the right eye and 490 μm in the left (Fig. 1). The patient was transferred to the neurology department, and treatment with fingolimod was withdrawn. At a follow-up visit to the neuro-ophthalmology department 20 days later, the macular oedema had fully resolved in both eyes (Fig. 2), and VA was restored bilaterally. Two months later, fingolimod was reintroduced to control MS. The patient was referred to the neuro-ophthalmology department 10 days later due to reduced VA (right eye: 0.7, left eye: 0.8). Cystoid macular oedema was present in both eyes; central macular thickness was 395 μm in the right eye and 420 μm in the left. Fingolimod was withdrawn once more, and neuro-ophthalmological and optical coherence tomography alterations resolved after a month. The macular oedema was not treated on either occasion; rather, it spontaneously and completely resolved following withdrawal of the drug.

In clinical trials, 0.5% of patients receiving fingolimod displayed macular oedema.[3] The summary of product characteristics recommends that patients be evaluated before treatment is started, with an ophthalmological evaluation to be performed at 3-4 months.[4] Fingolimod can cause vision loss due to macular oedema; this adverse reaction usually resolves following withdrawal of the drug, although cases have been described of visual impairment persisting months after withdrawal. Macular oedema is known to present more frequently in patients with diabetes mellitus and/or a history of uveitis. Our patient had no associated comorbidities; oedema developed less than 7 days after treatment onset. The literature includes other reports of macular oedema developing within 3-4 months of treatment onset,[5] although not as early as in our patient. We consider it important to begin performing ophthalmological reviews after treatment is started, and to expedite referral of patients at greater risk of macular oedema (patients with diabetes mellitus or history of uveitis) or who report reduced VA or blurred vision.

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Atypical paraneoplastic syndrome with no onconeuronal antibodies: A case report☆

Síndrome paraneoplásico atípico sin anticuerpos onconeuronales detectables: a propósito de un caso

Dear Editor:

Paraneoplastic neurological syndromes (PNS) constitute a heterogeneous group of immunopathogenic disorders caused by tumours located outside the nervous system. Before the diagnosis is established, we must rule out neurological complications resulting directly from the tumour or its treatment.[1] From a pathophysiological perspective, PNS are explained by the presence of common antigens in tumour cells and in some structures of the nervous system, with the result that the antitumour immune response also affects healthy cells.[2,3] According to the PNS diagnostic criteria, detection of both the onconeuronal antibodies and the primary tumour are 2 of the most useful factors when establishing diagnosis. However, not all patients present circulating antibodies[4]: these may go undetected in up to 50% of patients,[5] as in our case.

Our patient is a 68-year-old woman who presented progressive dyspnoea associated with pulmonary thromboembolism and deep vein thrombosis, as well as confusional syndrome and secondarily generalised partial seizures. After a 2-month improvement period, she once again presented confusional syndrome, gait ataxia, and recurrent seizures leading to status epilepticus.

The blood analysis displayed normal results (including thyroid and parathyroid hormone levels, vitamins, folic acid, CEA, and Ca 15.3); results for angiotensin-converting

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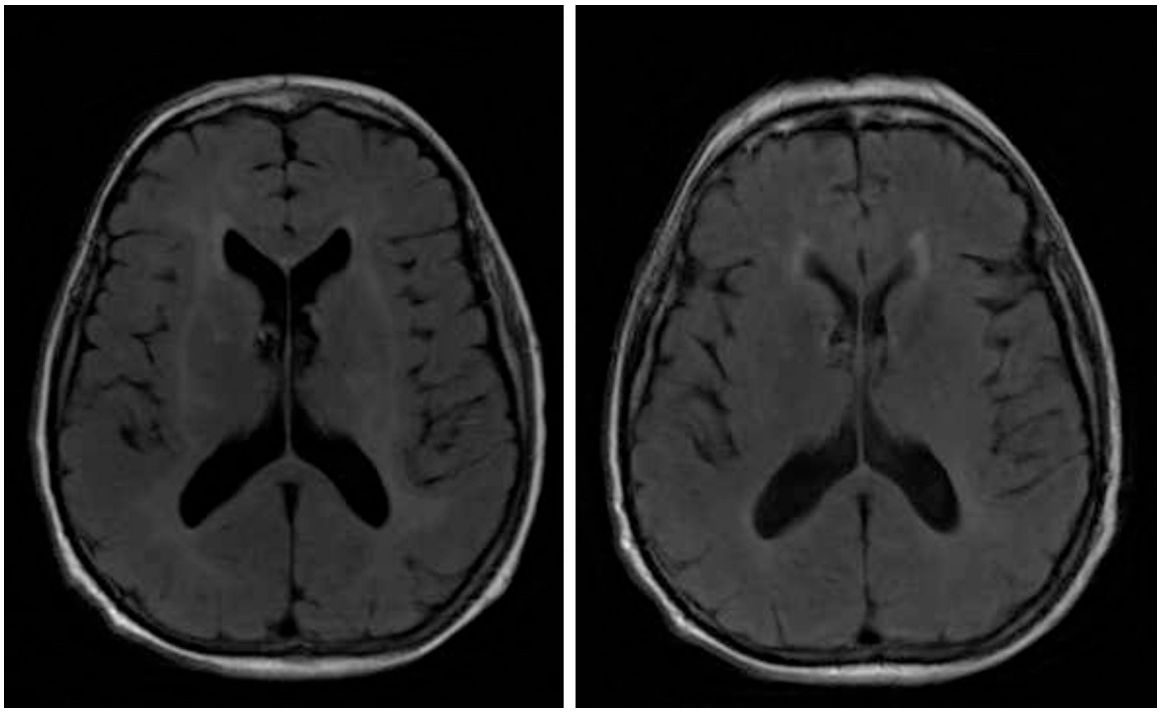

