Radiology Case Reports 19 (2024) 3529–3532

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Case Report

Gummatous neurosyphilisin an HIV-negative patient: Case report ☆,☆☆,★

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ARTICLE INFO

Article history:
Received 9 March 2024
Revised 10 May 2024
Accepted 11 May 2024

Keywords:
Syphilis
Neurosyphilis
HIV Infections
Neuroimaging
(MeSH)

ABSTRACT

Syphilis is a chronic infectious disease, which dates back to the XV century and is caused by the spirochete treponema pallidum, capable of invading the central nervous system in any of its stages- Its incidence has increased in parallel to the HIV/AIDS pandemic, and the synergism between both pathologies is such. that it has become a public health problem in recent years. Here we present the case of a 31-year-old female patient, who consulted for headache associated with decreased visual acuity and provided an unenhanced head CT showing hypodense lesions in both thalamic regions, serological tests for syphilis were reactive and those for HIV were not reactive. The brain MRI with spectroscopy was reported in favor of cerebral toxoplasmosis, which was later ruled out with a study of cerebrospinal fluid. Management with penicillin G sodium IV for 6 weeks was indicated, achieving complete imaging resolution of her lesions.

Introduction

Syphilis is a systemic sexually transmitted infectious disease caused by the spirochete treponema pallidum. It is a potentially serious entity that consists of different stages that define the severity of the disease. Although there is an effective treatment, we are far from eradicating this disease- Worldwide behavior shows an increase in incidence in recent years which has become a public health problem. WHO estimates that in 2020 there were 7.1 billion new syphilis infections [1,2].

☆ Competing Interests: 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.
☆☆ Financial Support and Sponsorship: None.
★ Acknowledgments: None.
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https://doi.org/10.1016/j.radcr.2024.05.036

Synergism that has been found between HIV infection and syphilis, may increase the risk of transmission and acquisition. Moreover, HIV infection can affect the evolution and response to treatment of syphilis [3,4].

An unusual case of an HIV-negative patient with gummatous neurosyphilis is reported.

Case report: gomatous neurosyphilis

This is a 31-year-old female patient, with no important pathological history with a headache of 2 weeks of evolution in the left temporo-parietal region, sometimes radiating to the ipsilateral cervical region, pulsating, with an intensity of 8/10 on the analogue pain scale, associated with decreased visual acuity. During this period, she consulted the emergency department several times, where she was prescribed with analgesics and discharged with an outpatient order for an unenhanced head CT (Fig. 1). On admission, she brought the study, which showed a left thalamic hypodense lesion of ischemic vs. infectious origin.

The initial evaluation showed no visual acuity or motor compromise, no suggestive data of neurological focality, blood biometry showed leukocytes 7.81 pmmc, neutrophils 86%, lymphocytes 12.0%, monocytes 1.5%, eosinophils 0.0%, VDRL reactive 27.65 dil and FTA abs positive, other paraclinical tests were within normality, HIV was not reactive.

In the MRI of the brain with spectroscopy, there were bilateral rounded focal lesions in deep basal ganglion region, isointense, in T1 and T2 influence, with accentuated enhancement of the contrast agent, with ring enhancement pattern with compressive effect on the third ventricle, due to the characteristics in favor of toxoplasmosis (Fig. 2).

A discussion on the case was held, where it was agreed that a joint assessment by the clinical neurology, neurosurgery and infectious diseases services was pertinent, as well as the study of cerebrospinal fluid, given the clinical impression of a gomatous neurosyphilis.

CSF results were received, showing pleocytosis and reactive VDRL, so she was prescribed sodium penicillin 4 million units intravenous every 4 hours for 14 days was established by the clinical infectious disease service.

