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Case Report

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Glucocorticoid-refractory painful cavernous sinus syndrome as a warning for occult skull-base infection: a case report of odontogenic mixed anaerobic empyema complicated by AICA-territory infarction

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Abstract

Background: Painful ophthalmoplegia is classically associated with Tolosa-Hunt syndrome; however, steroid-refractory or atypical presentations require urgent exclusion of infectious, neoplastic, vascular and inflammatory cavernous sinus lesions. We report an elderly patient with an occult odontogenic mixed anaerobic infection presenting as glucocorticoid-refractory painful cavernous sinus syndrome and complicated by acute anterior inferior cerebellar artery-territory infarction.

Case presentation: A 75-year-old man with hyperglycemia was admitted after two months of progressive headache, right ptosis and blurred vision in the left eye, followed by acute fever, confusion, dysarthria, gait ataxia and limb twitching. He had received glucocorticoids for a presumed diagnosis of Tolosa-Hunt syndrome without improvement. Examination showed nuchal rigidity, a dilated right pupil, left eye blindness, bilateral dysmetria, wide-based gait and bilateral Babinski signs. Contrast-enhanced MRI showed a continuous cord-like lesion extending from the clivus to the left cavernous sinus with ring enhancement and restricted diffusion, together with an acute infarct strictly confined to the anterior inferior cerebellar artery territory posterior to the lesion. Cerebrospinal fluid showed neutrophil-predominant pleocytosis, markedly elevated protein and a low cerebrospinal fluid/serum glucose ratio. Metagenomic next-generation sequencing identified a polymicrobial oral anaerobic community dominated by Prevotella intermedia, with Streptococcus constellatus also detected. A final diagnosis of odontogenic mixed anaerobic skull-base subdural empyema involving the clivus and cavernous sinus, complicated by probable local infectious vasculitis causing anterior inferior cerebellar artery-territory infarction, was made. Meropenem plus ornidazole and

acute infarction therapy were administered; the patient became afebrile, consciousness recovered and gait ataxia improved. At two months, follow-up MRI showed resolution of the empyema without new infarcts.

Conclusions: This case highlights glucocorticoid-refractory painful cavernous sinus syndrome as a warning presentation for occult skull-base infection. Paired cerebrospinal fluid/serum glucose ratio, careful dental source assessment and metagenomic next-generation sequencing can be decisive when routine cultures are unrevealing. Adjacent arterial infarction may reflect infectious vasculitis, but vascular imaging is needed to substantiate mechanism.

Keywords: Painful ophthalmoplegia; Tolosa-Hunt syndrome; Skull-base subdural empyema; Odontogenic infection; Metagenomic next-generation sequencing; Infectious vasculitis

Introduction

Tolosa-Hunt syndrome is a diagnosis of exclusion characterized by painful ophthalmoplegia and granulomatous inflammation of the cavernous sinus, superior orbital fissure or orbital apex. It may respond dramatically to glucocorticoids, yet normal non-contrast MRI and apparent steroid response do not exclude infection or malignancy. Red flags include older age, fever or systemic inflammation, cranial neuropathies beyond a single ocular motor nerve, visual loss, diabetes or immunosuppression, atypical or progressive course, and lack of steroid response.

Skull-base subdural empyema is uncommon, and a centrally arising clival lesion spreading along dural pathways to the cavernous sinus is exceptional. Oral anaerobes are

an important and often occult source of intracranial abscess. We report a case in which an initially presumed Tolosa-Hunt syndrome progressed despite glucocorticoids and was ultimately attributed to an odontogenic mixed anaerobic skull-base subdural empyema complicated by an adjacent artery-territory infarction. This report follows the CARE case-report structure and emphasizes diagnostic pitfalls, non-invasive multimodal imaging interpretation and mechanism-level inference.

