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Psychiatric manifestations and dysautonomia at the onset of focal epilepsy in adults: Clinical signs indicating autoimmune origin[☆]



Manifestaciones psiquiátricas y fenómenos disautonómicos en el comienzo de epilepsia focal del adulto. Señales clínicas de un origen autoinmune

Immune alterations may be the cause of some of the epilepsies considered to date to be cryptogenic, and they usually respond to immunotherapy. Some of the clinical features of this type of epilepsy are a personal or family history of autoimmune or neoplastic disease, subacute onset with high seizure frequency, multiple seizure foci, early resistance to antiepileptic drugs, neuropsychiatric symptoms, and in some cases rapidly progressive cognitive impairment.¹ Presence of signs of inflammation in magnetic resonance imaging (MRI) and cerebrospinal fluid (CSF) studies and the detection of antineuronal antibodies may help establish diagnosis.² Diagnosis and early treatment may have a crucial impact on seizure control and cognitive comorbidity.^{3,4} We describe the cases of 3 patients with adult-onset focal epilepsy. Psychiatric symptoms and dysautonomia led to the suspicion of autoimmune aetiology, which was confirmed by antibody tests.

The first patient was a 24-year-old man with no relevant personal history who experienced an epileptic seizure with head version to the left, disorientation, and generalised rigidity and postictal period. Two weeks previously, he had presented behavioural alterations, insomnia, and auto- and hetero-aggression which progressed to mutism and catatonia. He also presented self-limiting episodes of profuse sweating. No paroxysms were observed in the EEG. A brain MRI scan (Fig. 1A and B) revealed hyperintensities in the

frontal lobe bilaterally and in the posterior corpus callosum, with no contrast uptake. CSF and serum analyses confirmed the presence of anti-NMDA receptor antibodies (qualitative study) and tumour screening ruled out occult neoplasm. He received antiepileptic treatment during hospitalisation, as well as treatment with corticosteroids and immunosuppressants (cyclophosphamide and rituximab). A follow-up MRI scan showed that the size of the lesions had decreased. Psychiatric symptoms improved 2 weeks later, and the patient was discharged, presenting no further epileptic seizures and without receiving treatment. A follow-up laboratory test at one year showed negative results for serum anti-NMDA receptor antibodies.

The second patient was a 35-year-old woman with type 2 diabetes mellitus, vitiligo, and anxiety disorder of one year's progression, under follow-up with the psychiatry department. The patient responded poorly to benzodiazepines. She had fallen and lost consciousness on 3 occasions, which had been interpreted as syncope. The patient subsequently experienced complex partial seizures with symptoms of temporal lobe epilepsy in the dominant hemisphere, with piloerection, brief episodes of disorientation, jaw automatisms, and motor aphasia. These symptoms manifested daily for one year. Baseline brain MRI results were normal. Neuropsychological tests revealed difficulty performing verbal and visual memory tasks. After receiving 2 drugs in monotherapy, she continued experiencing seizures 2-3 times per week. She was admitted to the long-term continuous video-EEG monitoring unit, and experienced 74 seizures with symptoms of left anteromedial temporal lobe epilepsy. Interictal findings were located in the anteromedial region of the left temporal lobe. A second MRI scan revealed enlargement and hyperintensity of the amygdala and left hippocampal head (Fig. 1C). Presence of anti-LGI1 antibodies in the plasma was confirmed (levels of 275 pM; normal range: negative). Treatment with corticosteroids was started and seizures disappeared after 3 weeks. The patient was treated with oxcarbazepine for one year. A follow-up brain MRI scan (Fig. 1D) showed decreased severity of the findings in the initial scan; a new plasma study confirmed negative results for anti-LGI1 antibodies. Results from the neuropsychological study performed at one year were normal. The patient is currently receiving no treatment and remains asymptomatic.

