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ARTICLE

Medullary involvement in neurosyphilis: a report of 12 cases and a review of the literature

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Abstract

Study design Retrospective case series.

Objectives To describe the epidemiological, clinical, MRI and therapeutic features and the outcomes of patients with syphilitic myelitis in a third-level hospital in Marrakesh in southern Morocco.

Setting The Neurology Department, University Hospital Mohamed VI Marrakesh, Morocco.

Methods Twelve charts of persons with syphilitic myelitis over a period of 17 years were reviewed to determine demographics, presenting symptoms, clinical and radiological findings, biological features, treatment received and outcomes.

Results There were 120 reports of neurosyphilis. Twelve patients (10%) had syphilitic myelitis. Eleven patients (92%) were male with mean age of 44 at presentation. Tabes dorsalis was the most common clinical form. Cerebrospinal fluid analysis showed lymphocytic meningitis in nine patients (75%). Spine MRI was abnormal in four patients (33%). All patients were treated with 30 million units of aqueous penicillin G IV per day for 10 days, every 3 months. In follow-up, two patients (17%) with clinical syphilitic meningomyelitis improved significantly, eight patients (66%) with tabes dorsalis and subacute transverse myelitis showed partial improvement but clinical status was stationary for two patients (17%) with Erb paraplegia.

Conclusions All patients with myelopathy should undergo syphilitic serology because of nonspecific manifestations and curability of this disease.

Introduction

Neurosyphilis (NS) is a central nervous system infection caused by *Treponema pallidum*. NS can develop in the over 10% of patients that are inadequately treated or untreated [1]. Since the advent of penicillin therapy, symptomatic neurosyphilis is extremely rare; however, since 1980 and the epidemic of HIV, cases of syphilis have significantly increased worldwide. Recently, syphilis outbreaks have been reported in homosexual men [2, 3].

Neurosyphilis is characterized by clinical polymorphism and can be manifested as meningitis, parenchymatous or meningovascular involvement [4]; however, atypical or oligosymptomatic aspects have become more frequent [5]. Medullary involvement is rare in neurosyphilis and infrequently causes myelopathic syndromes. Diagnosing syphilitic myelitis is difficult because it mimics other common conditions such as spinal cord infarction, idiopathic transverse myelitis and acute disseminated encephalomyelitis [6, 7].

Syphilitic myelitis, as a potentially curable disease entity of NS, must be included in the differential diagnosis of myelopathy and strong suspicion and early treatment is essential to lessen sequelae [7]. Medullary involvement in neurosyphilis has not been well-documented and few cases have been reported in the literature; thus, we reviewed our patient population to document their clinical course.

Material and methods

We reviewed the medical records of 12 patients consecutively followed for syphilitic myelitis between January 2000 and December 2017.

Inclusion criteria were positive syphilitic serology (VDRL and TPHA) in cerebrospinal fluid (CSF) in patients with myelopathy and positive syphilitic serology in the

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blood. Records were analyzed to determine demographics, presenting symptoms, clinical and radiological findings, biological features, treatment received and outcomes.

The authors defined the recovery as follows:

Significant recovery: the ability to walk without assistance returns with complete disappearance of sphincter disturbances.

Partial recovery: the ability to walk is only possible with help or support and the patient retains some sphincter disturbances.

Stationary: there is a complete absence of any improvement in motor, sensory or sphincter disturbances.

Results

Demographic data, clinical features, investigations, treatment and outcome are summed up in Tables 1 and 2.

Demographic profile

Eleven individuals (92%) were male with a mean age of 44 years (33–57). Four patients had a history of risky sexual behavior (unprotected heterosexual intercourse). Two had a history of untreated genital ulcer (16%), and the median duration of illness after presenting ulceration was 20 years (8–33). Two cases of inadequately treated primary syphilis were noted while previous drug abuse was found in seven patients. No sexually transmitted infections such as hepatitis B and C, herpes, HIV and Neisseria gonorrhoeae were reported. Mean follow-up was 20 months (range 15–30 months).

Clinical features

Ten individuals had chronic myelopathy and two had subacute transverse myelitis. Tabes dorsalis was the most common clinical form of chronic myelopathy, being present in six patients. Syphilitic meningomyelitis was present in four individuals while two had a very slow progression of paralysis over many years known as Erb paraplegia.

