The clinical features of syphilitic myelitis with longitudinally extensive myelopathy on spinal magnetic resonance imaging: a case report and literature review

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Abstract

Background: Syphilitic myelitis as a bacterial infection caused by Treponema pallidum, is a very rare manifestation of neurosyphilis. The magnetic resonance imaging (MRI) appearance of longitudinally extensive myelopathy with syphilitic myelitis is not well documented and only a few cases have been reported about its' clinical features.

Case presentation: Herein, we report a patient who suffered from syphilitic myelitis with symptoms of sensory disturbance, with longitudinally extensive myelopathy with "flip-flop sign" on spinal MRI. This patient performed complete clinical and radiologic recovery after treatment. We also summarized the clinical features of syphilitic myelitis with longitudinally extensive myelopathy from the reported literatures published in English language. A total of 16 articles of 20 cases between January 1987 and December 2018 were identified. Of the 20 patients with syphilitic myelitis, the age of onset varied between 17 and 63 years. Sixteen patients were males (80%). Sixteen patients presented with the onset of sensory disturbance (80%), 15 with paraparesis (75%), 9 with urinary retention (45%). Eleven patients had high risk behavior (55%). Five patients had concomitant HIV infection (25%). Serological data showed 15 patients performed with positive venereal disease research laboratory (VDRL)/ treponema pallidum particle agglutination (TPHA), and 17 patients with positive VDRL/TPHA in cerebrospinal fluid (CSF). Seventeen patients with elevated cells and protein in CSF. On MRI, 16 patients showed abnormal signal intensities involved thoracic spine, 6 involved cervical, and 3 involved both cervical and thoracic spine. There were 3 patients performed with the "flip-flop sign". All the patients were treated with penicillin, and 15 patients were performed with a better prognosis.

Conclusions: Syphilitic myelitis is a relatively rare feature of Treponema pallidum infection. Early definite diagnosis and antibiotic therapy are crucial for minimizing neurological sequelae. Our case also raises awareness of syphilitic myelitis as an important complication of neurosyphilis due to homosexuality, especially in developing countries.

Introduction

Syphilis is a sexually-transmitted disease caused by Treponema pallidum infection. About 2.1 million pregnant women have active syphilis every year [1]. It is of both individual and public health issue

due to its direct morbidity, increased risk of human immunodeficiency virus (HIV) infection and lifelong morbidity especially in low-income countries [2]. It could progress over years through a series of clinical stages and result in irreversible neurological complications without treatment. One-third of patients with early syphilis have the manifestations of central nervous system, and neurosyphilis can also affect the brain, brainstem, spinal cord, meninges, nerve roots, and cerebral/spinal vessels [3]. The clinical presentations of neurosyphilis include acute lymphocytic meningitis (acute syphilitic meningitis), stroke (meningovascular syphilis), dementia (general paresis) and/or myelopathy (tabes dorsalis, meningomyelitis, syringomyelia) [4]. The clinical symptoms of syphilitic meningomyelitis usually develop at between 1 and 30 years after the initial infection [5]. The treatment with penicillin and corticosteroids can diminish the affected lesions with partially reversible. However, symptomatic neurosyphilis especially syphilitic myelitis and the clinical features have been infrequently reported [6].

Only a few cases of syphilitic myelitis have been documented in the international literature. To the best of our knowledge, there are only 19 cases about syphilitic myelitis were reported from the literatures [4, 7-21]. We herein report a case of syphilitic myelitis with longitudinally extensive myelopathy presenting with the characteristic of "flip-flop sign" on spinal MRI. We also summarized the clinical features of syphilitic myelitis with longitudinally extensive myelopathy from the prior reported literatures.

