et al*. first described the MR imaging findings in syphilitic meningomyelitis,[11] and only a few cases have been documented in the international literatures. Besides long extensive high-signal lesion on T2-weighted images of the spinal cord parenchyma, focal nodular enhancement and swelling spinal cord, there are two specific imaging features of syphilitic meningomyelitis mentioned,[12] one is "flip-flop sign" which has gadolinium-enhanced T1-weighted images and reversed

Table 1 Cases of syphilitic myelitis reported previously and current case.

Case	Age	Sex	Time to the initial infection of syphilis	Time between onset to nadir	MRI findings of spinal cord	Treatment	Recovery
Tashiro-1987[11]	31	M	7 months	10 days	Thoracic spinal cord, enhancement at the level of T3/4	Penicillin G with prednisolone	Yes(about 1 month later)
Strom-1991[14]	28	M	NA	6 months	Hyperintense on T2 from T6-8	Penicillin G with dexamethasone	Partial relief
Nabatame-1992[15]	46	M	NA	NA	Thoracic spinal cord, Candle guttering appearance and abnormal enhancement in the central part of spinal cord	Antibiotic treatment	Yes
Bulundwe-2000[16]	53	M	NA	11 months	Hyperintense with swelling on T2 from T3-6	Penicillin G	Yes
Tsui-2002[12]	52	F	2 years	5 days	Whole spinal cord, Candle guttering appearance and abnormal enhancement in the central part of spinal cord	Penicillin G with dexamethasone	wheelchair
Kikuchi-2003[17]	36	M	NA	3 months	Abnormal signals involving the whole spinal cord, Candle guttering appearance and flip-flop sign	Penicillin G	Yes(about 1 month later)
Matijošaitis 2006[18]	38	M	About 1.5 years	4 months	Hyperintense on T2 from T6-8, ring-like enhancement	Penicillin G with prednisone	Partial relief
Chilver-2009[19]	46	M	NA	7 days	Abnormal signals below T6, Candle guttering appearance and abnormal enhancement in the central part of spinal cord	Penicillin G with methylprednisolone	Yes(about 3 months later)
Dongmei He-2014[20]	63	M	NA	12 days	T6-11, Candle guttering appearance and abnormal enhancement in the central part of spinal cord	Ceftriaxone with methylprednisolone	Yes(about 3 months later)
Siu-2017[21]	41	M	NA	NA	spinal cord edema at C3 through T1 levels, with focal spinal cord enhancement at C6	Penicillin G	Yes(about1 week later)
Sun-2018[22]	50	F	NA	2.5 months	Hyperintense with swelling on T2 from T1 to T10, Candle guttering appearance with flip-flop sign	Penicillin G, Ceftriaxone with methylprednisolone	Yes(about1 week later)
This case	29	F	2 years	6 months	Whole thoracic spinal cord, Candle guttering appearance with flip-flop sign	Penicillin G with dexamethasone	Yes(about 6 months later)

low-signal intensities on T2-weighted images (Fig. 1), the other is "candle guttering appearance" which refers to abnormal peripheral enhancement in the spinal cord parenchyma (Fig. 2). Our patient's imaging findings had these two signs. "Flip-flop sign" reflects severe parenchymatous inflammation with blood–spinal cord barrier breach. The low-signal intensity of T2-weighted image (T2WI) may be due to rich proteins products during the infectious and inflammatory process after Treponema invasion.[13] It may be an indicative of different forms of granuloma. Similar characteristics could be seen occasionally in the MR image of tuberculoma and cryptococcoma as well.[9,10] The "candle guttering appearance" on MRI suggests that the pathological process of NS invasion of the spinal cord is from its surface. For the past 30 years, since MR became available in clinical practice, there are nine cases of syphilitic myelitis reported with spinal cord MR images. We conclude that among the documented cases with spinal cord MRI in Table 1,[11,12,14–22] the thoracic cord is the predominant part of involvement (10/12), whole spinal cord involvement for the other two cases, candle guttering appearance is the most common enhancing characteristics of the lesion (7/12), flip-flop sign may be seen occasionally in the stage probably with significant inflammation (3/12) . But these findings may be nonspecific and can be seen among other infectious myelopathies,[9,10] occasionally primary spinal cord tumor and intramedullary metastases,[23,24] which may need further differential diagnosis just like our case's situation. Unlike tabes dorsalis, most of the syphilitic meningomyelitis usually improve with penicillin treatment (complete 10/12, partial 2/12).

In conclusion, syphilitic myelitis is a very rare type of NS. Because of the nonspecific clinical and imaging findings, this treatable and potentially curable disease should be included in the differential diagnosis of unclear myelopathy. Serum and CSF serologic testing for syphilis are definitive in the diagnosis of these patients.

Disclaimer statements

Contributors None.

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Conflict of interest The authors declare no conflict of interests.

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