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''Sweet tears'': *Streptococcus salivarius* meningitis secondary to ethmoidal mucocele

«Lágrimas dulces»: meningitis bacteriana por *Streptococcus salivarius* secundario a mucocele etmoidal

Dear Editor:

Bacterial meningitis is associated with high morbidity and mortality rates. Some of the main pathogens that can cause the disease include *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* in the general population; and *Streptococcus agalactiae* and *Listeria monocytogenes* in neonates and immunosuppressed individuals, respectively. The recommended empirical treatment for community-acquired bacterial meningitis is a combination of cephalosporins and vancomycin, which may also be combined with another beta-lactam antibiotic.[1,2] *Streptococcus salivarius* meningitis is infrequent in our setting, and is mainly associated with spinal procedures.[3]

We present the case of a 54-year-old woman with no relevant medical or surgical history who visited the emergency department due to sudden-onset holocranial headache of 6 hours' progression, fever (38.5 °C), nausea, and vomiting. She also reported a 4-month history of ''sweet tears'' associated with right rhinorrhoea triggered by anterior flexion of the neck in both seated and standing positions; this may be attributable to decreased venous return and the transient increase in intracranial pressure. The physical examination revealed general discomfort, blood pressure of 158/89 mm Hg, heart rate of 106 bpm, room-air oxygen saturation of 95%, and rhythmic breathing with normal breath sounds. The neurological examination revealed somnolence (Glasgow Coma Scale: motor 6, verbal 4, eye 3). A head CT scan revealed no abnormal findings. Lumbar puncture revealed purulent CSF; opening pressure could not be measured. A CSF analysis showed 5360 leukocytes/μL (normal range: <5), 74% polymorphonuclear; a protein level of 173 mg/dL (normal range: <30); and a glucose level of 60 mg/dL (normal range: 40-70). A blood analysis revealed a serum glucose level of 154 mg/dL. The patient was diagnosed with bacterial meningitis.

We started intravenous empirical treatment with ceftriaxone 2 g every 12 hours, vancomycin 1 g every 12 hours, ampicillin 2 g every 4 hours, and a single dose of dexametha-

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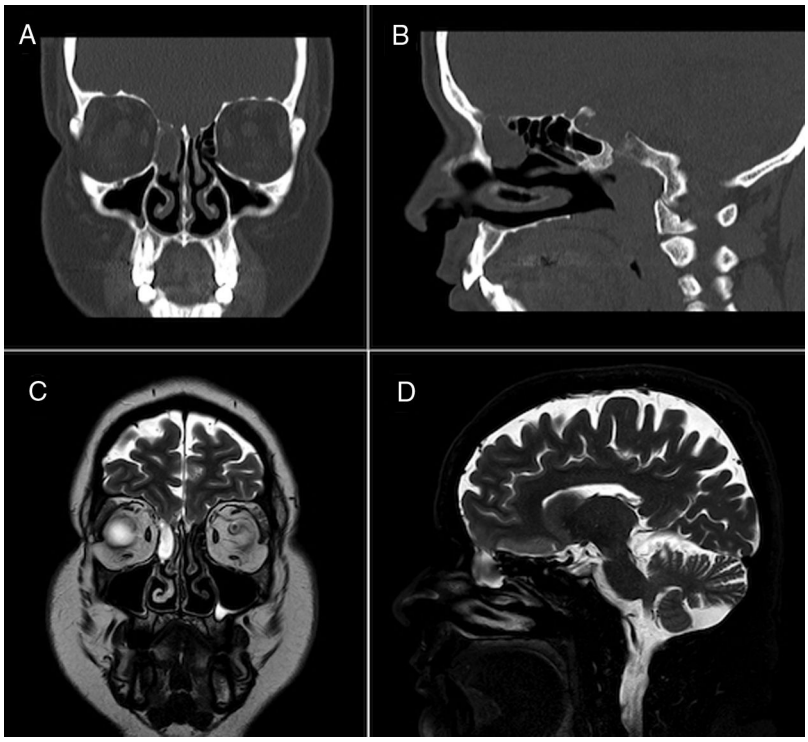

Figure 1 Coronal (A) and sagittal (B) face CT scans revealing a hypodense mass in the right anterior ethmoidal air cells and a defect in the ipsilateral cribriform plate. Coronal (C) and sagittal (D) brain MRI sequences confirming these findings and ruling out myelomeningocele.

sone 4 mg. Polymerase chain reaction (PCR) amplification of 16S rRNA genes in CSF yielded negative results for *S. pneumoniae*, *L. monocytogenes*, and *N. meningitidis* and positive results for *S. salivarius*, which is susceptible to cephalosporins. Blood culture findings (1:3) 48 h later were positive for *S. salivarius*.