Case Presentation

A 25-year-old man was admitted to the Department of Neurology with the symptoms of acute onset of sensory disturbance and numbness for 7 days. He was homosexual and exposed to unprotected intercourse. Neurological examination revealed the hypalgesia below T6 level. The other physical examinations were normal. Laboratory tests revealed the treponema pallidum particle agglutination (TPPA) and toluidine red unheated serumtest (TRUST) in serum were positive, and the serum rapid plasma reagin (RPR) was 1:16. However, antibody against HIV was negative. The levels of homocysteine, folic acid and vitamin B12 were 26μmol/L (0-15μmol/L), 2.59ng/ml (□5.4ng/ml)) and 325pg/mL (211-911pg/ml), respectively. The results of cerebrospinal fluid test (CSF) showed a higher

level of cells (110/uL) and protein (148mg/dl). The immunological tests of aquaporin 4 (AQP4)-IgG were negative both in serum and CSF. The other inflammatory, immune and infectious biomarkers of both CSF and serum were also unremarkable. The cranial MRI yielded normal findings. However, the spinal cord MRI showed abnormal longitudinally extensive T2 weighted hyperintensities involving the posterior columns from C7 through T6, with "flip-flop sign" on cervical spinal MRI (Figure 1 B and C, Figure 2 B and C). Focal enhancement was observed in the dorsal aspect of the thoracic cord on T1-weighted gadolinium-enhanced images at T3-T4 level (Figure 1 C, Figure 2 C).

With the treatment of penicillin (24-million IU/day) for two weeks, three months later, the symptoms of sensation disappeared. The abnormal hyperintensities of spinal MRI also dissolved with three months' follow up (Figure 3). Moreover, the laboratory data of CSF showed the reduced cells (24 /uL) and protein (65mg/dl). TPPA and TRUST (1:8) in serum were still positive. The examination in CSF showed TPPA was positive and TRUST was 1:1. The diagnosis of syphilitic myelitis was established according to the history of homosexuality, clinical manifestations, MRI findings with "flip-flop sign", also with the favorable prognosis by the penicillin treatment.

Literature search and selection

To better understand the clinical characteristics of syphilitic myelitis, we performed a literature search to identify other reports (reviews, case reports or case series) from January 1987 to December 2018, using the PubMed and web of science databases with the following terms, including "syphilis", "neurosyphilis", "syphilitic myelitis", "meningomyelitis", "central nervous system", "spine". All pertinent English language articles were retrieved. A hand-search by reviewing the reference sections of the retrieved articles was also performed.

Data Extraction

Two investigators collected data from the selected articles. The following data were extracted: the author, country, age, gender, symptoms, neurological examination, etiology, auxiliary examinations, therapy and outcome. In this article we also review the literatures of this rare condition.

A total of 16 articles of 20 cases between January 1987 and December 2018 were identified by preliminary literatures. The clinical characteristics of the involved cases were presented in Table 1. Of the 20 patients with syphilitic myelitis, the age of onset varied between 17 and 63 years. Sixteen patients were males (80%). The duration of symptoms was variable from 3 days to 9 months. Sixteen patients presented with the onset of sensory disturbance (80%), 15 with paraparesis (75%), 9 with urinary retention (45%), 2 with gait disorder (10%). Elven patients had a high risk behavior such as homosexuality or bisexuality (55%). Two patients presented with non-pruritic rash or erythematous with the diagnosis of secondary syphilis (10%). One patient was diagnosed as having syphilis and was treated previously (5%). Five patients had concomitant HIV infection (25%). Serological data showed 15 patients performed with positive venereal disease research laboratory test (VDRL) and/or high Treponema pallidum hemagglutination (TPHA), and 17 patients had positive VDRL/TPHA in CSF. We also found that raised protein was seen in 15 patients and pleocytosis was seen in 17 patients in CSF. On MRI, 16 patients showed abnormal signal intensities involved thoracic spine, 6 involved cervical, and 3 involved both cervical and thoracic spine. There were 3 patients performed with the "flip-flop sign". All the patients were treated with penicillin, and 15 patients were with a better prognosis.

Discussion

Syphilitic myelitis caused by Treponema pallidum is an extremely rare disease. Herein, we reported a rare case of 25-year-old young man presented with symptoms of sensory disturbance, due to syphilitic myelitis with longitudinally extensive myelopathy with "flip-flop sign" on spinal MRI. Furthermore, we also summarized the clinical features of syphilitic myelitis with longitudinally extensive myelopathy.