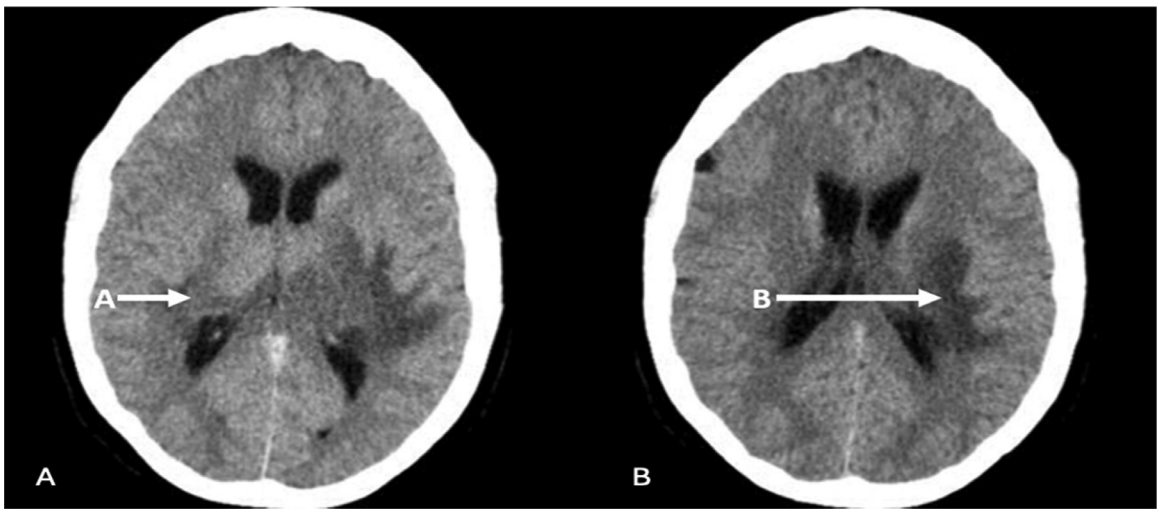

Fig. 1 – Admission CT Lesions in bilateral basal ganglia of left predominance, associated with left ventricular collapse towards midline. (A, B) Computed tomography.

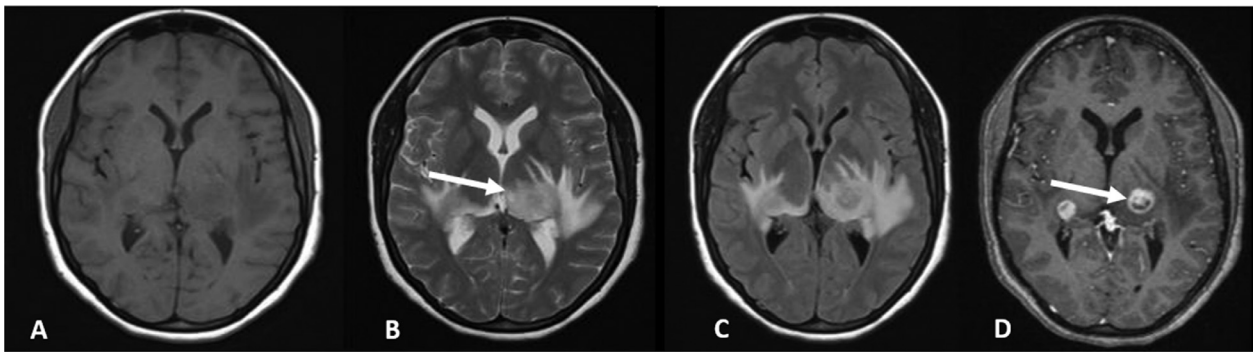

Fig. 2 – Admission MRI shows focal lesions in both basal ganglia regions in deep, thalamic location, (A) T1 axial T1-weighted image (B) T2 axial T1-weighted image (C) FLAIR image (D) contrast-enhanced image.

