

# Hypertrophic pachymeningitis post-neurosyphilis: case presentation

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## Abstract

**Introduction:** Hypertrophic pachymeningitis is an unusual and multifactorial disease characterized by thickening of the dura mater, secondary to a chronic inflammatory process. Clinical manifestations depend on the site of neurological involvement. Diagnosis requires integrating clinical, laboratory, imaging, and sometimes meningeal biopsy aspects. Treatment is tailored to the etiology, with Corticosteroids being the first-line medication.

**Case description:** A 67-year-old man presented with a progressive clinical picture over three years, consisting of intermittent headache, decreased visual acuity, temporal-spatial disorientation, depression, and gait disorder. A lumbar puncture revealed a reactive non-treponemal test and a brain nuclear magnetic resonance showed right frontotemporal pachymeningeal thickening and optic nerve involvement. He was diagnosed with hypertrophic pachymeningitis secondary to neurosyphilis. He was treated with antibiotic therapy and corticosteroids. The patient had an unfavorable outcome and died. **Conclusion:** This is one of the few case presentations of hypertrophic pachymeningitis caused by neurosyphilis, which provides important information to the literature. In the absence of early detection, and timely and appropriate treatment, the clinical course of the pathology is marked by progressive neurological deterioration, loss of vision, and even seizure status, leading to irreversible sequelae and may ultimately result in death.

**Keywords:** meningitis; neurosyphilis; diseases of the optic nerve; dura mater.

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## Paquimeningitis hipertrófica posneurosífilis: presentación de caso

### Resumen

**Introducción:** La paquimeningitis hipertrófica es una enfermedad inusual y multicausal que se caracteriza por un engrosamiento de la duramadre, secundario a un proceso inflamatorio crónico. Las manifestaciones clínicas dependen del lugar de la afectación neurológica. Para el diagnóstico se requiere integrar aspectos clínicos, de laboratorios, imagenológicos y en ocasiones biopsia meníngea. El tratamiento es según la etiología, siendo los corticoides los medicamentos de primera línea.

**Descripción del caso:** hombre de 67 años, con un cuadro clínico progresivo de tres años de evolución consistente en cefalea intermitente, disminución de la agudeza visual, desorientación temporoespacial, depresión y trastorno de la marcha. Se realizó una punción lumbar que evidenció una prueba no treponémica reactiva y se solicitó una resonancia magnética nuclear de cerebro con hallazgo de engrosamiento paquimeníngeo frontotemporal derecho y de nervios ópticos. Se le diagnosticó paquimeningitis hipertrófica secundaria a neurosífilis. Se dio tratamiento con antibioticoterapia y corticoesteroide. El paciente evolucionó de forma desfavorable y falleció.

**Conclusión:** Esta es una de las pocas presentaciones de caso de paquimeningitis hipertrófica causada por neurosífilis, la cual aporta información importante a la literatura. En ausencia de una detección temprana, tratamiento oportuno y adecuado, el curso clínico de la patología está marcada por un deterioro neurológico progresivo, pérdida de la visión e inclusive estatus convulsivo, dejando secuelas irreversibles e incluso puede progresar hasta la muerte.

**Palabras clave:** meningitis; neurosífilis; enfermedades del nervio óptico; duramadre.

## Paquimeningite hipertrófica pós-neurosífilis: apresentação de caso

### Resumo

**Introdução:** A paquimeningite hipertrófica é uma doença incomum e multicausal caracterizada por um espessamento da dura-máter, secundário a um processo inflamatório crônico. As manifestações clínicas dependem do local do comprometimento neurológico. O diagnóstico requer a integração de aspectos clínicos, laboratoriais, de imagem e, às vezes, biópsia meníngea. O tratamento é de acordo com a etiologia, sendo os corticosteroides os medicamentos de primeira linha.

**Descrição do caso:** Homem de 67 anos, com um quadro clínico progressivo de três anos de duração, consistindo em cefaleia intermitente, diminuição da acuidade visual, desorientação temporo-espacial, depressão e distúrbios de marcha. Foi realizada uma punção lombar que mostrou um teste não treponêmico reativo e uma ressonância magnética cerebral que evidenciou espessamento paquimeningeo frontotemporal direito e dos nervos ópticos. Foi diagnosticado com paquimeningite hipertrófica secundária a neurosífilis. Foi tratado com antibioticoterapia e corticosteroides. O paciente teve uma evolução desfavorável e faleceu.