In the pre-antibiotic era, syphilis was one of the most frequent cause of myelopathy [22]. Syphilitic meningomyelitis represents less than 3% of neurosyphilitic cases. The diagnosis is according to a high CSF white blood cell count (≥20mL) with either a reactive CSF VDRL test or a positive CSF antibody [15]. Syphilitic myelitis is a very rare but not well-recognized manifestation of neurosyphilis. It is a form of meningo-vascular syphilis with abnormalities confined to the spinal cord. The patients can present with sensory disturbance, lower extremity weakness, pyramidal signs, and variable degrees of

bladder and bowel dysfunction. Diagnosis is difficult as it mimic idiopathic transverse myelitis, spinal cord infarction, and acute disseminated encephalomyelitis or neuromyelitis optica spectrum disorders. On spinal MRI, longitudinally extensive myelopathy was in common, especially the feature of "flip-flop sign". Our case also suggested the presence of “flip-flop sign” in MR images may indicate syphilitic myelitis.

Syphilis is a sexually transmitted and systemic disease, and the most common mechanism of transmission is sexual intercourse. HIV and syphilis affect similar patient groups and co-infection is common. The neurological complications of both infections occasionally occur simultaneously during a clinical course. In the United States, 16% of all syphilis patients, and 28% of male syphilis patients were co-infected with HIV [23]. If syphilis is detected in a patient with an elevated CSF TPHA-albumin index, it is crucial to check for serum HIV antibodies. As for our case, 11 patients (55%) had a high risk behavior such as homosexual and/or bisexual individuals. Five patients had concomitant HIV infection (25%). Determining which of the infections, syphilis or HIV, is crucial for allowing for a prompt diagnosis and the initiation of appropriate treatment. Our case also raised the importance of the serious consequences of homosexuality or high risk of unprotected sexual intercourse.

Although there are several hypotheses, the exact origin of the disease remains unknown [24], which may due to reversible edema from infection or ischemia [13] In syphilitic myelitis, there is primary involvement of the meninges and vessels. It is pathologically characterized by meningeal inflammation and spinal cord ischemia and edema due to syphilitic vasculopathy. The MR abnormalities of the spinal cord probably result from meningeal inflammation and spinal cord ischemia. Spinal cord lesions which have resolved completely following treatment has been reported, and the disappearance of high-signal lesion may indicate that ischemic or inflammatory changes are reversible [25]. As for our case, The high intensity areas on T2- weighted, observed in our case, may indicate reversible ischemic change or inflammation [7].

The strengths of our case are showed as follows. Firstly, our case revealed extensive T2-weighted

abnormal signal in the spinal cord with "flip-flop sign". To the best of our knowledge, only 2 cases have been previously described of such longitudinally extensive T2-weighted hyperintensities with "flip-flop sign" [9, 14]. Secondly, the medical history of homosexuality, clinical presentations, physical examination, laboratory examinations of serum and CSF, the imaging findings of "flip-flop sign", treatment of penicillin and favorable prognosis all contributed to our diagnosis of syphilitic myelitis. Moreover, in view of the longitudinally extensive myelopathy on MRI, we perfected AQP4 in CSF and serum timely. The result was negative, and the misdiagnose of neuromyelitis optica spectrum disorders had been avoided. Thirdly, to date, our study was the largest number to explore the clinical features of syphilitic myelitis with longitudinally extensive myelopathy on spinal MRI.

Conclusion

In summary, syphilitic myelitis is a very rare manifestation of neurosyphilis. Early diagnosis and treatment are crucial because it represents a treatable and potentially reversible cause of myelopathy with penicillin. Our study also raises awareness of an important complication of neurosyphilis due to homosexuality. Attention is drawn upon the importance of doing serological tests for syphilis when presented with any atypical neurological situation. A high index of suspicion is necessary so that this potentially treatable disease would not be overlooked.

Abbreviations

VDRL: venereal disease research laboratory; TPHA: treponema pallidum hemagglutination assay; LETM: longitudinally extensive transverse myelitis; RPR: Rapid plasma reagin, TRUST: toluidine red unheated serum test; HIV: human immunodefciency virus; NA: not applicable; FTA -ABS: fluorescent treponemal antibody-absorption; MRI: magnetic resonance imaging; CSF: cerebrospinal fluid. AQP4: Aquaporin 4.