A biochemical study of nasal discharge revealed a glucose level of 51 mg/dL, 17 leukocytes/μL, and a protein level of 89 mg/dL.

Face CT (Fig. 1A and B) and brain MRI scans (Fig. 1C and D) revealed mucocele in the right ethmoidal air cells measuring 2 cm axially, and a 4-mm defect in the ipsilateral cribriform plate, related with the dural fistula, with MRI detecting no signs of myelomeningocele. The patient continued on ceftriaxone 2 g every 24 hours for 14 days, remaining asymptomatic at discharge. Two months later, the patient underwent surgical excision of the mucocele and endoscopic repair of the CSF fistula on an outpatient basis. After 2 years of follow-up, the patient remains asymptomatic and has presented no further episodes.

S. salivarius, which belongs to the viridans group of streptococci, is a commensal bacterium found in the orogastrointestinal and upper respiratory tracts. Despite its low virulence, it has been associated with bacteraemia, sinusitis, meningitis (approximately 0.3%-2.4% of cases), and endocarditis. Factors potentially favouring the development of *S. salivarius* meningitis include presence of CSF fistulas, sinusitis, brain abscesses, head trauma, and neoplasia.[3–5]

Diagnosis is made by isolating the pathogen in CSF cultures or by PCR. Cross-reaction with other *Streptococcus* species (*S. pneumoniae*) has been reported, which may result in aetiological misdiagnosis and underdiagnosis of the condition.[6] The genus *Streptococcus* presents adequate sensitivity to beta-lactams.

Although bacterial meningitis is a rare complication of spinal procedures (eg, lumbar puncture), it may have a fatal outcome.[7] In recent years, several cases have been reported of bacterial meningitis following spinal procedures. The most frequently identified pathogens were oral commensals (viridans group streptococci), which suggests the possibility of direct transmission by physicians through droplets if masks are not used during the procedure.[8–10] The literature includes only one case of *S. salivarius* meningitis secondary to sphenoid sinus mucocele,[5] resembling our own. Table 1 compares the clinical characteristics of previous cases of *S. salivarius* meningitis to the case presented here.

In conclusion, mucocele or CSF fistula should be suspected in patients with *S. salivarius* meningitis and no history of spinal procedures; neuroimaging studies should be performed in these patients. As spinal procedures constitute

Table 1 Clinical characteristics of previously reported cases of *Streptococcus salivarius* meningitis and of our own.

	Previous cases (n = 65)	Our patient
Male/female ratio	24/46:22/46	Woman
Age at diagnosis	44.5 (mean)[a]	54
Signs/symptoms		
Abnormal GCS score	30/53 (57%)	+
Headache	40/53 (75%)	+
Fever	44/53 (83%)	+
Nausea/vomiting	27/53 (51%)	+
Meningeal signs	37—39/53 (70%-74%)	—
Positive CSF culture	23/42	+
Positive blood culture	13/46	1:3
Initial treatment		
Cephalosporins	31/49 (63%)	+
Vancomycin	18/49 (37%)	+
Ampicillin	4/49 (8%)	+
Dexamethasone	3/49 (6%)	+
Risk factors		
Iatrogenesis	39/58 (67%)	—
CSF fistula	12/58 (21%)	—
Mucocele	1/58 (2%)	+
Other	13/65 (20%)	—
Survival	55/57	+

CSF: cerebrospinal fluid; GCS: Glasgow Coma Scale.
+: present; —: absent.
Source: taken from Wilson et al.[3]
[a] Age at diagnosis was not reported in 10 cases.

the main risk factor for *S. salivarius* meningitis, we should stress the need for systematic use of face masks during these procedures.