**Conclusão:** Este é um dos poucos casos relatados de paquimeningite hipertrófica causada por neurosífilis, o que contribui com informações importantes para a literatura. Na ausência de detecção precoce, tratamento oportuno e adequado, o curso clínico da patologia é marcado por um deterioro neurológico progressivo, perda de visão e até mesmo status convulsivo, deixando sequelas irreversíveis e podendo progredir até a morte.

**Palavras-chave:** meningite; neurosífilis; doenças do nervo óptico; dura-máter.

## INTRODUCTION

Hypertrophic pachymeningitis (HP) is a rare condition characterized by thickening of the cranial or spinal dura mater in a localized or diffuse manner secondary to a chronic inflammatory process. Few cases have been documented in the literature, with an estimated prevalence of 0.949 per 100,000 inhabitants (1,2). The etiology is multifactorial, with cases described of rheumatologic, neoplastic, immunologic, infectious, and idiopathic origin (3).

Clinical manifestations depend on the site of neurological involvement, whether cranial, craniospinal, or spinal, with asymptomatic forms or even severe neurological alterations (4). Diagnosis requires integrating clinical, laboratory, and imaging aspects, and sometimes a meningeal biopsy is necessary (1).

Treatment depends on the etiology. Corticosteroids have been documented as first-line medications; however, cases requiring decompressive surgical management have also been reported (1,4-5). Early diagnosis and timely management can prevent permanent damage and improve the prognosis of the condition (1). Thus, the objective of this study was to describe a case of pachymeningitis secondary to neurosyphilis.

## CASE DESCRIPTION

The case involves a 67-year-old man with a history of bilateral optic neuritis and HP of unstudied etiology, without any other significant personal or family history. He presented with a progressive clinical picture over 3 years consisting of intermittent headache, decreased visual acuity, temporal-spatial disorientation, depression, and gait disorder, leading to severe dependency on activities of daily living, prompting admission to a healthcare facility.

Upon admission, he was disoriented in time and space, had multidomain memory deficits, scored 12/30 points on the Montreal Cognitive Assessment (MOCA), exhibited incoherent bradylyalic speech, marked bilateral visual acuity decrease, generalized decreased muscle strength (4/5) according to the Daniels scale with mild spasticity, hyperreflexia, and gait apraxia. Hospitalization was decided based on these findings.

On the first day of hospitalization, blood chemistry tests (glucose, creatinine, blood urea nitrogen, bilirubin, electrolytes, and transaminases) showed normal results; likewise, antigen tests for SARS-CoV-2 and human immunodeficiency virus (HIV) were non-reactive, serum *venereal disease research laboratory* (VDRL) test was positive, antinuclear antibodies (ANA) were negative, extractable nuclear antigens (ENA) were negative, cytoplasmic and

perinuclear antineutrophil cytoplasmic antibodies (C and P ANCA) were negative, complement C3 and C4 were not consumed, and C-reactive protein and erythrocyte sedimentation rate were normal.

On the second day of hospitalization, a lumbar puncture (LP) revealed slight mononuclear pleocytosis with proteinorrhachia and a reactive VDRL at 1:24 dilutions (Table 1).

Based on these results, neurosyphilis was diagnosed, and management was initiated with *penicilina cristalina* (4 million units intravenously every 4 hours for 14 days) and prednisolone (50 mg orally daily). A brain magnetic resonance imaging (MRI) was requested, revealing marked diffuse thickening of the right frontotemporal pachymeninges, cerebellar tentorium, and optic nerves. HP caused by neurosyphilis was diagnosed (Figure 1).