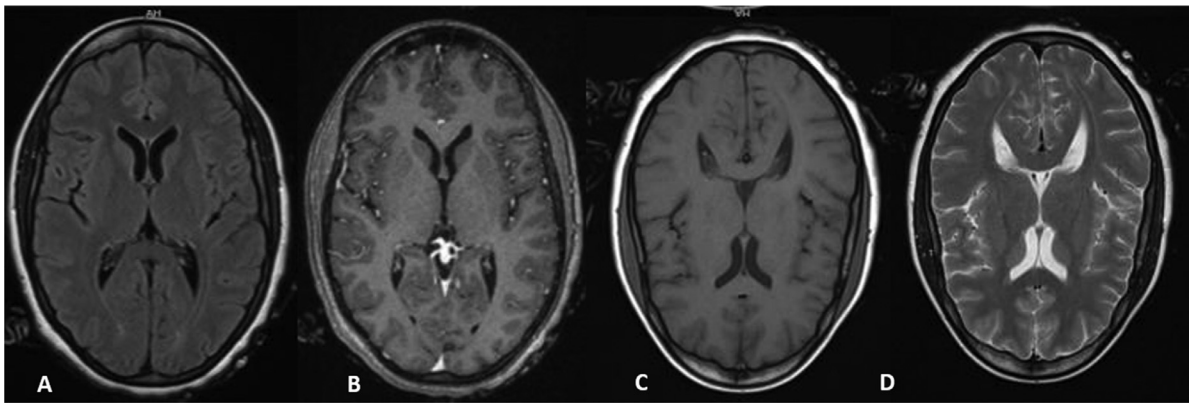

Fig. 3 – MRI 6 months after initiation of medical treatment, complete imaging remission is documented A T1 axial T1-weighted image (B) T2 axial T1-weighted image (C) FLAIR image (D) contrast-enhanced image.

Serology for toxoplasmosis was received, IGG antibody 0.06 ui/mL and IGM antibody: 0.0 ui/mL (normal), cerebrospinal fluid culture was negative, ruling out cerebral toxoplasmosis.

Once the 14-day treatment plan was completed, a notable reduction of the lesion was observed in the control MRI, however, it was decided to extend the treatment until completing 6 weeks of penicillin treatment, achieving complete symptomatic and imaging remission at 6 months (Fig. 3).

Discussion

Neurosyphilis is the result of central nervous system involvement due to invasion by the spirochete Treponema pallidum. It can occur at any stage of the disease; however, it is more frequent in the tertiary stage. Its classification varies depending on the symptomatology, as well as the region involved in asymptomatic neurosyphilis, interstitial neurosyphilis in its meningeal or meningovascular forms, the latter can present with implications at the cerebral or spinal level, parenchymal neurosyphilis within which the tabes dorsalis syndrome and general paresis stand out, and gummatous neurosyphilis, the least frequent form [5,6].

Gomatous neurosyphilis is considered a rare condition of the brain, 0.1% to 0.5% of patients diagnosed with syphilis, with up to 10 years elapsing before presentation in immunocompetent patients, under normal conditions these individuals, even without treatment, are able to eliminate treponema pallidum from the central nervous system, with meningovascular neurosyphilis being the most common form of presentation in these patients [4,7].

In immunocompromised patients, the onset of neurosyphilis occurs earlier, even months after infection [4]. In HIV-positive patients, neurosyphilis presents more aggressively. Historical cohorts date a series of patients with neurosyphilis, contrasting those patients who are HIV carriers with individuals seronegative for the infection, finding a higher probability of neurosyphilis in those with positive VDRL in blood and HIV coinfection than in those seronegative for the disease (OR: 62.37 CI: 95% (32.1-119.1) $P: < .001$) [8].

Most case reports allude to a greater probability of developing neurosyphilis in immunocompromised individuals, within these HIV carriers: however, some studies report discrepancies, such as the one conducted in Colombia, which consisted of a descriptive cross-sectional study of patients with neurosyphilis who attended a tertiary level center for 5 years, including 16 patients, 11 of whom had definite neurosyphilis and 11 probable neurosyphilis. Coinfection with HIV was determined in only a quarter of the patients [9].