Case presentation

History and initial course

A 75-year-old man was admitted with a 2-month history of recurrent headache and a 1-day history of acute ptosis and gait difficulty. Two months prior, he developed persistent left-sided head and periorbital pain of no apparent cause, accompanied by dental pain, nausea, and vomiting, with episodic exacerbations. He subsequently developed right ptosis and blurred vision in the left eye. A non-contrast brain MRI at a local hospital was unremarkable. Based on the combination of headache and ophthalmoplegia, a diagnosis of Tolosa-Hunt syndrome was made. He received intravenous methylprednisolone 40 mg daily for two weeks, followed by oral methylprednisolone 25 mg daily as maintenance therapy. Throughout the course of glucocorticoid treatment, his headache and ophthalmoplegia showed no improvement.

One day prior to admission, the patient acutely developed fever, dizziness, gait instability, choking on liquids, delayed verbal responses, confusion, and intermittent limb twitching. On admission, his temperature was 38.3°C. He was restless and had pronounced nuchal rigidity. The left eye had no light perception, and visual acuity was decreased in the right eye. The right pupil was 5 mm in diameter and sluggishly reactive

to light; extraocular movements were normal without nystagmus. Bilateral heel-to-shin testing revealed dysmetria, and his gait was wide-based. Babinski signs were positive bilaterally. Muscle strength was 5/5 in all limbs, and superficial and deep sensation were intact. Laboratory investigations showed a neutrophil percentage of 77.7%, high-sensitivity C-reactive protein of 22.6 mg/L, and a random blood glucose of 18.4 mmol/L. The remaining laboratory tests were unremarkable.

Investigations and diagnostic reasoning

The patient exhibited confusion, dysarthria, truncal ataxia, and a wide-based gait. Neuroimaging revealed diffusion-restricted lesions in the left cerebellar hemisphere, middle cerebellar peduncle, and cerebellar tonsil, localizing to the cerebellum and its brainstem connections. However, a cerebellar lesion alone could not account for the right dilated pupil, bilateral optic nerve involvement, or cavernous sinus cranial neuropathies, suggesting the presence of two distinct intracranial lesions.

Contrast-enhanced brain MRI revealed two key lesions (Figure 1). The first was a continuous cord-like lesion extending from the clivus at the skull base laterally into the left cavernous sinus. This lesion showed marked hyperintensity on diffusion-weighted imaging (DWI) and thin, uniform ring enhancement after contrast administration. MR spectroscopy (MRS) was suggestive of an infectious process, evidenced by low signal-to-noise ratio (SNR), reduced creatine (Cr) peak, markedly decreased N-acetylaspartate (NAA) peak with a reduced NAA/choline (Cho) ratio, and elevated lipid/lactate (LL) peaks. These characteristic imaging features, combined with the acute infectious course, were highly suggestive of a subdural empyema. Its pattern of spread along the dural pathways explained the concurrent cavernous sinus syndrome. Posterior to this empyema,

in the left cerebellar hemisphere, a lesion strictly confined to the territory of the anterior inferior cerebellar artery (AICA) and exhibiting a typical arterial infarct pattern was observed. On MRS, this AICA-territory lesion similarly demonstrated a decreased NAA peak and an elevated lactate (Lac) peak, metabolic abnormalities consistent with ischemic injury. However, contrast-enhanced imaging showed no ring enhancement, thereby excluding a parenchymal abscess.

