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Case Report

The great imitator behind an ischemic stroke: a case of meningovascular syphilis

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ABSTRACT

Neurosyphilis is a rare but reversible cause of ischemic stroke. We report a 41-year-old male with no cardiovascular risk factors initially diagnosed with Bell's palsy for left facial weakness. Four days later, he developed left-sided hemiparesis and dysarthria. Neuroimaging confirmed a right nucleocapsular ischemic stroke. Cerebrospinal fluid analysis revealed pleocytosis (39 cells/μL), elevated protein (191.9 mg/dL), and a reactive VDRL, confirming meningovascular neurosyphilis. Treatment with 14 days of intravenous Penicillin G led to complete clinical recovery after six months. This case highlights "the great imitator" during a global resurgence of syphilis. This clinical evolution highlights how isolated cranial nerve deficits can act as a deceptive precursor to a endarteritis obliterans, masking a systemic infection behind a seemingly benign presentation. In young patients with stroke and no vascular risk factors, neurosyphilis should be considered, particularly when preceded by cranial nerve deficits.

1. Introduction

Syphilis is a sexually transmitted infection that can present with heterogeneous clinical manifestations. Neurosyphilis, particularly in its meningovascular form, represents a rare but potentially reversible cause of ischemic stroke.

2. Case report

We report the case of a 41-year-old man, born in Italy, with an unremarkable past medical history. On hospital day 1 he presented to the Emergency Department with left facial weakness. A non-contrast brain CT scan was performed and was unremarkable; he was therefore discharged with a diagnosis of Bell's palsy. Four days later, he returned to the same Emergency Department due to left-sided hemiparesis, deviation of the oral commissure and dysarthria. A brain CT angiography revealed a newly developed cortico-subcortical hypodense area at the level of the genu of the internal capsule, consistent with ischemic stroke. Laboratory tests showed mild neutrophilic leukocytosis and intravenous alteplase was administered.

A post-thrombolysis brain CT scan performed on hospital day 5 demonstrated subtle hypodensity of the posterior limb of the internal capsule, the tail of the caudate nucleus, and the right lentiform nucleus, consistent with recent ischemia. Brain MRI confirmed findings compatible with a subacute ischemic lesion (Fig. 1A–C).

On hospital day 13 a lumbar puncture was performed. Cerebrospinal fluid (CSF) analysis revealed slightly opalescent fluid with elevated protein levels (191.9 mg/dL) and 39 cells/μL, of which 94.9% were mononuclear cells. The FilmArray panel for neurotropic pathogens and CSF cultures were negative.

Given the suspicion of an inflammatory demyelinating disorder, including neuromyelitis optica spectrum disorder or multiple sclerosis, empiric intravenous corticosteroid therapy and intravenous immunoglobulins were administered for four days while CSF testing for anti-MOG and anti-AQP4 antibodies was underway; subsequent results were negative. Additional investigations, including HIV testing,

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QuantiFeron-TB Gold, rectal swab for enterovirus and two sets of blood cultures were all negative.

He had no previous history of syphilis and did not report any prior chancres or rash. Due to suspicion of neurosyphilis, serum anti-*Treponema pallidum* antibodies were detected (24.47), with a positive serum VDRL titer of 1:32. Therefore, a second lumbar puncture was performed, showing reactive CSF VDRL. As the reference laboratory performed only qualitative CSF VDRL testing, a quantitative CSF VDRL titer was not available. A diagnosis of neurosyphilis was established, and intravenous penicillin G therapy was initiated on hospital day 22.

On hospital day 38, a brain CT scan with and without contrast showed clearer demarcation of the ischemic lesion in the right internal capsule and resolution of the previously observed contrast enhancement.

The patient completed intravenous penicillin G therapy on hospital day 66. On the same day, an additional intramuscular dose of benzylpenicillin was administered. Six months after the event, the patient had achieved complete neurological recovery, with restoration of autonomous walking and independent daily activities. No repeat cerebrospinal fluid examination or follow-up neuroimaging was performed.