Investigations

CSF analysis showed lymphocytic meningitis in nine individuals: Cell count was 20–690 cells/mm^3 (average 252, 44 cells/mm^3) and protein 0, 3–1, 64 g/l (average 0.8 g/l). Two CSF analyses were normal. One case had albuminocytologic dissociation with cell counts <3 cells/mm^3 and hyperproteinurachia at 2, 97 g/l. CSF venereal disease research laboratory (VDRL) was reactive while HIV serology was negative in all cases.

Neuroimaging findings

Magnetic resonance imaging (MRI) of the spine was abnormal in four individuals (Figs. 1–3). Syringomyelia was present in one case and spinal cord atrophy in two cases. All cases had hyperintense signals on T2 sequences in the spinal cord.

Treatment and outcome

All patients were treated with 30 million units of aqueous penicillin G IV per day for 10 days, every 3 months. Patients received an average of four courses of penicillin G for their treatment (range 3–6 courses). On a follow-up of patients for an average of 21 months (range 15–30), it was found that two patients (17%) with clinical syphilitic meningomyelitis improved significantly, eight patients (66%) with tabes dorsalis and subacute transverse myelitis showed partial improvement but clinical status was stationary for two patients (17%) with Erb paraplegia.

Repeated CSF analysis performed at the end of the third course of treatment showed partial improvement of lymphocytic pleocytosis, regression of the protein level in all patients, negative CSF–VDRL in seven cases, while the other five had negative serology 6 months later. Spine MRI was repeated in one patient (case 7) and showed that the hyperintensity had disappeared with generalized dorsal spinal cord atrophy.

Discussion

Neurosyphilis caused by the spirochete *Treponema pallidum* is an endemic infection of the central nervous system. It is an important sexually transmitted disease [1]. Neurosyphilis is generally known as a late manifestation of syphilis, but neurological involvement can also be seen in early syphilis [8], and *T. pallidum* can be found in the CSF of patients with primary syphilis [9]. The incidence of syphilis has increased in person with a history of immunosuppression and same sex. Clinical and epidemiological data have changed considerably compared to the pre-antibiotic era [10]. Yahyaoui et al. [11] reported a series of 201 individuals between 1986 and 1997 and Rafai et al. [12] reported on 55 cases over a period of 12 years. The prevalence of NS in sub-Saharan Africa is not negligible. In Guinea, Cisse et al. [13] reported 82 cases between 1986 and 1991 and 28 cases between 1992 and 2000 and in South Africa, Timmermans and Carr [10] collected 161 cases over a period of 10 years. In the United States, the number of cases of late syphilis has been slowly increasing every year since 1993 (17.2% per year) [14] while a northern Indian study reported 25 cases of NS over 13 years [15].

Table 1 Demographics, MRI and recovery patients with syphilitic myelitis

	Age (years)/ sex	History	Duration of symptoms	Clinical findings	Diagnostic category	MRI findings	Follow-up duration	Recovery
Case 1	38/M	—	3 months	−Flaccid paraplegia −Hypoesthesia with a low level of sensitivity at T10 −Neurogenic bladder	Subacute transverse myelitis	Normal	15 months	Partial improvement of the motor deficit with regression of sphincter disturbances
Case 2	40/M	—	6 months	−Posterior cord syndrome (proprioceptive ataxia, impaired position and vibration sense) −Pyramidal syndrome in lower limbs	Tabes dorsalis	Normal	20 months	Partial recovery of the motor deficit with possibility of walking with help
Case 3	42/M	−Primary syphilis treated in 1990	4 years	−Spastic paraplegia −Hypoesthesia with a low level of sensitivity at T12 −Bilateral babinski −Anal hypotonia −Neurogenic bladder	Erb paraplegia	Normal	18 months	Stationary without any motor, sensory or sphincter disturbances improvement moderate disability
Case 4	54/F	—	4 years	−Left-side predominant spastic tetraparesis. −Neurogenic bladder	Erb paraplegia	Cervico-osteoarthritic myelopathy on narrow cervical canal without true compression of the dural sheath.	20 months	Stationary with moderate disability
Case 5	41/M	−History of unprotected sex	4 months	−Paraparesis −Hypoesthesia with a low level of sensitivity at T6 −Anal hypotonia. −Neurogenic bladder	Syphilitic meningomyelitis	Sagittal T2-weighted image of the spinal cord shows continuous intramedullary high signal intensity from T1 to T3	20 months	Favorable with possibility of walking without support and complete disappearance of sphincter disturbances
Case 6	33/M	Primary syphilis treated in 1992	1 year	−Paraparesis −Radicular syndrome of the lower limbs −Impaired position and vibration sense	Tabes dorsalis	Normal	20 months	Partial recovery of the motor deficit with possibility of walking with support
Case 7	44/M	—	1 year	−Paraparesis −Pyramidal syndrome in lower limbs	Syphilitic meningomyelitis	Sagittal mid-slice view of the cervicothoracic spine shows hypointense signals on T1 sequences and hyperintense signals on T2 in the cord extending from C7 to T4, compatible with syringomyelia. Follow-up cervicothoracic spine MRI at 30 months showed that the syringomyelia had disappeared with generalized dorsal cord atrophy	30 months	Significant with ability to walk without help