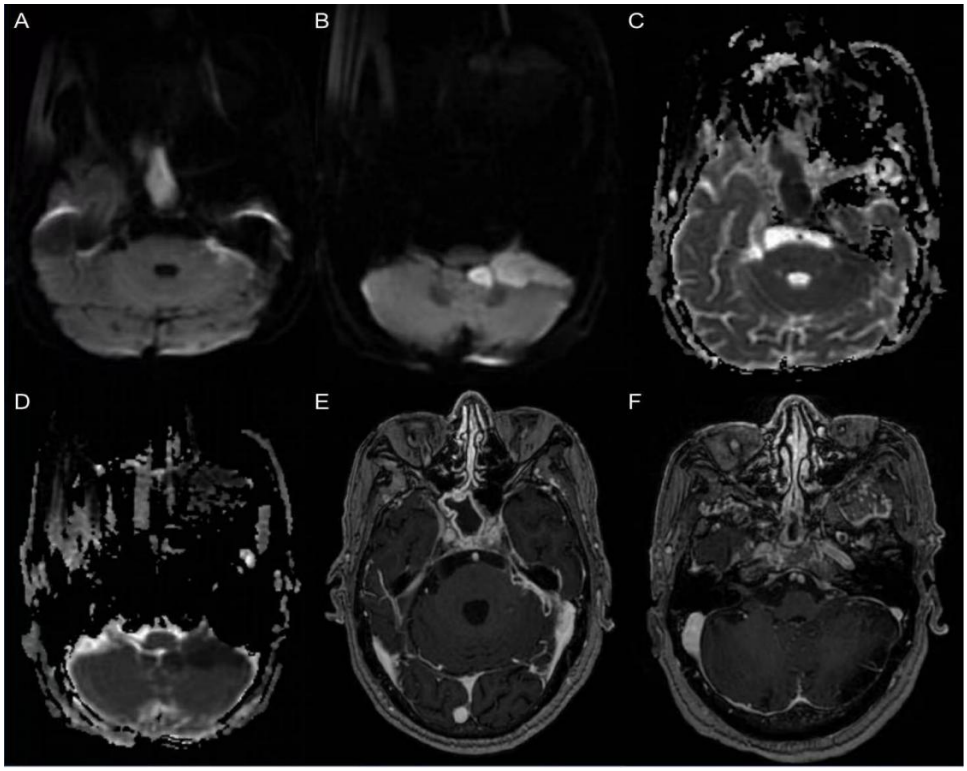


Figure 1. Brain MRI on admission. (A) DWI shows a hyperintense lesion involving the clivus and cavernous sinus. (B) DWI shows a hyperintense lesion in the left cerebellar hemisphere. (C) ADC shows a hypointense lesion in the clivus and cavernous sinus region. (D) ADC shows a hypointense lesion in the left cerebellar hemisphere. (E) Post-contrast T1-weighted imaging shows ring enhancement of the clivus and cavernous sinus lesion. (F) Post-contrast T1-weighted imaging shows no significant enhancement in the left cerebellar lesion.

Of note, the clival component of the empyema was midline and cord-like in configuration, extending across the midline along the skull-base dura, suggesting that the inflammatory process was not confined to the left cavernous sinus.

On imaging, the close anatomical proximity between the posterior wall of the subdural empyema and the AICA, together with MRS findings of ischemic and inflammatory metabolic abnormalities within the AICA territory, strongly indicated that the arterial infarction was secondary to the infection. Two potential mechanisms of vascular injury were considered: first, direct extension of the local inflammatory process from the subdural empyema to the adjacent AICA wall, inducing infectious vasculitis, luminal stenosis, and in situ thrombosis; second, detachment of septic microthrombi or emboli from the cavernous sinus, causing distal embolization of the AICA branch [1,2]. Given the tight anatomical relationship between the posterior wall of the subdural empyema and the AICA, infectious vasculitis appeared more plausible than septic embolization in accounting for the arterial infarction in this case. To validate this hypothesis and guide targeted therapy, identifying the pathogen and its source became imperative. We therefore proceeded immediately with lumbar puncture. No vascular imaging (MRA/CTA or high-resolution vessel-wall MRI) was performed; the mechanism of arterial injury was therefore inferred from anatomic contiguity and the microbial spectrum (see Discussion).

CSF analysis revealed a slightly turbid, yellowish fluid with a positive Pandy test. The leukocyte count was 1153 × 10^6/L, with 92.3% segmented neutrophils and 7.7% mononuclear cells. The protein level was 2.88 g/L, chloride 112 mmol/L, and glucose 3.25 mmol/L, with a simultaneous blood glucose of 18.4 mmol/L. Given the patient's prolonged glucocorticoid-induced immunosuppression and stress hyperglycemia, the CSF-to-blood glucose ratio was only 0.18, far below the normal cutoff of 0.5, indicating substantial glucose consumption by pathogens within the central nervous system—a

hallmark of occult suppurative infection with hypoglycorrhachia [3]. Together with the markedly elevated protein level and neutrophilic pleocytosis, these findings indicated severe blood-brain barrier disruption and acute suppurative intracranial infection.

