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Case Series

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Neurosyphilis in the Modern Era: A Case Series

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ABSTRACT

Ten cases of syphilis with central nervous system involvement were reported. All patients had HIV-negative status. Seven patients tested positive for treponemal antibodies in both serum and CSF. Five patients had progressive dementia with prominent psychiatric symptoms. All developed extrapyramidal syndrome after exposure to antipsychotic medication. Two patients had meningo-encephalitic illness. Neuro-imaging showed cortical atrophy more marked at the frontotemporal region with ventricular prominence. CSF revealed increased protein and lymphocytic pleocytosis. One patient presented with recurrent stroke. None of them improved due to the advanced state of disease. Multisegmental demyelination noted in 2 patients predominantly involving the dorsal cord, they were tested positive in serum only. One had a good recovery and the other showed no improvement in deficit.

Key-words: Neurosyphilis, Central nervous system, Dementia, Meningoencephalitis, Myelitis

INTRODUCTION

Neurosyphilis is a chronic and potentially debilitating manifestation of syphilis caused by the bacterium Treponema pallidum. It occurs when the infection invades the central nervous system and can present with a wide range of clinical features depending on the stage and immune status of the patient [1]. The disease can affect any part of the nervous system, including the brain, spinal cord, and meninges, and may present years after the initial infection if left untreated [2,3].

Historically, neurosyphilis was a common complication of untreated syphilis, often leading to severe neurological impairment or death. With the advent of antibiotics, particularly penicillin, its incidence declined dramatically. However, recent decades have witnessed a resurgence of syphilis globally, including neurosyphilis, likely due to increased high-risk sexual behavior, suboptimal screening, and healthcare disparities [4,5].

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The clinical manifestations of neurosyphilis are varied and can be classified into several forms, including asymptomatic neurosyphilis, meningeal syphilis, meningovascular syphilis, general paresis, and tabes dorsalis [6]. Early symptoms may include headache, confusion, and cranial nerve abnormalities, while late-stage disease may lead to dementia, psychiatric disturbances, sensory ataxia, and myelopathy [7,8].

Neurosyphilis is often underdiagnosed due to its protean manifestations that can mimic other neurological and psychiatric conditions. Diagnosis requires a high index of suspicion, particularly in patients with atypical neuropsychiatric presentations. Confirmatory testing includes serological assays such as the Venereal Disease Research Laboratory (VDRL) test and the Treponema pallidum hemagglutination assay (TPHA), both in serum and cerebrospinal fluid (CSF) [6,9]. MRI findings such as cortical atrophy, infarcts, or demyelination can support the diagnosis in conjunction with clinical and laboratory findings [10].

Timely diagnosis and prompt initiation of antibiotic therapy are crucial in preventing irreversible neurological damage. Penicillin remains the treatment of choice and has proven effective in many cases, particularly when administered in the early stages of the disease [11].

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In this case series, we report ten HIV-negative patients diagnosed with neurosyphilis over an extended period. The objective is to illustrate the diverse clinical presentations, imaging findings, and outcomes, thereby emphasizing the importance of considering neurosyphilis in the differential diagnosis of unexplained neuropsychiatric symptoms.

CASE 1: Dementia Presentation

A 45-year-old male (R.R.) presented with progressive memory loss, behavioral disturbances, and psychiatric symptoms. He had previously been under psychiatric care and was misdiagnosed with a functional psychosis. Neurological examination revealed diminished pupillary response suggestive of Argyll Robertson pupils. Serum treponemal tests were positive, and CSF analysis was suggestive of neurosyphilis, although CSF VDRL was not performed. MRI brain showed significant frontotemporal cortical atrophy with associated ventricular dilatation (Fig. 1i, 1ii). Despite appropriate antibiotic treatment, there was no clinical improvement.