Table 1 (continued)

	Age (years)/ sex	History	Duration of symptoms	Clinical findings	Diagnostic category	MRI findings	Follow-up duration	Recovery
Case 8	38/M	Untreated genital ulcer in 1998.	8 months	−Pyramidal syndrome in lower limbs −Impaired position and vibration sense	Tabes dorsalis	Normal	15 months	Partial recovery of the motor deficit with possibility of walking with support
Case 9	57/M	Untreated genital ulcer in 1975	1 month	−Flaccid paraparesis −Hypoesthesia with a low level of sensitivity at T6 −Anal hypotonia	Subacute transverse myelitis	Sagittal T2-weighted image of the spinal cord shows continuous high signal intensity from T3 to T9 without enhancement at the sagittal gadolinium-enhanced image	30 months	Partial recovery of the motor deficit and the patient still has some sphincter disturbances
Case 10	46/M	History of unprotected sex	3 years	−Posterior cord syndrome (proprioceptive ataxia, impaired position and vibration sense)	Tabes dorsalis	Normal	20 months	Partial improvement of the motor deficit with ability to walk with help
Case 11	51/M	History of unprotected sex	3 years	−Radicular syndrome in the lower limbs (proximal and distal motor deficiency with areflexia) −Posterior cord syndrome (proprioceptive ataxia, impaired position and vibration sense) −Neurogenic bladder	Tabes dorsalis	L4-L5 and L5-S1 disc herniation without root conflict	30 months	Partial recovery of the motor deficit with possibility of walking with support and improvement of sphincter disturbances
Case 12	48/M	−History of unprotected sex	3 years	−Pyramidal syndrome in lower limbs. −Impaired position and vibration sense −Neurogenic bladder	Tabes dorsalis	Sagittal T2-weighted image of the spinal cord shows continuous high signal intensity from T6 to T11 with spinal cord atrophy at T1−T6 level	18 months	Partial recovery of the motor deficit with possibility of walking with support and the patient still has some sphincter disturbances