The third patient was a 62-year-old man with no relevant personal history, who was admitted due to a 2-month

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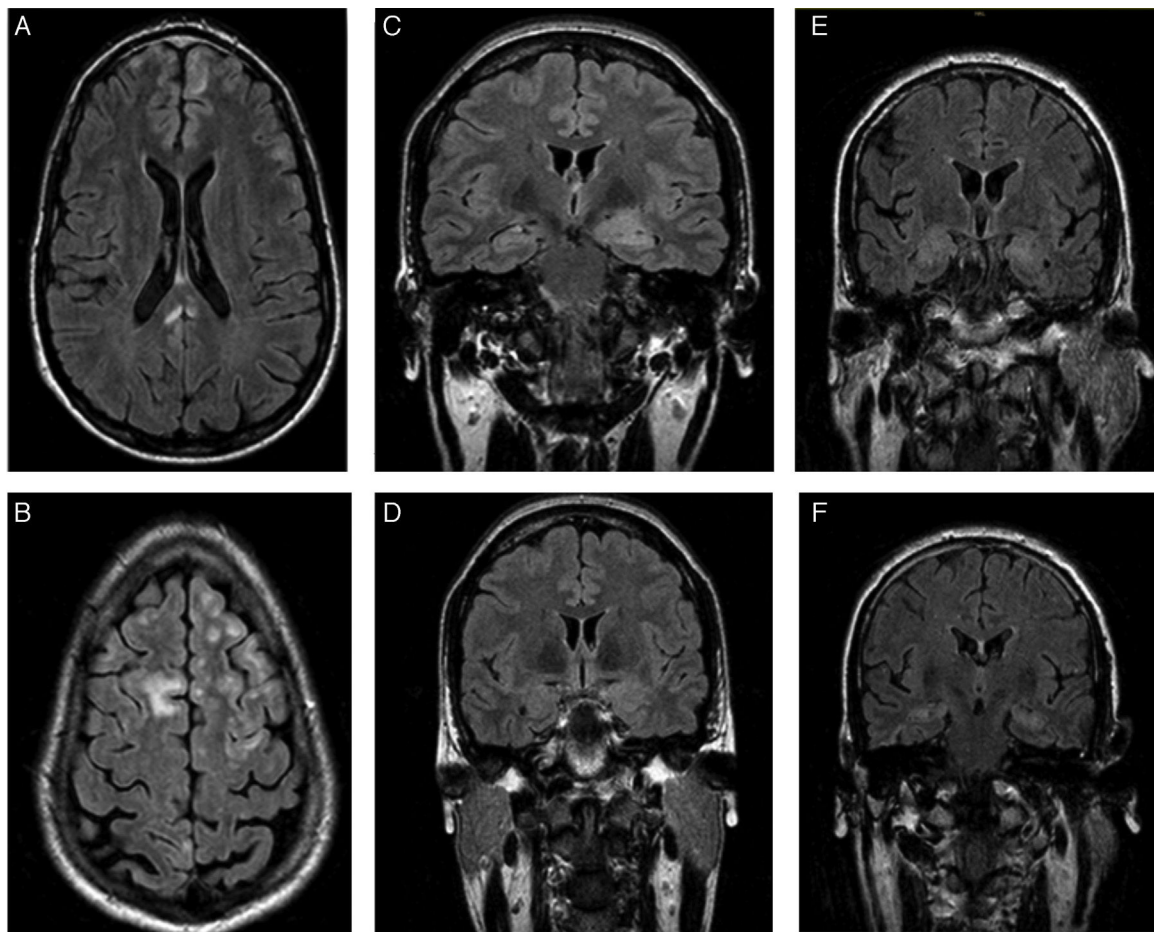


Figure 1 Patients' brain MRI scans. A and B) FLAIR sequence of the first patient, revealing bilateral frontal subcentimeter lesions and a T2-hyperintense lesion in the posterior corpus callosum with no contrast uptake. C and D) Diagnostic and follow-up FLAIR sequences of the second patient, showing enlargement and increased signal in the amygdala and left hippocampal head, and a subsequent decrease in size and signal. E and F) Diagnostic FLAIR sequence of the third patient, showing increased signal in both hippocampi.

history of apathy and episodes of disorientation with behavioural alterations and visual hallucinations. He concomitantly presented complex partial seizures with head version to the right and generalised rigidity. During admission, he presented 5 episodes of vasovagal syncope. The video-EEG recording showed interictal paroxysms in the left temporal lobe. The brain MRI scan and laboratory tests (vitamin B₁₂, pholate, TSH, 14.3.3 protein, tumour markers, and serology and autoimmune tests) yielded normal results. A second brain MRI scan (Fig. 1E and F) revealed increased signal intensity in both hippocampi; serum tests confirmed the presence of anti-LGI1 antibodies (levels of 188 pM). The tumour screening ruled out occult neoplasm.