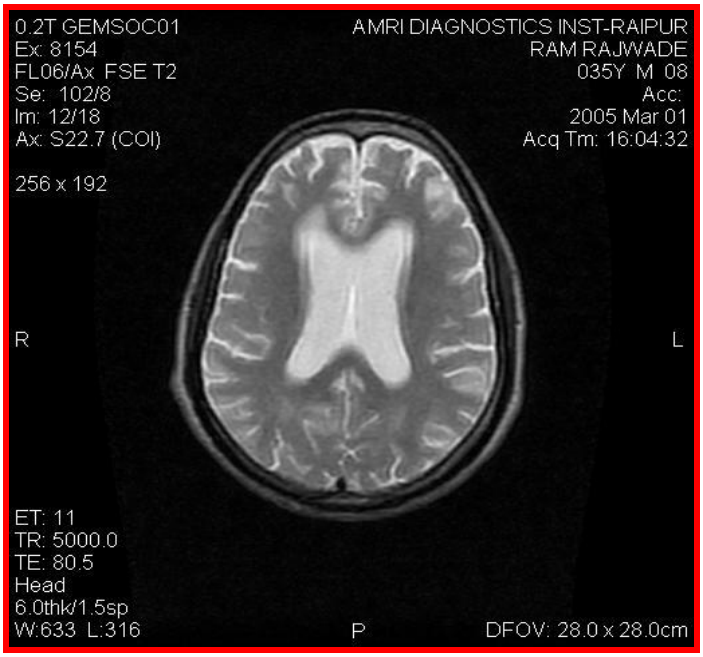

Fig. 1i: Axial T2-weighted MRI – Marked frontotemporal cortical atrophy with dilated lateral ventricles.

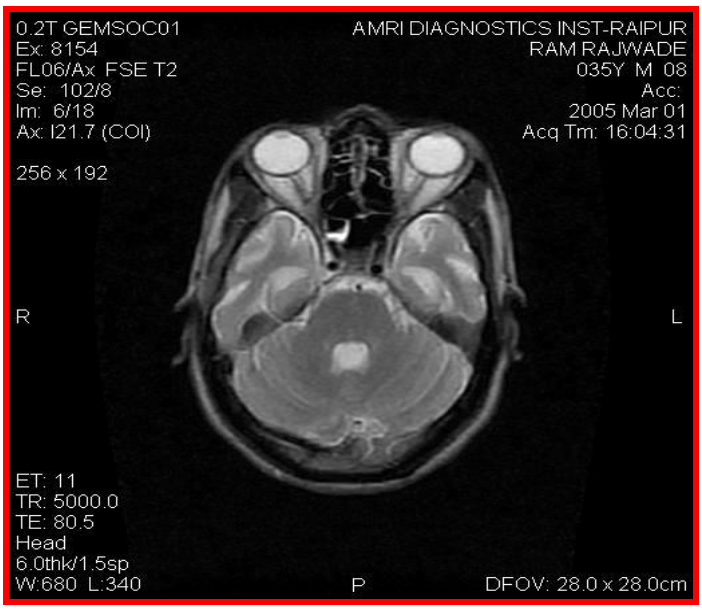

Fig. 1ii: Coronal T1-weighted MRI – Symmetrical frontal lobe volume loss and widened Sylvian fissures.

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CASE 2: Dementia with Confirmed CSF Positivity

A 39-year-old male (K) presented with short-term memory impairment, disorganized behavior, and reduced executive function. Both serum and CSF treponemal antibody tests were positive. CSF analysis showed elevated protein (108.7 mg/dL) and lymphocytic pleocytosis (10 cells/mm³). MRI revealed bilateral frontotemporal atrophy and ventricular enlargement (Fig. 2i, 2ii). Despite treatment, the patient showed no measurable recovery in cognition.