Table 2 CFS profile of patients with syphilitic myelitis

	CSF analysis	Repeat CSF analysis at the end of the third cure of Peni G
Case 1	−Cell counts <3 cells/mm^3 −Albuminorachia: 0.43 g −VDRL1/16, TPHA: +++	−Cell counts <3 cells/mm^3 −Albuminorachia: 0.23 g − VDRL -
Case 2	−Lymphocytic meningitis: (cell counts: 350 lymphocytes/mm^3, hyperalbuminorachia at 0.77 g /l) −VDRL 1/32, TPHA 1/5120	−Regression of the lymphocytic meningitis (cell counts :150 lymphocytes/mm^3, hyperalbuminorachia at 0.5 g/l) −(VDRL: 1/2, TPHA 1/260)
Case 3	−Lymphocytic meningitis: (cell counts 128 lymphocytes/mm^3 Hyperalbuminorachia at 0.90 g/l) −VDRL ½, TPHA 1/530	−Cell counts<3 cells/mm^3 −Albuminorachia: 0.22 g −VDRL -
Case 4	−Cell counts <3 cells/mm^3 −Albuminorachia: 0.22 g/l −VDRL: ½, TPHA: 1/650	−Cell counts<3 cells/mm^3 −Albuminorachia: 0.20 g/l −VDRL -
Case 5	−Lymphocytic meningitis: (Cell counts: 200 lymphocytes/mm^3, hyperalbuminorachia at 1.36 g/l) −VDRL 1/4, TPHA 1/2560	−Regression of the lymphocytic meningitis (Cell counts: 80 lymphocytes/mm^3, hyperalbuminorachia at 0.80 g/l) −VDRL -
Case 6	−Lymphocytic meningitis (cell counts: 98% of lymphocyte with hyperproteinurachia at 0.5 g/l). −VDRL: 1/8, TPHA: 1/2960	−Regression of the lymphocytic meningitis (cell counts: 20% of lymphocyte, proteinurachia at 0.4 g/l). −(VDRL: 1/2, TPHA 1/640).
Case 7	−Lymphocytic meningitis: (Cell counts: 24 lymphocytes/mm^3, hyperalbuminorachia 0.81 g/l) −VDRL ¼,TPHA 1/2560	−Cell counts <3 cells/mm^3 −Albuminorachia: 0.18 g −VDRL -
Case 8	−Lymphocytic meningitis: (Cell counts: 20 lymphocytes/mm^3, hyperalbuminorachia at 0.60 g/l) −VDRL 1/4, TPHA 1/640	−Cell counts<3 cells/mm^3 −Albuminorachia: 0.28 g −VDRL -
Case 9	−Lymphocytic meningitis: (Cell counts 320 lymphocytes/mm^3, hyperalbuminorachia at 0.90 g/l) −VDRL 1/16, TPHA 1/2560	−Regression of the lymphocytic meningitis (160 lymphocytes/mm^3, normoproteinorachia at 0.28 g/l) −(VDRL 1/4, TPHA 1/1280)
Case 10	−Lymphocytic meningitis: (Cell counts 690 lymphocytes/mm^3, hyperalbuminorachia at 0.67 g/l) −VDRL: 1/64, TPHA: 1/10240	−Regression of the lymphocytic meningitis (560 lymphocytes/mm^3, normoalbuminorachia at 0.30 g/l). −(VDRL: 1/8, TPHA 1/1280)
Case 11	−Lymphocytic meningitis: (Cell counts 310 lymphocytes/mm^3, hyperalbuminorachia at 0.71 g/l). −VDRL: 1/16; TPHA: 1/5120.	−Regression of lymphocytic meningitis: (Cell counts 110 lymphocytes/mm^3, hyperalbuminorachia at 0.5 g/l). −(VDRL: 1/2, TPHA 1/2560)
Case 12	−Cell counts <3 cells/mm^3 −Hyperproteinorachia: 2.97 g /l −VDRL 1/4; TPHA 1/2560	Cell counts<3 cells/mm^3 −Albuminorachia: 0.4 g −VDRL -

Clinical forms of NS are variable and generally divided into five major entities: asymptomatic, parenchymatous, meningeal, meningovascular, and gummatous. Clinical aspects are usually nonspecific and can be observed during the evolution of the disease. Several forms can be seen on the same patient [10].

Treponema pallidum infection can affect different parts of the central nervous system (the meninges, the brain, the brainstem, the spinal cord, the nerve roots, but also the cerebral and spinal blood vessels), so the neurosyphilis can present in various forms making the diagnosis difficult [16]. Thirty percent of patients with *T. pallidum* have CSF abnormalities indicative of an invasion of the central nervous system by the body, but only a portion of these have symptomatic neurosyphilis [16]. The concomitant presence of immunosuppressive agents or conditions such as HIV/AIDS may alter the characteristics of neurosyphilis [16].