3. Discussion

Early symptomatic neurosyphilis often manifests as acute meningitis, frequently involving the cranial nerves which may be the result of extensive basilar meningitis [1]. While Bell's palsy is commonly idiopathic, clinicians should always think about syphilis: involvement of cranial nerve VII is one of the most common cranial neuropathies in the basilar meningitis associated with *Treponema pallidum* infection [1]. Early cranial neuropathies may therefore represent an initial warning sign of meningovascular neurosyphilis and should prompt careful diagnostic evaluation in order to prevent progression to ischemic cerebrovascular complications. The four-day interval between the initial facial palsy and the subsequent hemiparesis highlights the critical window during which the infection progressed from a purely meningeal process to a meningovascular event [1,4].

In the European Union during 2025 there was an increase of 34% of new infections from 2021 to 41% from 2018 [8,10]. In 2022 alone, the U.S. reported 207,255 total syphilis cases, including 3755 cases of congenital syphilis—the highest number recorded since 1991 [9,10].

This resurgence indicates that neurosyphilis should no longer be viewed as a historical curiosity; it is estimated that 3% to 5% of syphilis cases result in neurological, ocular, or otic complications [1]. In a 41-year-old patient with no traditional cardiovascular risk factors, the etiological work-up for an ischemic stroke should evaluate infectious or inflammatory causes, as neurosyphilis [6]. The treponema can cause stroke at any stage of the disease, though typically it occurs 5 to 10 years after the initial infection [1]. The ischemic stroke observed in the genu of the internal capsule represents the clinical endpoint of *endarteritis obliterans* [1]. This process involves an inflammatory vasculitis of small- and medium-sized cerebral vessels, where fibroblastic and inflammatory proliferation of the adventitia and intima leads to arterial stenosis and subsequent thrombosis [1,5]. In this patient, MRI findings confirmed an infarct in the territory of the middle cerebral artery (MCA) and its perforating branches, which are the most commonly affected [1,5].

The first step in the evaluation of late neurosyphilis is serum treponemal testing. If this test turns out negative, the diagnosis can be excluded. These tests remain reactive for life in virtually all individuals regardless of previous treatment. The non-treponemal serum tests may become non reactive in late neurosyphilis, especially in tabes dorsalis [1,5].

The diagnosis of late neurosyphilis can be done with a positive CSF non-treponemal test. Even if the CSF non-treponemal tests turn out negative the diagnosis can be established with a count of white blood cells (WBC) $>$ 5 cells/ μL and/or CSF protein concentration $>$45 mg/dL in the absence of other plausible causes [2,5].

The diagnosis in this case was secured via CSF analysis which tested positive for VDRL. Nevertheless the patient's CSF mirrored the parameters discussed in recent literature:

- Pleocytosis: the patient exhibited 39 cells/μL. Non-specific pleocytosis, defined as $>$5 cells/μL, is considered a sensitive marker of neuroinvasion [2,5].
- Protein Levels: CSF protein was significantly elevated at 191.9 mg/dL. Protein levels above 45 mg/dL are supportive of late neurosyphilis [1,2].
- VDRL Sensitivity: The CSF VDRL was reactive. Although the VDRL test is the "gold standard" for specificity, its sensitivity is highly variable (27%–98%) [1,2].