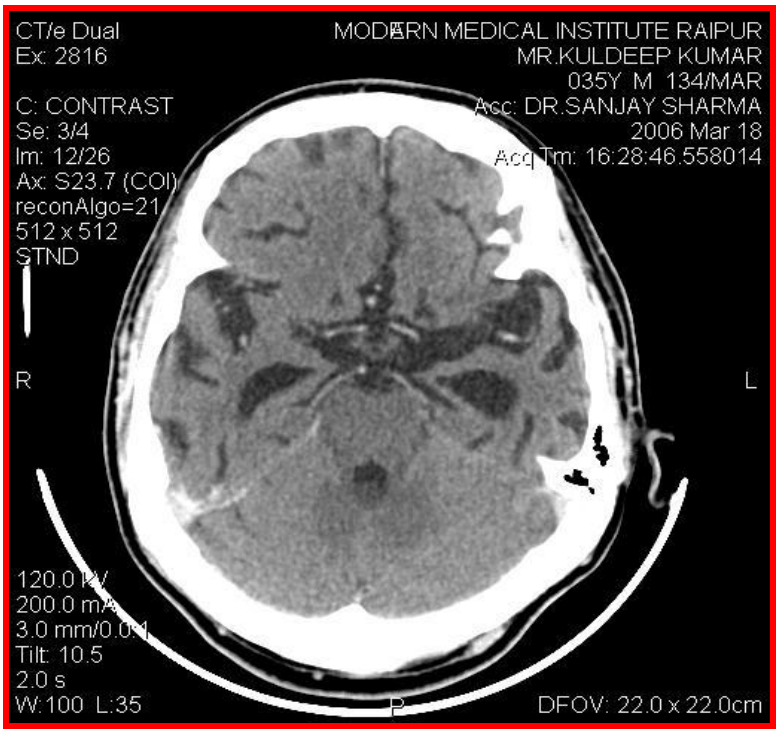

Fig. 2i: Axial FLAIR MRI – Prominent sulci in the frontal lobes indicating cortical thinning.

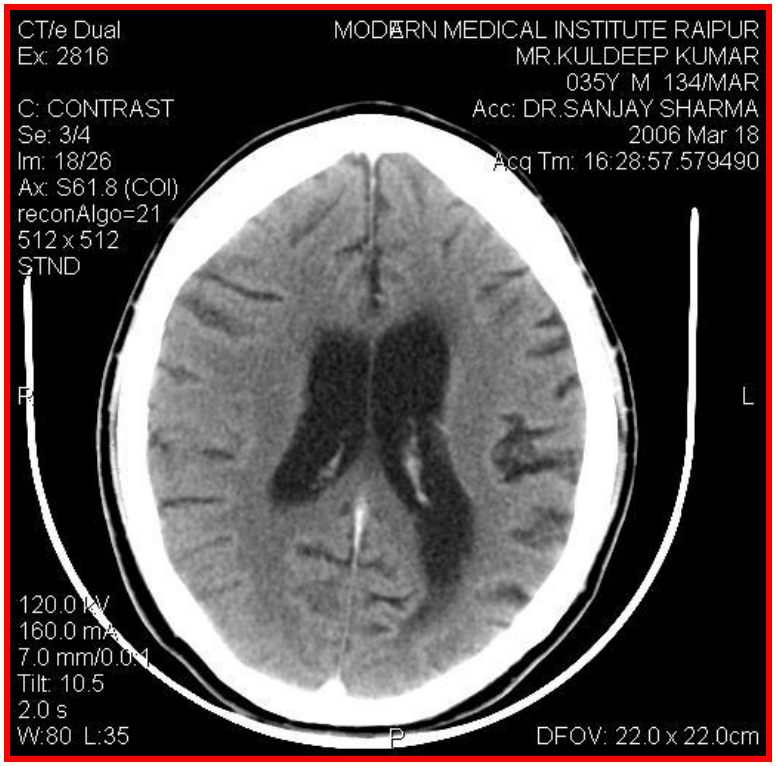

Fig. 2ii: Sagittal T1-weighted MRI – Dilated third ventricle and diffuse brain atrophy.

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CASE 3: Dementia with High Serum Titer

A 38-year-old male (A.S) developed cognitive decline and apathy over several months. Serum VDRL was reactive at 1:16 dilution, and TPHA was positive. CSF analysis revealed elevated protein (57.7 mg/dL), 100 cells/mm³, non-reactive VDRL, and positive TPHA. MRI brain demonstrated diffuse cortical atrophy (Fig. 3i, 3ii).