Only a few cases of nontabetic syphilis affecting the spinal cord are described in the literature [17]. Pathophysiologically, syphilitic myelitis has not only been associated

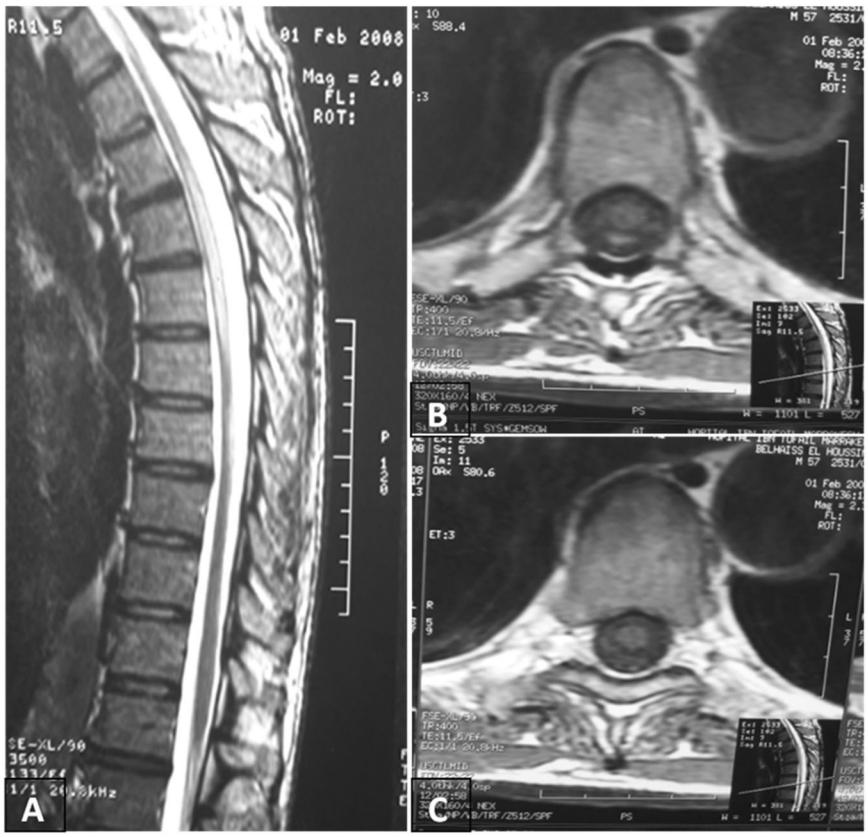

Fig. 1 **a** Sagittal T2-weighted image of the spinal cord shows continuous high signal intensity from T3 to T9 without enhancement at the T1-weighted axial gadolinium-enhanced image (**b**, **c**)