The patient had responded poorly to conventional anti-infective therapy. Given the low positivity rate and time-consuming nature of traditional bacterial cultures, which are inadequate for the diagnostic needs of critically ill patients, cerebrospinal fluid was sent for metagenomic next-generation sequencing (mNGS). mNGS revealed a characteristic polymicrobial spectrum with a clear abundance gradient: Prevotella intermedia at 38.2% relative abundance (the predominant pathogen), Porphyromonas gingivalis (9.4%), Bacteroides heparinolyticus (7.7%), Streptococcus constellatus (4.2%), Tannerella forsythia (2.4%), Fusobacterium nucleatum (2.2%), and Epstein-Barr virus (EBV, 4.8%).

The mNGS results revealed a microbial community dominated by obligate anaerobic bacteria indigenous to the oral cavity and periodontium [4], with a clear abundance gradient and no common contaminant strains. Combined with the patient's history of dental pain, this confirmed an occult odontogenic infection. The predominant organism, Prevotella intermedia, along with other anaerobes, facilitated the formation of a skull-base subdural empyema by disrupting tissue barriers and creating an anaerobic microenvironment; the lesion extended along dural pathways from the clivus to the cavernous sinus. The vascular invasive property of Streptococcus constellatus provided the pathogenetic basis for the infarction in the AICA territory adjacent to the subdural empyema. EBV, detected as a result of latent reactivation under immunosuppression, was considered a non-causative bystander.

Diagnosis

Odontogenic mixed anaerobic infection causing a skull-base subdural empyema (involving the clivus and cavernous sinus), complicated by acute infarction in the anterior inferior cerebellar artery (AICA) territory secondary to probable local infectious vasculitis.

Treatment and outcome

Based on the mNGS results, the anti-infective regimen was adjusted to meropenem combined with ornidazole, together with medications for acute cerebral infarction (aspirin, atorvastatin, and butylphthalide). Following treatment, the patient became afebrile, regained full consciousness, and showed progressive improvement in gait ataxia. Repeat MRI at 2 months demonstrated resolution of the subdural empyema (Figure 2), with no new infarcts.

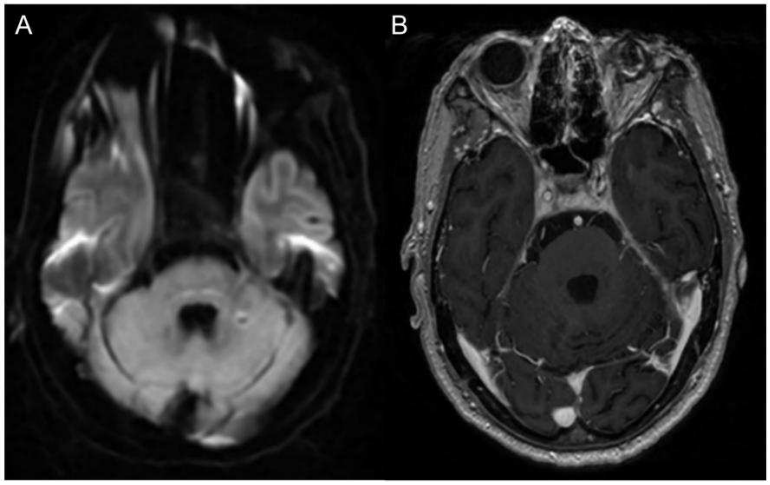


Figure 2. Brain MRI at 2-month follow-up. (A) DWI shows no hyperintense lesion. (B) Post-contrast T1-weighted imaging demonstrates resolution of the abnormal enhancement in the clival–cavernous sinus region compared with the initial scan.