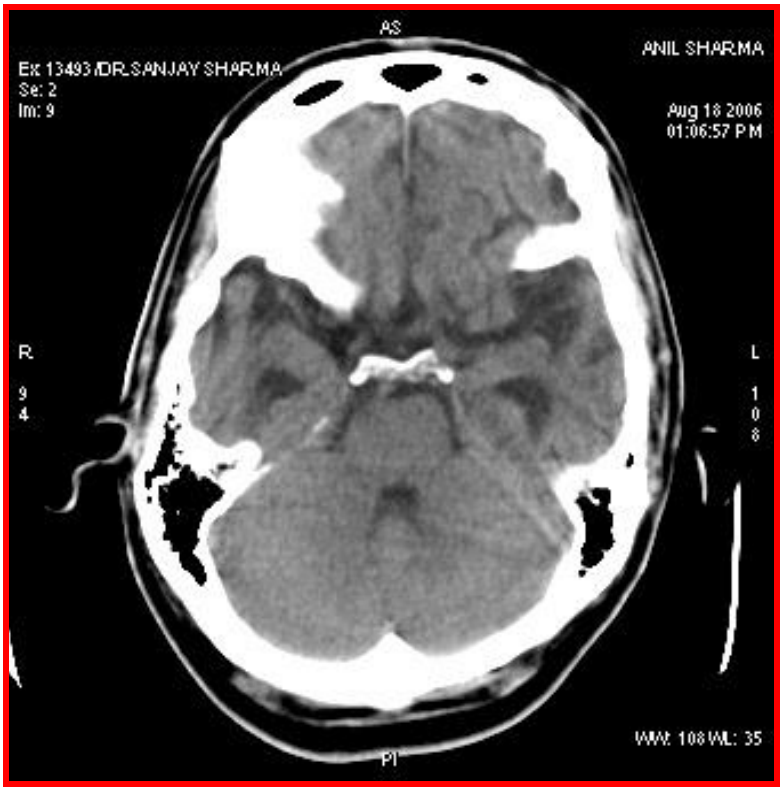

Fig. 3i: Axial T2-weighted MRI – Diffuse cortical atrophy with mild ventricular enlargement.

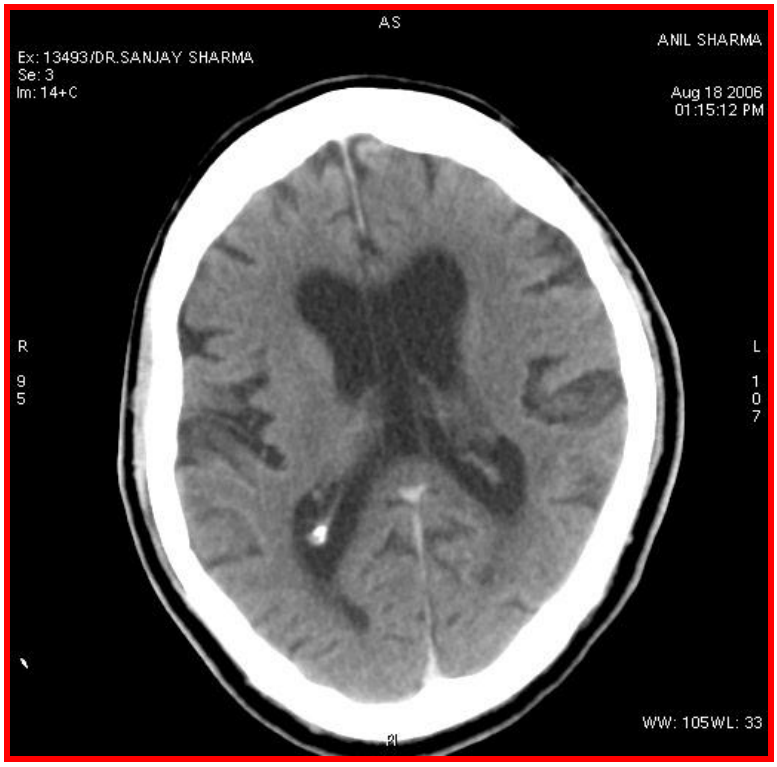

Fig. 3ii: Coronal T1-weighted MRI – Frontoparietal cortical thinning. Axial T2-weighted MRI – Diffuse cortical atrophy.