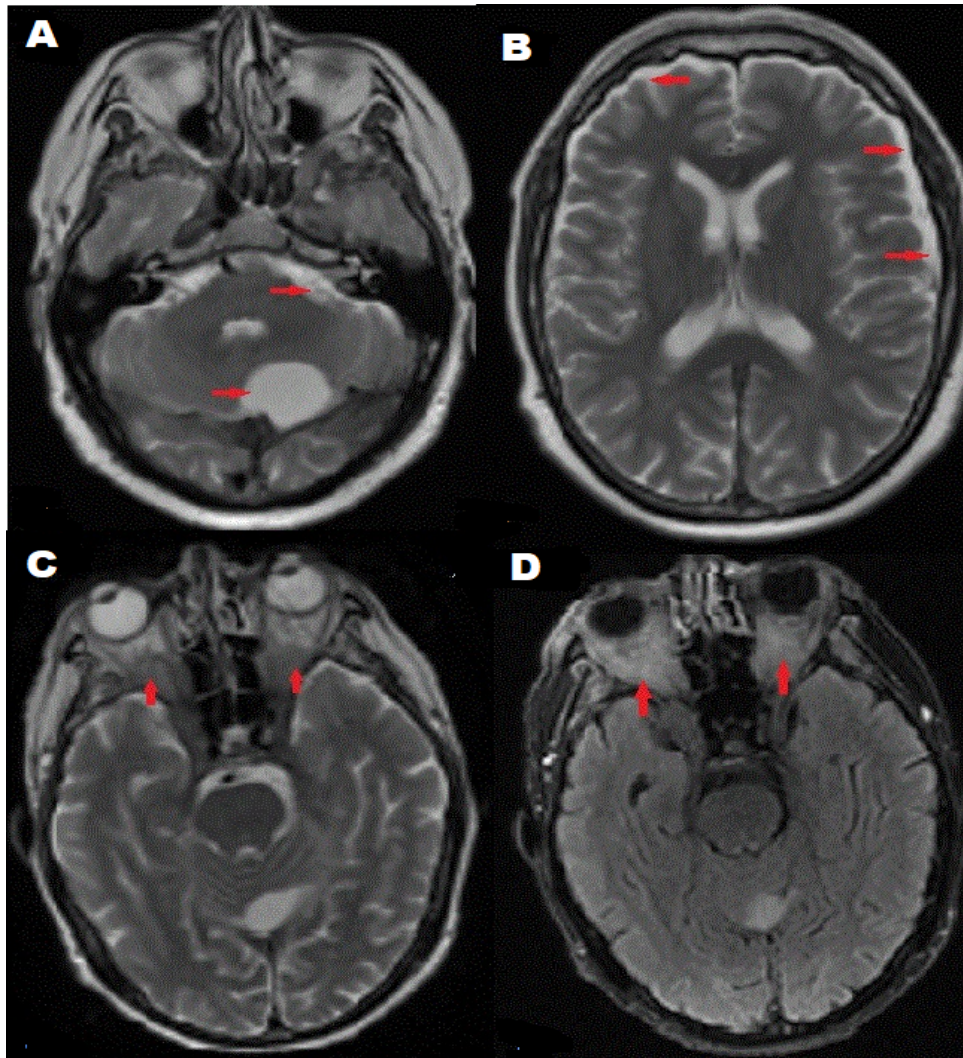
On the fourth day of hospitalization, the patient presented with refractory myoclonic status epilepticus, evidenced by clinical symptoms and video telemetry. He required management in the intensive care unit with ventilatory support and infusion of midazolam (5 mg intravenous per hour) and *Valproic Acid* (500 mg intravenous every 8 hours). On the sixth day of hospitalization, video telemetry control was requested, showing evidence of super-refractory status. The patient had an unfavorable outcome and died on the twelfth day of hospitalization.

**Table 1.** Cerebrospinal Fluid Characteristics

Characteristics	Results	Normal Value
<b>CSF Cytochemistry</b>		
CSF Glucose	37 mg/dl	≥60% of blood glucose
Proteins	70 mg/dl	35-45 mg/dl
<b>CSF Cytology</b>		
Color	Colorless	Colorless
Appearance	Transparent	Transparent
Red Blood Cells	0/Ul	0/Ul
Leukocyte count	5 × mm <sup>3</sup>	<5 × mm <sup>3</sup>
Mononuclear cells	5 × mm <sup>3</sup>	<5 × mm <sup>3</sup>
<b>Microbiological Examination</b>		
VDRL	Reactive 1:24 dilutions	Non-reactive
India ink	Negative	Negative
GRAM Stain	Negative	Negative
ADA Test	Negative	Negative
TB PCR	Negative	Negative
Film Array LCR	Negative	Negative
Bacterial Culture	Negative	Negative
<b>Blood Chemistry</b>		
Serum Glucose	91 mg/dl	70 to 100 mg/dl

CSF: cerebrospinal fluid; ADA: adenosine deaminase; TB PCR: polymerase chain reaction for *Mycobacterium tuberculosis*; Film Array LCR: polymerase chain reaction for multiple pathogens.