Discussion

Summary of the case and its novelty. We report an elderly patient with an indolent, steroid-refractory painful cavernous sinus syndrome that was ultimately attributed to an odontogenic mixed anaerobic skull-base subdural empyema extending from the clivus

along dural pathways to the cavernous sinus, complicated by an acute infarct strictly confined to the adjacent AICA territory. Subdural empyema involving the skull base is uncommon, and a cord-like collection arising centrally at the clivus and spreading along the dura is exceptional; cases caused by periodontally derived mixed anaerobic flora and further complicated by adjacent infectious vasculitis with cerebellar artery infarction are, to our knowledge, exceedingly rare. The insidious course—progressing from chronic headache and ophthalmoplegia that mimicked glucocorticoid-responsive Tolosa-Hunt syndrome to fever, meningismus and stroke within two months—makes this case a clinically instructive model of diagnostic delay.

Background: occult odontogenic intracranial infection. Oral anaerobes are an important and frequently occult source of intracranial abscess. A nationwide population-based cohort study confirmed that a substantial proportion of intracranial subdural empyemas are caused by oral cavity bacteria and that diagnosis is often delayed because the primary odontogenic focus is clinically silent [6]. Periodontal pathogens can reach the intracranial compartment through contiguous spread or hematogenous seeding, and the resulting polymicrobial, synergy-driven infections are notoriously difficult to recover by conventional culture, particularly after empirical antibiotics or under anaerobic conditions [4,5]. In the present case, the only early clues to the dental origin were a history of dental pain and the later CSF mNGS spectrum; no dedicated dental evaluation had been performed before admission, illustrating how easily this source is overlooked.

Pathogen identification and the mechanism of the arterial infarct. In this case, mNGS of the cerebrospinal fluid revealed a polymicrobial community dominated by obligate anaerobes indigenous to the oral cavity and periodontium, with a clear

abundance gradient: Prevotella intermedia (38.2%), Porphyromonas gingivalis, Bacteroides heparinolyticus, Tannerella forsythia and Fusobacterium nucleatum—several of them members of the "red complex," highly specific biomarkers of periodontal infection [5]—together with Streptococcus constellatus, an organism with recognized vascular invasiveness [8,9]. This community structure suggests synergistic pathogenicity: the P. intermedia-dominated anaerobic consortium, adept at disrupting tissue barriers and establishing an anaerobic microenvironment, likely drove the formation and dural spread of the empyema, whereas the vascular-invasive S. constellatus plausibly mediated inflammatory injury to the adjacent arterial wall.

Two mechanisms could account for the AICA-territory infarct: local extension of the inflammatory process to the AICA wall with infectious vasculitis, luminal stenosis and in situ thrombosis; or septic embolization from the cavernous sinus region to a distal AICA branch [1,2]. Given the tight anatomic contiguity between the posterior wall of the empyema and the infarct, infectious vasculitis appeared more plausible than embolism. We acknowledge, however, that no vascular imaging was performed to confirm this mechanism (see Limitations). The value of mNGS here was decisive: conventional cultures are slow and frequently negative in mixed anaerobic and partially treated infections, whereas mNGS rapidly identified the pathogen spectrum and its likely source and directly guided the switch to meropenem plus ornidazole [7].

Diagnostic pitfalls: glucocorticoids and the EBV signal. The initial misdiagnosis of Tolosa-Hunt syndrome and the ensuing two weeks of glucocorticoid therapy were key precipitating factors. By suppressing local innate immunity, glucocorticoids neither controlled the primary infection nor relieved symptoms; instead, they masked disease

progression, facilitated suppurative tissue breakdown and may have promoted the extension toward the cavernous sinus and the adjacent artery [10]. Notably, a normal non-contrast MRI and a presumptive steroid response do not exclude infection or malignancy; in retrospect, the absence of any response to glucocorticoids, together with fever, meningismus and multiple cranial neuropathies, should have prompted earlier contrast-enhanced imaging and lumbar puncture. EBV detected by mNGS was interpreted as reactivation of latent virus under the dual immunosuppression of severe infection and glucocorticoid therapy, a non-causative bystander rather than a contributor to the abscess or the vascular injury.