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CASE 4: Dementia, Partial Workup

A 38-year-old male (A.D) presented with progressive cognitive dysfunction. Serum VDRL was reactive (1:8). CSF protein was elevated (67.3 mg/dL) with occasional lymphocytes. CSF TPHA was positive, but VDRL was non-reactive. MRI showed cerebral atrophy (Fig. 4i, 4ii). Despite treatment, neurological status did not improve.

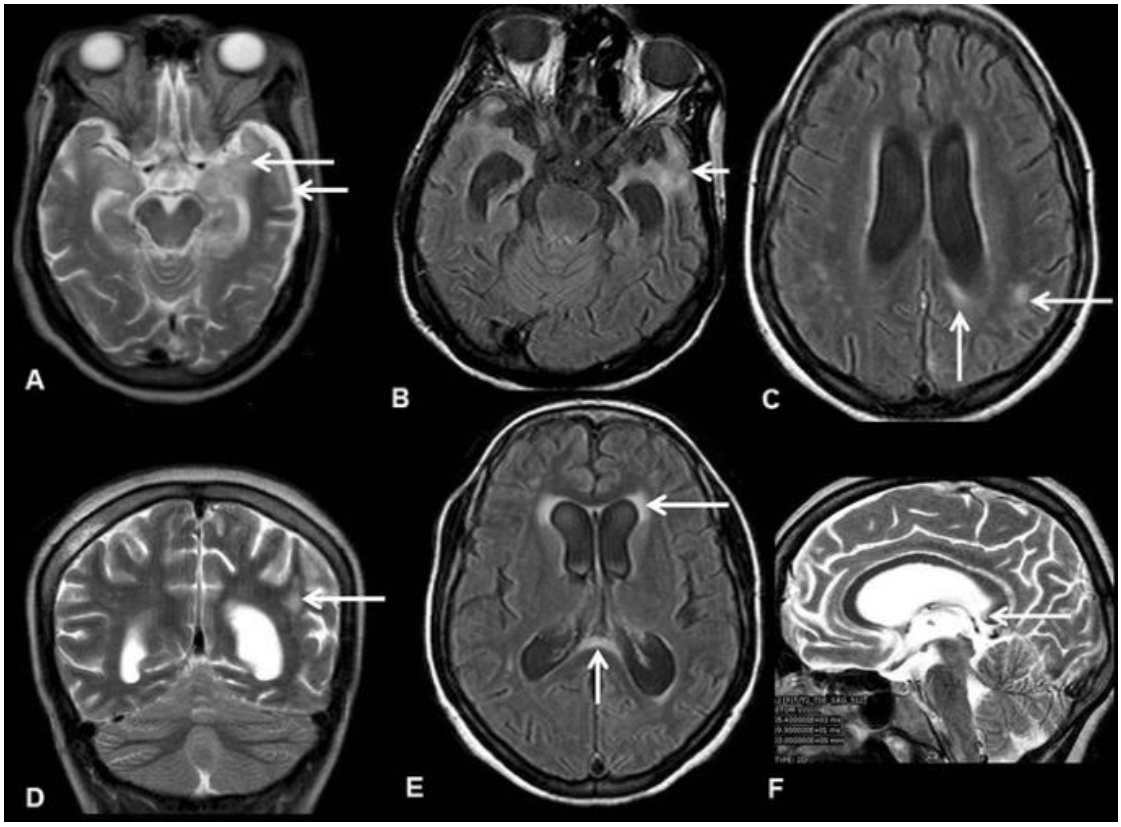

Fig. 4i: Sagittal T2-weighted MRI Spine – Long-segment hyperintensity involving posterior cord from C6 to T12.