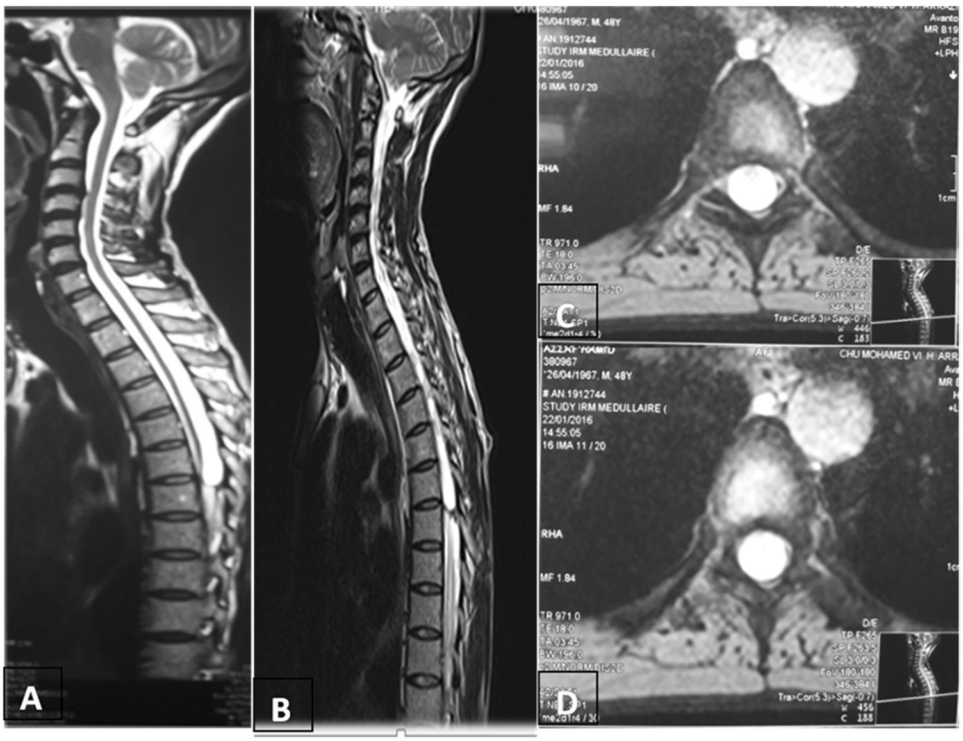

Fig. 2 **a** Sagittal T2-weighted image of the spinal cord shows spinal cord atrophy at T1−T6 level with continuous high signal intensity from T6 to T11 (**b**). **c**, **d** Axial T2-weighted image at T7/T8 level

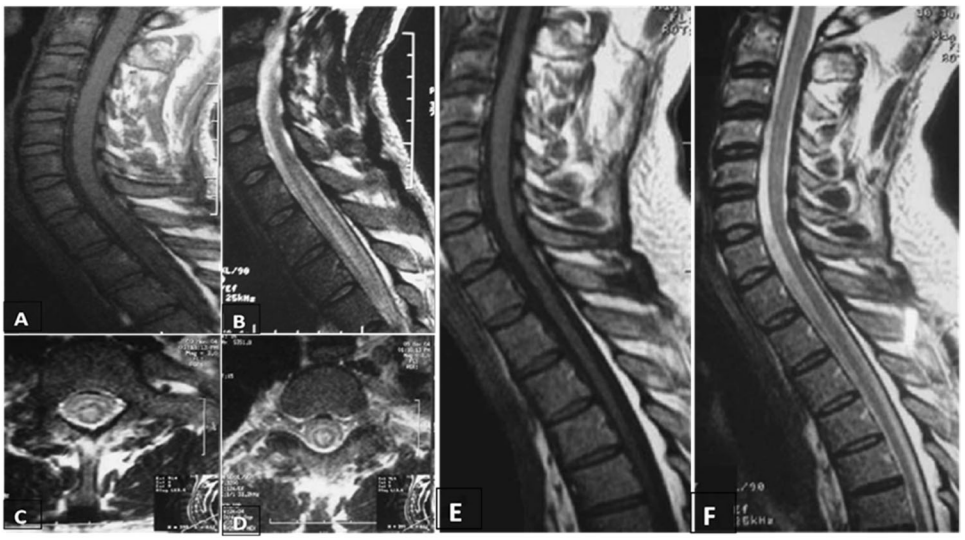

Fig. 3 **a** Sagittal image of the thoracic spinal cord shows hypointense signals on T1 sequence. **b** Hyperintense signals on T2 in the cord extending from C7 to T4, compatible with syringomyelia. **c**, **d** Axial view at the level of T3 shows hyperintense signals on T2 corresponding to a fluid-filled central cavity. **e**, **f** Follow-up cervicothoracic spine MRI at 30 months showed that the intramedullary high intensity areas on T2-weighted images disappeared with generalized dorsal cord atrophy

with meningomyelitis, cord atrophy or meningovascular disease, but also with compression of the spinal cord by gummae or syphilitic osteitis. Direct contamination of the marrow by the bacterium is rare [6].

Tabes dorsalis is the most well-known form of parenchymatous neurosyphilis, occurring in six of our patients. Its incidence has significantly decreased in the post-antibiotic era with a relative increase in the incidence of meningovascular forms [18]. Tabes dorsalis usually occurs 15–30 years after the primary infection presents with impaired position and vibration sense, subacute to chronic sensory ataxia, and lancinating pains. Throbbing or lightning-like pain affects the legs and abdomen. Physical examination reveals hyperreflexia, pupillary abnormalities and Argyll Robertson pupils: abolition of the photomotor reflex (contraction of the pupils in the light), with preserved contraction on accommodation. Gait is ataxic and often ulcers of the feet and Charcot joints can be present [16]. Syphilitic meningomyelitis was present in four of our patients. It is described as progressively worsening paraplegia with variable sensory and sphincter disturbances and abolition of superficial abdominal reflexes [16].