Lamotrigine was administered, achieving no positive response, and was substituted with lacosamide. After autoimmune aetiology was confirmed, corticosteroid treatment was started; this resolved the symptoms. The patient died 2 months later due to respiratory infection with *Pneumocystis jirovecii*.

A lack of typical clinical manifestations of autoimmune encephalitis may delay diagnosis.⁴ Epileptic seizures

in isolation are rare in autoimmune epilepsies. In our series, psychiatric manifestations and dysautonomia⁵ were key symptoms leading to the diagnosis of autoimmune aetiology.^{6,7} CSF determination of antibodies, exclusion of other causes, and negative tumour screening results for occult neoplasm helped diagnose the aetiology. Up to 50% of cases of autoimmune encephalitis respond to first-line treatment with corticosteroids, plasmapheresis, or immunoglobulins. The remaining 50% respond to cyclophosphamide and/or rituximab. Early immunological treatment is associated with a better response and may prevent progression to cognitive impairment. The time lapse between symptom onset and treatment onset is greater in refractory cases than in responding patients.^{4,8}

Psychiatric manifestations and dysautonomia associated with epileptic seizures may be signs permitting diagnosis and early treatment of autoimmune epilepsies.

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Recurrent lacrimal neuralgia secondary to ophthalmological procedures[☆]



Neuralgia lagrimal recurrente desencadenada por procedimientos oftalmológicos

Dear Editor:

Lacrimal neuralgia, an infrequent cause of orbital and peri-orbital pain, was first described in 2013.¹ The 2 patients presented in the original description had constant pain in the areas innervated by the lacrimal nerve (the lateral part of the upper lid and adjacent area of the temple). Accompanying symptoms were sensory dysfunction and hypersensitivity upon palpation of the lacrimal nerve in the superolateral angle of the orbit. In both cases, diagnosis was confirmed by a deep anaesthetic block of the lacrimal nerve with lidocaine 2%; however, pain was alleviated only for a few hours. In subsequent cases,^{2–4} a simpler anaesthetic technique was used: a superficial block of the lacrimal nerve by a subcutaneous injection of bupivacaine 0.5%, which has been shown to be useful as a short- and long-term diagnostic and therapeutic technique. To date, 7 cases of lacrimal neuralgia have been published, most of them primary or idiopathic. Only one case secondary to ophthalmic surgery has been reported³; in this case, pain was paroxysmal, with multiple episodes per day lasting 1–2 minutes. This case showed that lacrimal neuralgia can have a compressive or traumatic origin. We present a new case of lacrimal neuralgia secondary to ophthalmological procedures.

Our patient was a 53-year-old man with wet age-related macular degeneration and migraine with aura as the only relevant history. The patient visited our hospital due to a 15-month history of pain limited to a very small (3 cm diameter) area in the left temple, manifesting for the first time after a session of argon laser photodynamic therapy of the left eye. Pain was intense (8 on a 0–10 numeric scale), oppressive, and manifested in episodes lasting up to 72 hours which appeared only when he visited the ophthalmologist to receive intravitreal injections of aflibercept (anti-vascular endothelial growth factor [anti-VEGF]) every 3 months. He simultaneously presented allodynia and hyperalgesia in the treated area. Examination during the intercritical period revealed hypersensitivity to palpation of the left lacrimal nerve and hyperalgesia in the affected area (Fig. 1). No other significant findings were observed in the neurological or systemic examinations. A brain magnetic resonance study was performed, revealing only signs compatible with mild microangiopathy.

The patient visited our department on 2 subsequent occasions due to new episodes of pain, which had started



Figure 1 Hyperalgesic area delimited during the examination of the patient in the first consultation.

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