Declarations

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Availability of Data and Materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request

Authors' contributions

JLY and WXW examined, evaluated the patient and drafted the manuscript. DMX help collect the data. WLH participated in the design of the case-report and helped to draft the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The study was approved by the Institutional Ethical Committee of Beijing Chaoyang Hospital, Capital Medical University.

Consent for publication

Written informed consent was obtained from the patient for publication of this Case Report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

Competing interests

The authors declare that they have no competing interests

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Table

Table 1. The clinical features of syphilitic myelitis with longitudinally extensive myelopathy for 20 patients

Case series	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Ref	[7]	[8]	[9]	[9]	[10]	[11]	[12]	[13]	[14]	[15]	[16]	[17]	[4]	[18]	[18]	[19]	[20]	[21]	[21]	Our case
Age	46	31	17	29	17	28	63	57	36	46	63	38	32	35	30	49	41	36	49	25
Gender	M	M	F	F	M	M	M	F	M	M	M	M	M	M	F	M	M	M	M	M
Clinical Features	Gait, sensory disturbance, dysuria	Sensory disturbance, paraparesis	Paraparesis, sensory disturbance, urinary retention	Numbness, sensory disturbance, paraparesis	Paraplegia	Chorioretinitis, spastic paraparesis	Sensory deficit, weakness, urinary disturbance	Paraplegia, urinary retention	Pain, paraparesis	Numbness, pain	Pain, weakness	Pain, weakness, numbness, retained urination	Tingling, numbness	Acute transverse myelitis	Acute transverse myelitis	Gait, paresthesia, loss of pain and temperature, urinary retention	Unconscious, numbness	Paresthesia, ascending paresis in inferior limbs	Loss of bilateral strength, sensory impairment	Sensory disturbance,numbness
Duration	2 weeks	10 days	8 days	9 months	NA	180 days	60 days	3 days	4 months	7 days	12 days	4 months	4 months	2 weeks	1 month	2 weeks	NA	NA	NA	7 days
High risk behavior	NA	+	+	+	NA	+	NA	NA	NA	+	NA	+	+	+	NA	+	+	NA	NA	+
HIV infection	NA	NA	NA	NA	+	-	-	-	-	-	-	-	-	-	-	+	+	+	+	-
Blood VDRL	NA	1:640	1:4	1:4	1:16	NA	NA	1:8	Reactive	1:64	1:16	RPR (1:128)	1:16	Reactive	Non-reactive	Reactive	RPR +	NA	NA	TRUST+ RPR (1:16)
Blood TPHA	NA	>1:20480	Reactive	Reactive	FTA-ABS(1:6400)	NA	NA	FTA (3+) TPHA (2+)	1:5120	1:81920	Reactive	4+	1:160	1:5120	1:1280	1:2560	+	NA	NA	+
CSF protein (mg/dl)	High	94	52	54	106	94	200	Normal	243	72	91.70	88	40	123	57	79	NA	NA	NA	148