Laterality of the cranial neuropathy. The right-sided ptosis and pupillary involvement appeared discordant with the predominantly left-sided cavernous sinus enhancement. However, the clival component of the empyema was midline and cord-like, crossing the midline along the skull-base dura, so the inflammatory process was unlikely to be confined to the left cavernous sinus. Asymmetric bilateral dural involvement, or inflammatory encasement of the cisternal segment of the oculomotor nerve at the skull base, offers a plausible explanation for the right-sided levator palpebrae weakness and is consistent with the dural spread pattern observed on MRI.

Clinical implications. This case offers three practical lessons. First, progressive painful ophthalmoplegia that is refractory to glucocorticoids should routinely trigger exclusion of infectious cavernous sinus lesions with contrast-enhanced MRI and CSF analysis, regardless of an initially normal non-contrast scan. Second, CSF glucose must always be interpreted as a paired CSF-to-serum ratio; here the ratio of 0.18—despite a seemingly normal absolute glucose—revealed marked hypoglycorrhachia and redirected

the diagnosis toward occult suppurative infection [3]. Third, when conventional cultures are unrevealing in a suspected intracranial abscess, CSF mNGS can rapidly identify mixed anaerobic pathogens and the odontogenic source, enabling targeted antimicrobial therapy. Systematic dental assessment should be part of the work-up whenever oral anaerobes are detected intracranially.

Limitations.

This is a single case report, and the proposed causal chain—odontogenic infection, skull-base subdural empyema, infectious vasculitis and AICA-territory infarction—is inferential. High-resolution vessel-wall imaging or catheter angiography was not performed to directly demonstrate arteritis or luminal stenosis, and the infectious-vasculitis mechanism remains a radiologic–microbiologic inference rather than a proven one. No formal dental examination or imaging was obtained to localize the odontogenic focus, which rests on clinical history and the mNGS spectrum. Although the cavernous sinus component appeared predominantly left-sided on the available images, the midline clival origin of the empyema makes subtle bilateral dural involvement likely rather than exceptional; nevertheless, dedicated thin-slice review of the complete imaging study would be required to define the full extent of skull-base involvement. The two-month follow-up, although showing radiologic resolution, is short for assessing long-term neurological recovery and late vascular complications. Finally, mNGS detects nucleic acid and cannot by itself distinguish infection from colonization; the abundance gradient, clinical context and treatment response support, but do not prove, the pathogenicity of each detected organism.

Conclusions.

Glucocorticoid-refractory painful cavernous sinus syndrome should be regarded as a red-flag presentation for occult skull-base infection rather than steroid-unresponsive Tolosa-Hunt syndrome. A paired CSF/serum glucose ratio, systematic assessment for a dental source, and CSF mNGS can be decisive when conventional cultures are unrevealing. Adjacent arterial-territory infarction in this setting may reflect infectious vasculitis, but dedicated vascular imaging is required to substantiate the mechanism and should be pursued whenever feasible.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal upon request.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

YW and YL contributed equally to this work and share first authorship. YW drafted the manuscript and interpreted the neuroimaging findings. YL collected the clinical data and participated in patient management. TC performed the metagenomic next-generation sequencing analysis. CW contributed to the imaging interpretation. XX and HW conceived the study and revised the manuscript critically for important intellectual content. HL supervised the study and approved the final version for submission. All authors read and approved the final manuscript.

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List of abbreviations

ADC: apparent diffusion coefficient

AICA: anterior inferior cerebellar artery

Cho: choline

Cr: creatine

CTA: computed tomography angiography

DWI: diffusion-weighted imaging

EBV: Epstein-Barr virus

Lac: lactate

LL: lipid/lactate

MRA: magnetic resonance angiography

MRI: magnetic resonance imaging

mNGS: metagenomic next-generation sequencing

MRS: magnetic resonance spectroscopy

NAA: N-acetylaspartate

SNR: signal-to-noise ratio

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