Macroscopically, it is evident as soft, well-defined lesions, which adhere to the pia mater due to an accumulation of nodular granulomatous material, resulting in the appearance of neoplastic lesions, which can be a diagnostic challenge. Microscopically, its pathology shows inflammatory granulomas composed of lymphocytes and plasma cells, accompanied by microvascular intimal thickening and perivascular inflammation, which is less common in other granulomatous lesions, so it should be considered as a differential diagnosis of intracranial space-occupying lesions, especially in the context of patients with syphilis [10–12].

Diagnosis is made with clinical suspicion and history, cerebrospinal fluid findings and pathological examinations such as Warthin-Starry staining which allows isolation of Treponema pallidum in tissue. Laboratory tests can be nontreponemal and treponemal. Among the nontreponemal are the rapid plasma reagin test (RPR), the VDRL and the unheated toluidine red in serum test (TRUST). These measure the levels of IgG and IgM antibodies to cardiolipin-lecithin-cholesterol antigen. Treponemal tests include Treponema pallidum particle agglutination (TPPA), fluorescent treponemal antibody absorption (FTA-ABS), automated enzyme immunoassays (EIA), and chemiluminescent immunoassays (CIA) [13].

In most forms of neurosyphilis, the CSF study shows the presence of pleocytosis, glycorrhachia within normal ranges, protein levels are increased, with values between 45 and 200 mg/dL. Except for cases of tabes dorsalis and meningitis. The VDRL test in cerebrospinal fluid, has a high specificity so it is largely used as a diagnostic criterion, however, has a low sensitivity, having a negative result does not rule out the disease,

it is important a correlation of clinical findings, Even in adequately treated patients, VDRL can remain active for a period of time. Cases have been reported in HIV-negative patients with reactive syphilis serology, and normal CSF cultures and cytochemicals [13,14].

Imaging studies such as cranial computed axial tomography can demonstrate focal hypodense lesions sometimes accompanied by contrast enhancement with or without mass effect [12]. On the other hand, MRI can show lesions that can be hypo- or isointense in T1 and hyperintense in T2 and FLAIR, these methods do not distinguish between gum and a neoplastic lesion, however, complementary studies such as spectroscopy can be useful in determining different types of lesions, differentiating tumor processes from infectious ones. In this case, MRI of the brain with spectroscopy showed bilateral rounded focal lesions in the deep basal ganglion region, isointense, in T1 and T2 influence, with accentuated enhancement of the contrast agent, ring enhancement pattern with compressive effect on the third ventricle, which is consistent with the findings described in the literature.

Penicillin is the first line treatment for neurosyphilis, it is indicated 24 million international units every day for 14 days-In the case of our patient, we opted for 6 weeks extended scheme, achieving as a result, a complete symptomatic and imaging remission at 6 months. Other second and third line options are available such as ceftriaxone and Doxycycline respectively [9].

Conclusion

Tertiary syphilis can give rise to a wide range of clinical manifestations, among them, gummatous neurosyphilis, which is an infrequent presentation, due to the wide use of penicillin, becoming a diagnostic challenge and it is common to confuse it with entities such as cerebral toxoplasmosis from a clinical and imaging point of view as occurred in our case.

It is important in HIV seronegative patients to suspect gummatous neurosyphilisas one of the main differential diagnoses of space-occupying lesions.

The radiological pattern of ring enhancement of lesions of the central nervous system in studies such as magnetic resonance imaging can occur in various pathologies, so it is essential a correct clinical correlation and laboratory studies such as VDRL in cerebrospinal fluid, which is an indispensable tool to clarify the diagnosis.

Patient consent

I certify that I have obtained the patient's written informed consent for publication. This document ensures that a clear explanation of the purpose of the publication has been provided, and that the patient has voluntarily and knowingly consented to the publication.

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