Two of our patients were diagnosed with Erb's paraplegia defined as an attack of the lateral column with a degeneration of pyramidal tracts. It is a variant of meningomyelitis characterized by spasmodic paraparesis that worsens progressively and is associated with urge incontinence. The evolution is slowly progressive to a bedridden state in 10−15 years [19]. Two final cases had syphilitic transverse myelitis with sudden onset of paraplegia and loss of sensation [16].

Diagnosis of syphilitic myelitis is problematic as it mimics other causes of myelopathy. Establishing the diagnosis of neurosyphilis requires CSF analysis. The CSF cell count (usually lymphocytes) are increased, protein concentration is raised and glucose reduced or normal [20]. In our series, CSF analysis showed lymphocytic meningitis in nine patients and ten individuals had hyperalbuminorachia and normoglycorachia. The VDRL and rapid plasma reagin (RPR) tests are more sensitive in the early stages of the disease but become negative later in the majority of cases [21]. The CSF VDRL test is very specific for active NS, but it has low sensitivity. The diagnosis of NS is confirmed by positive CSF VDRL. If CSF VDRL is negative, CSF fluorescent treponemal antibody absorption (FTA) testing is used to establish the diagnosis because it is highly sensitive; and experts believe that the diagnosis of NS can be excluded if FTA-abs test on the CSF is negative [20, 22]. *Treponema pallidum* haemagglutination test [23] and molecular tests including PCR [24] are also assays used to diagnose neurosyphilis; and they are generally characterized by their high specificity and sensitivity.

MRI of the spine was performed in all our patients and was abnormal in four. Few reports in the literature have described the MRI abnormalities in syphilitic myelitis. The first descriptions of MRI abnormalities in syphilitic myelitis reported by Tashiro et al. [25] in 1987 were short-segment with high signal intensity in the thoracic cord on T2-weighted images and abnormal peripheral enhancement. In case 5, the spinal MRI showed similar appearance with continuous intramedullary high signal intensity from T1 to T3. The classic appearance of syphilitic myelitis is abnormal enhancement in the superficial parts of spinal cord parenchyma (candle guttering appearance), low signal intensity on T2-weighted imaging and high intensity on gadolinium-enhanced T1-weighted imaging (flip-flop sign) [26].

High-signal lesions of the spinal cord parenchyma extending confined to the central portion and extending over multiple levels on T2-weighted imaging and abnormal enhancement on gadolinium-enhanced T1-weighted images have been described [7]. This radiological aspect was noted in two individuals in our series having an extensive

hypersignal exceeding three levels on T2-weighted imaging (Figs. 1 and 2). The difference in our two cases was the absence of contrast enhancement after gadolinium injection.

The literature indicates that intramedullary high intensity areas on T2-weighted images and gadolinium-enhancement on T1-weighted images disappear after antibiotic therapy and prednisolone [25, 27] and this was seen in case 7 (Fig. 3). Additionally, this individual had generalized dorsal cord atrophy on follow-up MRI 2.5 years post penicillin therapy been previously observed at advanced stages of the post disease [28]. Moreover, case 12 (Fig. 2) was seen after 3 years of disease evolution and had medullary atrophy on his first spine MRI.

Syphilitic spinal meningitis, as a cause of syringomyelia, has rarely been described in the literature; and only a few cases have been reported [29]. This rare form of syphilitic myelitis was found in case 7 (Fig. 3) as syrinx caused by syphilitic spinal meningitis due to the improvement of symptoms, disappearance of the syringomyelia cavity at the spinal MRI after penicillin treatment, and the absence of any other causes of syringomyelia, particularly basal intracranial arachnoiditis and cerebellar octopia.

We note radiologic normality of medullary MRI in 8 of 12 cases despite the presence of clinical symptoms of SCI; thus we conclude that syphilitic myelitis is not always accompanied by changes in spine MRI. The medullary abnormalities found in four cases of the series and previous cases reported in the literature were also localized at the level of the thoracic marrow which brings into question whether this is a simple coincidence or there is a physiopathological explanation for this location in the cord.

Conclusion

Syphilitic myelitis has no specific clinical or imaging findings. Only the practice of serologic testing for syphilis in all patients with myelopathy can diagnose this potentially treatable disease.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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