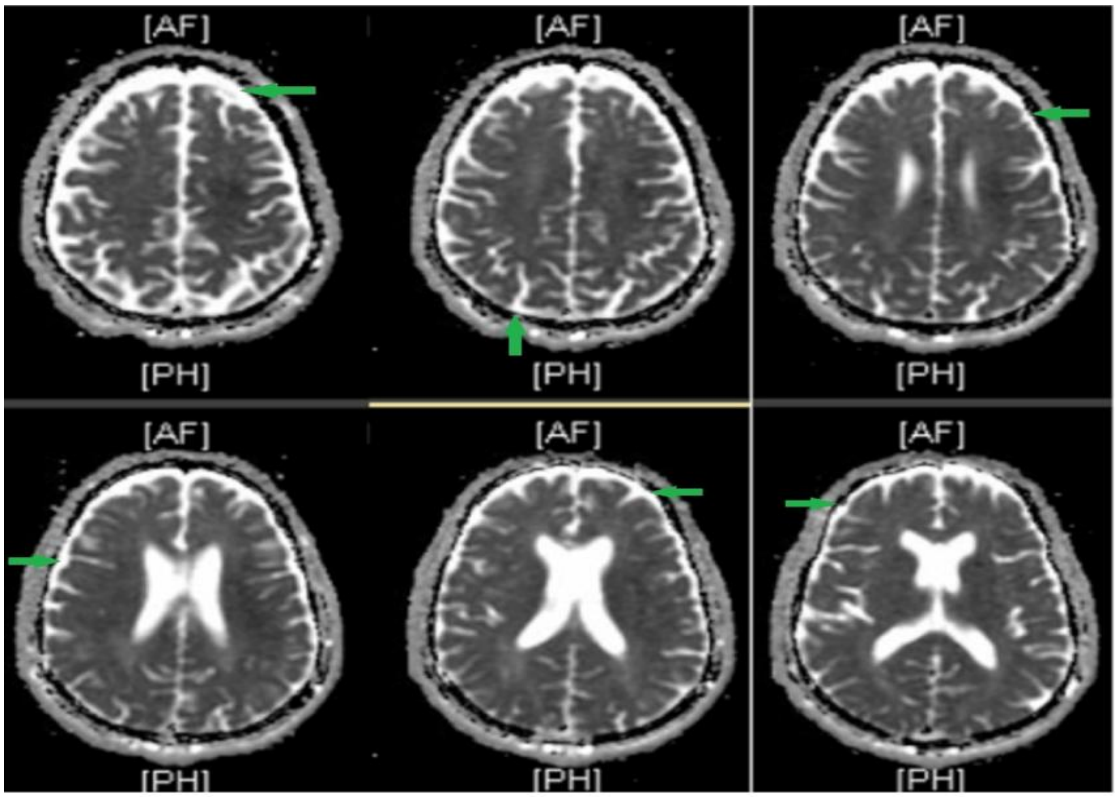

Fig. 4ii: Axial T2-weighted MRI Spine – Central cord hyperintensity with preserved peripheral signal.

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CASE 5: Dementia with Positive CSF Findings

A 40-year-old male (P.K) exhibited disorientation, decreased concentration, and personality changes. CSF and serum VDRL/TPHA were reactive. CSF protein was elevated (79.9 mg/dL) with 98 cells/mm³. MRI brain revealed diffuse atrophy with enlarged ventricles (Fig. 5i, 5ii). There was no functional improvement after treatment.

These five cases represent the paretic form of neurosyphilis, confirmed by serology and imaging. The neuroimaging consistently showed cortical atrophy, predominantly in the frontotemporal regions. All patients demonstrated minimal to no clinical recovery despite therapy, emphasizing the progressive nature of neurosyphilitic dementia and the critical importance of early diagnosis.