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CLIPPERS syndrome: A case report

Síndrome CLIPPERS. A propósito de un caso

Dear Editor:

We present the case of a 44-year-old man with history of primary haemophagocytic lymphohistiocytosis (homozygous carrier of the Ala91Val mutation) and splenectomy. He presented a 2-month history of sudden-onset, progressive numbness and tingling in the soles of the feet, leg rigidity triggered by physical activity, and gait instability. In addition to these symptoms, the patient had developed numbness and tingling in the palms of both hands 48 hours before coming to hospital. He had no epidemiological history of interest.

The physical examination revealed diffuse exaggeration of stretch reflexes, with sustained ankle clonus, bilateral Babinski sign, and spasticity; tactile hypoaesthesia and hypalgesia in the soles of the feet; right leg dysmetria on the heel-to-knee test; and ataxic gait, with positive Romberg sign.

A neurophysiological study including electromyography, nerve conduction studies, and cortical stimulation revealed prolonged motor nerve conduction latencies in the lower limbs, predominantly in the right leg. A brain and spinal cord T2-weighted FLAIR MRI scan (Fig. 1) revealed numerous punctiform hyperintense foci, particularly in the middle cerebellar peduncles, pons, and corticospinal tracts, predominantly on the left side; the lesions showed paramagnetic contrast uptake.

A blood test yielded normal results; serology tests were negative for HIV, syphilis, *Borrelia*, *Brucella*, HTLV-1, cytomegalovirus, herpesvirus family, and hepatitis B and C viruses; and an autoimmunity study revealed no alterations. A CSF analysis revealed lymphocytic pleocytosis, associated with high levels of CD4 + T cells, and high protein levels; no tumour cells or signs of CNS infection were detected. CSF and serum results were negative for onconeuronal and antineutrophil antibodies. A whole-body PET scan was conducted to rule out lymphomatous, inflammatory, systemic, or tumoural diseases.

Given the recent fluctuation of neurological symptoms, we started treatment with intravenous methylprednisolone 1 g/day for 5 days, followed by decreasing doses of oral prednisone, starting at 1 mg/kg/day. Weakness and rigidity improved and gait instability resolved 72 hours after treatment onset.

The patient returned to our centre for a follow-up consultation one month later; prednisone dose at that time was 0.5 mg/kg/day. In a follow-up brain and spinal cord MRI study, T2-weighted FLAIR sequences revealed the disappearance of all punctiform hyperintensities; furthermore, no gadolinium-enhancing lesions were observed (Fig. 2).

Having ruled out other systemic diseases, the patient was diagnosed with chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids (CLIPPERS syndrome).

CLIPPERS syndrome is an entity of unknown aetiology, first described by Pittock et al.[1] in 2010; approximately 60 cases have since been described worldwide.[2,3] Its incidence is unknown. The syndrome predominantly affects men, and is most common in patients with a median age of 50 years.[2]

From a clinical viewpoint, CLIPPERS syndrome can present with a wide range of symptoms, although the most frequent are diplopia, ataxic gait, and spasticity.[4] Differential diagnosis includes a wide range of diseases; laboratory analysis reveals high CSF protein levels and lymphocytic pleocytosis with high levels of CD4 + T cells.[1]

The diagnostic criteria for CLIPPERS syndrome include subacute neurological symptoms, clinical signs of brainstem involvement, and characteristic radiological images. Brain MRI typically reveals punctiform hyperintensities (<3 mm in diameter) on T2-weighted FLAIR sequences (''salt and pepper sign''), which show gadolinium uptake, with no perilesional mass effect; the lesions appear bilaterally in the pons, cerebellum, and less frequently the spinal cord.[5] Diagnostic criteria include complete radiological resolution after high-dose corticosteroid therapy and absence of an alternative diagnosis.[1,5] Biopsy of CNS tissue is indicated only in case of atypical findings. In these cases, anatomical pathology studies show perivascular lymphohistiocytic infiltrate, predominantly of CD4 + T cells.[1]

The pathogenic mechanisms of CLIPPERS syndrome remain unknown; it has been hypothesised that the condition may be an inflammatory response to other disease, is of autoimmune origin, or constitutes a variant of lymphoma.

The syndrome usually responds rapidly to corticosteroid therapy. An appropriate treatment schedule is methylprednisolone boluses dosed at 1 g/day for 3-5 days, followed by prednisone dosed at 1 mg/kg/day, with slowly decreasing doses; the optimal duration of treatment is

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