**Figure 1. Brain magnetic resonance imaging with contrast.** A) T2 sequence: hyperintensity due to infratentorial cerebellar tentorium meningeal thickening in ovoid form. B) T2 sequence: hyperintensity due to frontotemporoparietal meningeal thickening. C) T2 sequence: hyperintensity due to meningeal thickening affecting the optic nerves in the distal infraorbital and canalicular segment. D) Flair sequence with hyperintensity due to meningeal thickening of the optic nerves in their anterior infraorbital segment



This research considered Law 1581 of 2012, which refers to the protection of personal data (6). Written informed consent was requested and accepted by the responsible family member of the subject for the publication of the case, taking into account the patient's cognitive state.

## DISCUSSION

HP is an unusual condition characterized by thickening of the cranial or spinal dura mater in a localized or diffuse manner secondary to chronic inflammatory processes (1,6). The causes are multiple, but the most common is idiopathic, followed by vasculitis secondary to ANCA. Cases have also been reported in tuberculosis, systemic lupus erythematosus, Sjögren's syndrome, rheumatoid arthritis, Wegener's granulomatosis, multifocal fibrosclerosis, sarcoidosis, temporal arteritis, meningeal carcinomatosis, lymphoma, Lyme disease, HIV infection, and neurosyphilis, which has few cases described in the literature (2,7-10).

The disease has three clinical presentation forms, depending on the location: spinal, craniospinal, and cranial. The latter is the most frequent (79%) and predominates in males over 50 years old (4,11,12). It has been documented that the most common symptom is headache (92%), followed by the involvement of cranial nerves, with the optic nerve being the most affected (25%), manifested by visual impairment. Other

less frequent presentations include hearing loss, altered consciousness, loss of strength, ataxia, sensory alteration, and seizures (7,11,13-15).

Laboratory tests in blood will depend on the etiology of HP. ANCA and immunoglobulin IgC4 are the most recognized for ruling out autoimmune vasculitis, ANA, ENA, and rheumatoid factor for studying rheumatologic diseases (systemic lupus erythematosus, Sjögren's syndrome, or rheumatoid arthritis). HIV and VDRL laboratories seek infectious etiology (AIDS and syphilis). Other laboratories that may be nonspecific include white blood cell count in the blood, which may be present in 57% of cases, C-reactive protein in 79%, and erythrocyte sedimentation rate in 87% (1,7,8).

The most common findings in cerebrospinal fluid are hyperproteinorrachia and lymphocytic predominance pleocytosis; however, a normal result or other relevant data such as a reactive VDRL, which confirms neurosyphilis pathology, may be detected (9).

In imaging studies, MRI can show in T1-weighted images structural alterations in the base cisterns; in T2-weighted images, edema can be found, and with gadolinium (contrast medium) T1-weighted images, documenting enhancement of more than 2 millimeters, which would evidence thickening of the dura mater in all cases (4). In idiopathic HP

and tuberculous meningitis, the posterior fossa is the most affected; in autoimmune vasculitis, it is in the frontal, parietal, and occipital lobes, and in neurosyphilis, the case report shows marked diffuse thickening of the right frontotemporal meninges, cerebellar tentorium, and optic nerves (7,10).

Dural biopsy is considered the gold standard test for the etiological diagnosis of HP. It is performed in doubtful cases that require confirmation and to exclude other causes of the disease. Characteristic findings of meningeal fibrosis, plasma cells, and lymphocytic infiltrate have been documented (11).

Treatment is focused on the cause. *Corticoides* therapy is the first-line pharmacological option; however, it usually leads to temporary improvement of symptoms. Recurrence rate is documented in 16% of cases in the literature, which are better controlled with corticosteroid administration followed by immunosuppressants such as cyclophosphamide and azathioprine. Long-term benefits have also been reported with rituximab (biological) (4,12). Surgical management is limited to cases with severe neurological deficits that do not respond to medication (5).

Early diagnosis, as well as timely and adequate management, is associated with a lower risk of neurological sequelae, especially neuro-ophthalmological ones, improving the prognosis of

the pathology and the patient's quality of life (11,13,14). During the writing of the article, the limited research on HP caused by neurosyphilis was recognized as a limitation, but it presents an opportunity to contribute information about the disease.

In conclusion, this is one of the few case reports of PH caused by neurosyphilis, which provides important information to the literature. Its clinical presentation is varied, and studies of LP, MRI with contrast medium, and, if necessary, biopsy are required to confirm and exclude other causes. In the absence of early detection and timely and adequate treatment, the clinical course of the pathology is marked by progressive neurological deterioration, loss of vision, and even convulsive status, leading to irreversible sequelae and ultimately death.

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## CONFLICT OF INTEREST

The researchers declare no conflicts of interest.

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