Management followed the recommended first-line therapy: intravenous Aqueous Crystalline Penicillin G (18 to 24 million units per day) for 14 days [3,11]. Before the diagnosis of neurosyphilis was established, intravenous alteplase was administered under the initial suspicion of acute ischemic stroke, but it did not result in any clinical improvement. Empiric corticosteroid therapy was also started during the initial work-up for a possible autoimmune/inflammatory disorder; however, it was promptly discontinued once this hypothesis was excluded, and it provided only mild transient relief of headache, without meaningful neurological benefit. These observations suggest that the patient's

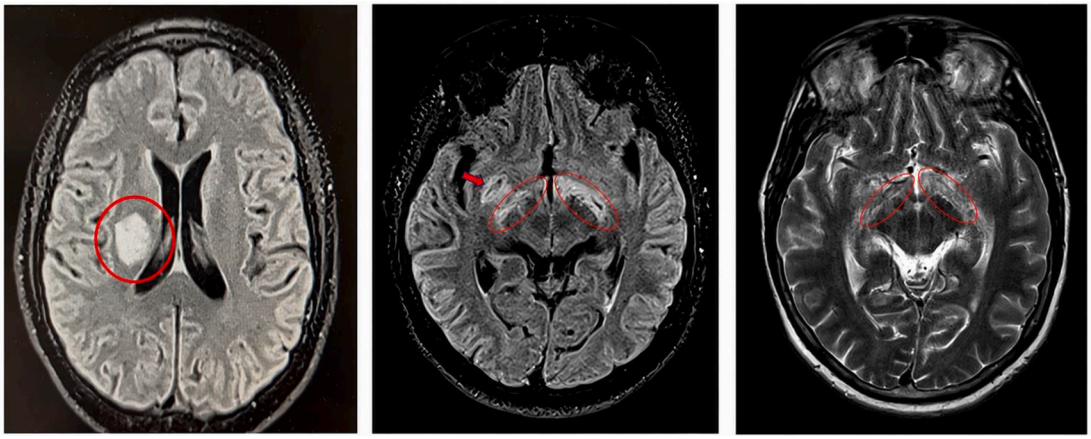

Fig. 1. A: Brain MRI showing an area of altered signal in the right nucleocapsular region involving the body and tail of the caudate nucleus, the posterior limb of the internal capsule, and the posterior portion of the lentiform nucleus, with minimal peripheral extension to the anterior portion of the lentiform nucleus, consistent with an acute/subacute ischemic lesion. B, C: **Bilateral involvement of the optic tracts with extension to the right caudate-commissural region**.

recovery was attributable to targeted antimicrobial therapy rather than to the preceding thrombolytic or corticosteroid treatment. The clinical team also administered an additional intramuscular dose of benzathine penicillin G (BPG) upon completion. Recent reviews have questioned the use of this supplemental BPG dose, noting that the practice is not strictly supported by data but originates from the historical belief that T. pallidum may replicate more slowly in late-stage disease [1]. While 10–14 days of IV penicillin is generally enough to eradicate the infection, the use of BPG remains a common clinical practice to ensure prolonged treponemicidal concentrations in the blood [1,3,11].

4. Conclusion

The patient's initial presentation of left facial weakness—initially dismissed as Bell's palsy—is an illustration of why syphilis is called "the great imitator" [6,7]. The complete clinical recovery of the patient after six months is a testament to the reversibility of meningovascular neurosyphilis when caught early. As syphilis rates continue to increase globally, this case serves as a critical reminder: in the absence of clear cardiovascular risk, an ischemic stroke—especially one preceded by cranial nerve deficits—can be neurosyphilis until proven otherwise. Suspicion of neurosyphilis should be raised as early as possible in order to allow prompt diagnosis and treatment, ensuring the best possible recovery for the patient.

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CRediT authorship contribution statement

Emilio Altavilla: Writing – review & editing, Writing – original draft, Conceptualization. **Luca Bortolani:** Writing – review & editing. **Anna Carraro:** Writing – review & editing, Methodology, Conceptualization. **Alberico Parente:** Methodology. **Blerta Kertusha:** Writing – review & editing. **Daniela Di Trento:** Conceptualization. **Ermanno Notarianni:** Supervision, Investigation. **Gabriella d'Ettorre:** Supervision. **Miriam Lichtner:** Supervision. **Cosmo Del Borgo:** Validation, Supervision, Project administration, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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