CSF cells (/uL)	Pleocytosis	120	75	20	180	120	498	Pleocytosis	346	113	303	18	40	115	170	202	NA	NA	NA	110
CSF VDRL	Reactive	1:80	Non-Reactive	Non-Reactive	NA	+	+	1:2	NA	NA	Reactive	1:16	+	Reactive	Reactive	NA	+	NA	NA	NA
CSF TPHA	Reactive	1:5120	Non-Reactive	Reactive	FTA-ABS (1:100)	TPHA +	NA	NA	FTA-ABS (1:320), TPHA (1:640)	NA	NA	NA	NA	NA	NA	+	NA	NA	NA	NA
Spinal MRI	High T2 intensity, abnormal Gd-DTPA enhanced	T3/4 wedge-shaped Gd-DTPA enhanced high intensity, swollen spinal cord	Below the C4 diffuse high signal, candle gutter ring appearance	T1-T11 abnormal signal, flip-flop sign	NA	T6-T8	LETM, Gadolinium enhancement	Extensive central high T2 signal, enhancement of the dorsal T8-T9	Diffuse high T2 signal, flip-flop sign	T2-T6 high signal, focal Gd-DTPA enhancement	T6-T11 high signal, focal Gd-DTPA enhancment	Ventral part on the level of T6–T7	T5-T12 hyperintense signals	Spine-cord edema from D4 to conus medullaris	Spine-cord edema from cervicodorsal up to conus	High-intensity lesions from C4 to T6	Spinal cord edema from C3-T1	Signal impairment in the spinal cord (T2-T12)	Diffuse hypersignal at several levels	Longitudinally extensive T2 hyperintensities involving from C7 to T6
Treatment	Antibiotic therapy	Penicillin, prednisolone	Penicillin	Penicillin, cephalosporins	Penicillin	Penicillin, dexamethasone	Penicillin, dexamethasone	Antibiotic therapy.	Penicillin	Penicillin, methylprednisolone	Ceftriaxone, methylprednisolone	Penicillin, prednisone	Penicillin	Procaine penicillin, Methyl prednisole	Procaine penicillin, donapezil	Penicillin potassium, methylprednisolone	Penicillin	Penicillin	Penicillin	Penicillin	Penicillin
Follow-up duration	NA	16 days	14 days	1 month	NA	NA	2 years	4 weeks	28 days	21 days	30 days	NA	14 days	6 months	Lost	two weeks	1 week	NA	NA	3 months
Status	Improved	Improved	Complete remission	Improved	Spasticity	NA	Improved	Non improved	Improved	Improved	Improved	Positive effect	NA	Same	NA	Improved	Improved	Complete improvement	Partial improvement	Improved
Repeat CSF finding	NA	TPHA (1:2560), VDRL (1:40)	Cells 9/uL, protein 38mg/dl	NA	Non-reactive	NA	NA	NA	Reduced	N	cells 34/uL, protein 45.4 mg/dl	NA	NA	NA	NA	NA	MA	NA	NA	cells 24/uL, protein 65 mg/dl, TPPA +, TRUST 1:1.
Repeat blood	NA	TPHA (1:10240),	NA	NA	NA	NA	NA	NA	NA	VDRL (1:16)	RPR (1:4)	RPR (1:64)	NA	NA	NA	NA	NA	NA	NA	TPPA (+), TRUST

finding																				(1:8)
	VDRL (1:160)																			
Repeat MRI finding	Disappearance of intramedullary high intensity areas	Reduction in the intensity of lesions	Reduction in the intensity of lesions	Reduction in the intensity of lesions	NA	NA	NA	Disappearance of the high signal lesion on T2-weighted images	Gadolinium enhancement disappeared, the high signal intensity diminished	NA	Reduction in the intensity of lesions	NA	NA	NA	NA	Reduction in the size of the cervical and thoracic cord lesions	NA	NA	NA	Dissolved with three months' follow up

Ref: reference; M: male, F: female; NA: not applicable; VDRL: venereal disease research laboratory; TPHA: treponema pallidum hemagglutination assay; LETM: longitudinally extensive transverse myelitis; RPR: Rapid plasma reagin, TRUST: toluidine red unheated serum test; T: thoracic; C: cervical; CSF: cerebrospinal fluid; HIV: human immunodefciency virus; NA: not applicable; FTA -ABS: fluorescent treponemal antibody-absorption; +, positive.

Figures

Figure 1

Figure 1. The spinal cord MRI showed abnormal longitudinally extensive T2 weighted hyperintensities involving the posterior columns from C7 through T6, with "flip-flop sign" on cervical spinal MRI.

Figure 2

Figure 2. The spinal cord MRI showed abnormal longitudinally extensive T2 weighted hyperintensities involving the posterior columns from C7 through T6, with "flip-flop sign" on cervical spinal MRI. Focal enhancement was observed in the dorsal aspect of the thoracic cord on T1- weighted gadolinium-enhanced images at T3-T4 level.

Figure 3

Figure 3. The abnormal hyperintensities of spinal MRI also dissolved with three months' follow up.

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