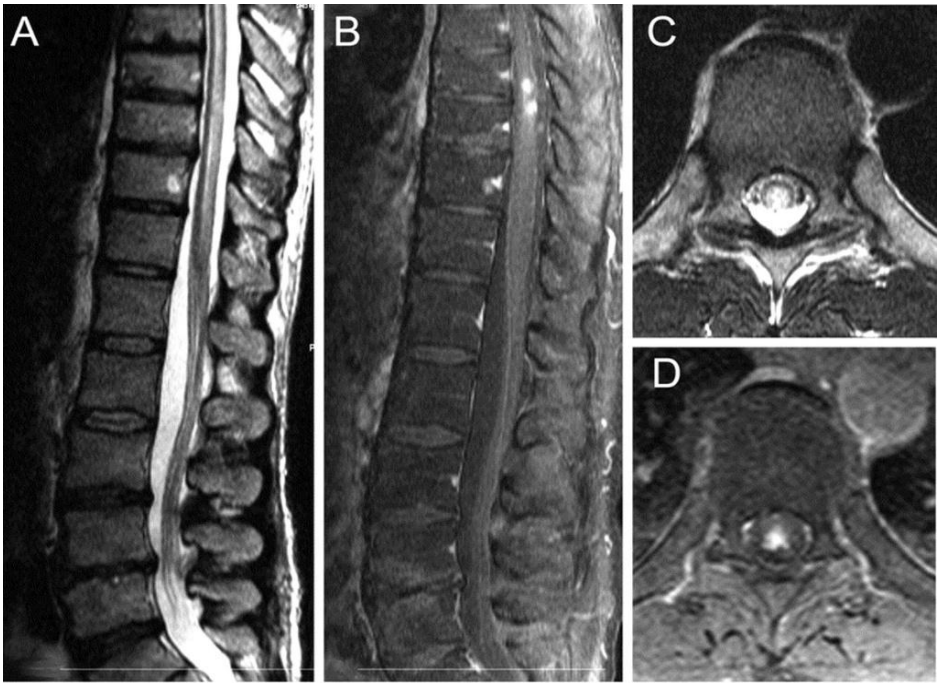

Fig. 5i: Sagittal T2-weighted MRI Spine – Dorsal cord demyelination from upper thoracic to lumbar segments.

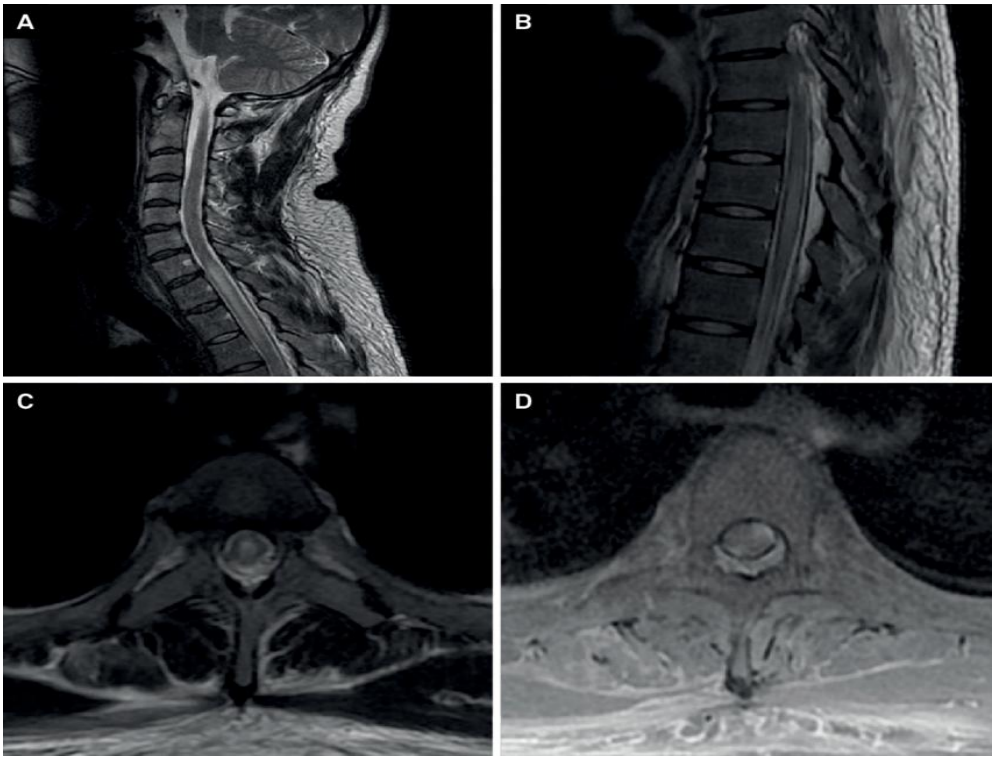

Fig. 5ii: Axial T2-weighted MRI Spine – Patchy cord edema and signal alteration in thoracic region

