

Infraorbital neuralgia: A diagnostic possibility in patients with zygomatic arch pain^{☆,☆☆}

Neuralgia del infraorbitario: un diagnóstico a considerar en pacientes con dolor malar

Dear Editor:

Neuralgia of the infraorbital nerve is an unusual cause of facial pain. The patient experiences paroxysmal or constant discomfort, often in the form of stabbing pain, in the distribution area of the infraorbital nerve.¹ The sensation is associated with hypersensitivity to palpation in the infraorbital notch.

The infraorbital nerve is a branch of the maxillary nerve. It originates in the infraorbital canal of the upper jaw and then follows the anterior and superior dental canal, branching off towards the incisor and canine roots and towards the mucous membranes of the anterior part of the inferior meatus.²

We present the case of a patient with left zygomatic arch pain refractory to medical treatment that was temporarily resolved with an infraorbital nerve block.

Our patient was a man aged 39 years with no relevant medical history. He made an appointment with the headache service because he had been experiencing continuous burning pain with no apparent cause over a 16-month period. Pain intensity was 5 out of 10 on the visual analog scale (VAS, with 0 indicating no pain and 10, the worst pain imaginable); it was located in the left zygomatic arch. He also experienced infrequent exacerbations lasting about an hour during which pain intensity was 9/10 on the VAS. Neurological examination yielded the surprising finding that this pain could be provoked by palpation of the nerve in the infraorbital notch. No other concomitant data of interest were observed.

Before attending our service, he had been assessed by the otorhinolaryngology and maxillofacial surgery departments. MRI and facial CT scans had been performed and neither yielded pathological findings.

Pain responded partially to naproxen but did not abate with a daily dose of 200 mg of lamotrigine.³ Since we suspected neuralgia of the infraorbital nerve, we performed an anesthetic block with 1 cm³ of lidocaine.⁴ Cessation of pain for 2 weeks confirmed the diagnosis (code 13.7 in the second edition of the International Headache Classification [ICHD-2]).⁵

We later performed several anesthetic blocks that were temporarily effective. Results did not change on the one occasion when anesthetic block was associated with a cor-

ticosteroid. We continued looking for a means of long-term pain resolution since it was not achieved with amitriptyline dosed at 25 mg daily and carbamazepine was not well tolerated. Partial improvement of symptoms has currently been achieved with pregabalin dosed at 150 mg daily.

When doctors suspect infraorbital neuralgia, they must rule out other symptomatic causes in order to assign a diagnosis. Doctors should determine if there is any history of traumatic episodes.⁶ Where no such history is present, they must rule out other secondary causes, mainly neoplasms that can cause these symptoms due to haematogenous, lymphatic, or perineural spread. For these reasons, imaging studies are recommended for all these patients.^{7,8} Once all the above have been ruled out, we can consider primary neuralgia^{9,10} and confirm the diagnosis after achieving pain relief with anesthetic nerve block.

Infraorbital neuralgia may be refractory to medical treatment, which generally includes analgesic, anti-inflammatory, anti-epileptic, or antidepressant drugs.¹¹ Other therapy alternatives include electrical transdermal nerve stimulation in extremely resistant cases.¹²

Cases of terminal branch neuralgia of the trigeminal nerve are rare and they frequently manifest as continuous pain. In contrast, cases of central involvement of the trigeminal nerve are generally associated with painful paroxysms.^{13–15} Considering these neuralgias and palpating the nerve territories corresponding to the painful area may provide effective treatment alternatives for symptoms that are frequently persistent and incapacitating. Nerve block is among the essential diagnostic criteria for these neuralgias, and it may therefore be suggested as a first therapeutic step, as in our case.

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Leptomeningeal amyloidosis due to A25T TTR mutation: A case report^{☆,☆☆}

Amiloidosis leptomeníngea debida a la mutación A25T TTR. A propósito de un caso

Dear Editor:

Leptomeningeal amyloidosis is a rare form of amyloidosis caused by a limited spectrum of mutations in the transthyretin gene (TTR), including the mutation in which threonine replaces alanine at codon 25. We describe the case of a patient with the A25T TTR variant. Only one report of such a case exists in published literature.^{1,2}

The patient was a 53-year-old woman with a 4-year history of progressive symptoms of vertigo, paraparesis, and ataxic gait. One month before, she had experienced sudden neurosensory hearing loss. A neurological examination revealed normal higher functions and right-sided hypoacusia. Deep tendon reflexes were present and generalised, with intact bilateral extensor plantar reflexes. We found moderate paresis of the right leg with tactile hypoaesthesia and hypopalaesthesia in both legs. Ataxic gait was also present. The CSF study revealed hyperproteinaemia (177 mg/dL) and xanthochromia. The electromyography study ruled out peripheral neuropathy. Cranial and spinal cord magnetic resonance imaging revealed superficial siderosis in the left sylvian fissure and signs of chronic bleed in CSF (Fig. 1). Both studies found thickened meninges with gadolinium uptake (see Fig. 1). The meningeal biopsy revealed abundant interstitial and perivascular amyloid deposits that were positive for TTR (see Fig. 1). A genetic study confirmed presence of the A25T TTR mutation. The patient had two healthy children who declined to undergo a genetic study. The patient's mother had died of an undiagnosed disease with similar symptoms at the age of 60. The

patient did not undergo studies to rule out the diagnosis of amyloidosis.

Leptomeningeal amyloidosis associated with TTR mutations is a rare but fatal form of amyloidosis. The A25T TTR mutation found in our patient was previously reported in a Japanese patient who also developed superficial siderosis and died due to multiple intracranial haemorrhages. The autopsy confirmed selective amyloid deposition in the leptomeninges.^{1,2}

Our patient presented both clinical signs and radiological findings compatible with superficial siderosis. Superficial siderosis of the central nervous system is caused by haemosiderin deposition in the leptomeninges and the surface of the brain. These deposits are the result of continuous or recurrent bleeding in the subarachnoid space which are due to multiple causes.³ This presentation was described in the published case of A25T TTR mutation, as well as in other cases of familial amyloidosis in which deposition predominantly affects the meninges.^{4,5} As a whole, these data stress the importance of considering leptomeningeal amyloidosis as an infrequent cause of superficial siderosis.

At present, there are no specific treatments for leptomeningeal amyloidosis. Liver transplantation, the treatment of choice for preventing the progression of neuropathy associated with most TTR mutations, is not effective in these cases; cells of the choroid plexus are the main producers of TTR in the brain.⁶ Tafamidis is an inhibitor that selectively binds to TTR in plasma and stabilises the tetrameric structure of amyloid, thereby preventing deposition.^{7,8} Unfortunately, there are no data suggesting that tafamidis would be able to cross the blood-brain barrier, and it is therefore not regarded as a means of slowing the course of the disease in cases of leptomeningeal amyloidosis (personal communication with Dr. Said). Intraventricular administration of a specific anti-sense oligonucleotide for TTR in the brains of transgenic mice with a mutated human TTR gene results in dose-dependent decreases in TTR expression in the choroid plexus. This is a compelling treatment strategy for these patients.⁶

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