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DISCUSSION

Our case series highlights the diverse clinical presentations of neurosyphilis, including dementia, meningoencephalitis, stroke, and myelitis. Neurosyphilis is often referred to as "the great imitator" because of its ability to mimic various neurological and psychiatric conditions. In this series, the diagnosis was supported by a combination of serological tests, cerebrospinal fluid analysis, and neuroimaging.

Five patients presented with progressive cognitive decline and behavioral changes, consistent with the paretic form of neurosyphilis. All five showed frontotemporal cortical atrophy on MRI, which aligns with literature indicating predilection for these regions in syphilitic dementia [12]. Psychiatric symptoms were prominent and worsened with antipsychotics, a pattern also reported by Conde-Sendín et al., reinforcing the need for differential diagnosis in atypical psychiatric cases [13].

Two patients manifested with meningoencephalitic symptoms, including fever, altered mental status, and CSF pleocytosis. These findings are consistent with classic descriptions of acute symptomatic neurosyphilis [14].

One patient presented with recurrent strokes, which were attributed to meningovascular syphilis. Neuroimaging showed multiple subcortical infarcts and diffuse cortical atrophy. This form is known to cause cerebrovascular events due to endarteritis obliterans, as described by Flint et al. and others [15,16].

Two cases of spinal neurosyphilis (myelitis) demonstrated long-segment demyelination predominantly involving the dorsal cord. This is an uncommon but documented presentation. Berger emphasized the diagnostic challenges and variability in imaging findings for such cases [17]. MRI findings in our patients supported the diagnosis, and serological tests confirmed the treponemal etiology.

Treatment with intravenous penicillin was initiated in all cases. However, the clinical outcomes varied. Only one patient (a myelitis case) showed marked improvement. The rest either showed no recovery or deteriorated further. This highlights the importance of early diagnosis and treatment before irreversible neurological damage occurs [18].

Despite the availability of serologic testing and imaging, neurosyphilis often remains underdiagnosed, particularly in patients with neuropsychiatric symptoms lacking a clear etiology. As emphasized by Timmermans and Carr, the disease is frequently misdiagnosed due to its protean manifestations [19].

The resurgence of syphilis globally further underlines the importance of maintaining a high index of suspicion. Neuroimaging findings, especially frontotemporal atrophy and spinal cord demyelination, while not specific, should prompt testing in relevant clinical scenarios [20,21].

Our findings support prior evidence highlighting the importance of considering neurosyphilis in patients with unexplained cognitive decline, psychiatric symptoms, or spinal cord syndromes. Early diagnosis is critical. A multidisciplinary approach—including neurologists, psychiatrists, and infectious disease experts—can enhance detection and management, ultimately improving patient outcomes in this potentially reversible yet often underdiagnosed condition [22].

CONCLUSIONS

Neurosyphilis is a complex disease that can manifest in various forms, including dementia, meningoencephalitis, and myelitis. Early recognition and treatment are crucial to prevent long-term damage and improve outcomes. Clinicians should consider neurosyphilis in patients with neurological symptoms, particularly those with untreated syphilis. A thorough diagnostic workup, including serological tests and cerebrospinal fluid analysis, is essential for diagnosis.

Prompt treatment with antibiotics can help alleviate symptoms and prevent further progression of the disease. Awareness and timely intervention are key to managing neurosyphilis effectively and improving patient outcomes. Further studies are warranted to better understand the disease.

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CONTRIBUTION OF AUTHORS

One author has only contributed to this article.

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