Figure 1 Brain MRI. T2-weighted FLAIR sequence. A) Baseline: bilateral diffuse involvement of the white matter, except for the U-shaped fibres. B) Three months after tumour resection: decreased leukoencephalopathy (barely visible).

enzyme, long-chain fatty acids, serum and urine protein test, and immunofixation were also normal. The autoimmunity study (anti-DNA antibodies, IgM and IgG anti-cardiolipin antibodies, anti-Cenp-B antibodies, anti-histone antibodies, anti-Jo-1/HRS antibodies, anti-nucleosome antibodies, anti-PCNA antibodies, anti-PM/Scl antibodies, anti-ribosomal P antibodies, anti-topo I (Scl-70) antibodies, anti-Sm antibodies, anti-RNP/Sm antibodies, anti-SSA/Ro60 antibodies, anti-SS-A/Ro52 antibodies, anti-SS-B/La antibodies, antimicrosomal antibodies, TSH receptor antibodies, antithyroglobulin antibodies) yielded normal results, with the exception of those for anti-nuclear antibodies. Serology tests for syphilis, HIV, and JC virus returned negative results. The CSF analysis only revealed high protein levels (118 mg/dL), with negative results for Gram staining, cultures, and cytology study. No intracellular onconeural antibodies or surface antigen antibodies were detected in the serum or the CSF (anti-Hu, Yo, Ri, CV2, PNMA 2 [Ma2/Ta], amphiphysin, recoverin, Sox1, titin, Zic 4, GAD65, and Tr [DNCR]).

A brain MRI scan revealed bilateral supratentorial leukoencephalopathy, with no gadolinium contrast enhancement or specific findings (Fig. 1). Several electroencephalography (EEG) studies revealed diffuse slowing with occasional epileptiform activity. An electromyography study revealed an asymmetrical demyelinating/axonal sensorimotor polyneuropathy of distal predominance, which was more pronounced in the lower limbs.

We ruled out thiamine deficiency, toxic-metabolic, inflammatory, and infectious encephalopathy. Given suspicion of atypical PNS, complementary tests were performed, revealing an invasive ductal carcinoma in the left breast (Fig. 2), with no signs of metastasis. After surgical resection of the tumour and hormone therapy with exemestane and radiation therapy, the patient progressed favourably, showing normal results in a neurological examination and EEG study at 3 months. A brain MRI scan revealed that leukoencephalopathy had significantly decreased and was barely visible (Fig. 1).

Having ruled out other causes and in the absence of a better explanation, we diagnosed the patient with atypical PNS (acute encephalopathy, secondarily generalised partial seizures, and asymmetric demyelinating/axonal sensorimotor polyneuropathy). The favourable clinical outcome and the normal MRI, EEG, and CSF findings after tumour treatment (without immunosuppressants) suggests that a coincidental association is unlikely and points to a definitive diagnosis of PNS.

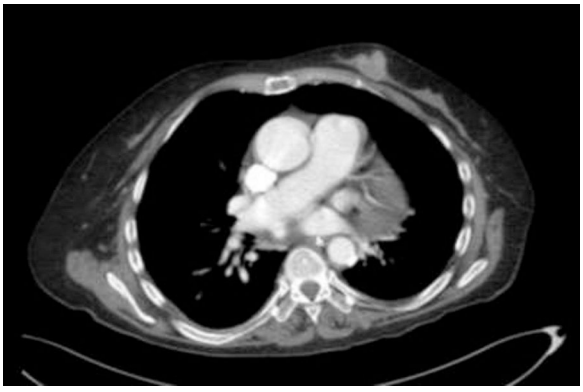

Figure 2 Full-body CT scan. Nodular lesion with poorly-defined edges in the left thoracic wall, corresponding to breast cancer.

We stress the importance of maintaining a high level of suspicion of PNS (a potentially curable disease) in cases of neurological alterations of unknown cause, once other conditions have been ruled out, even in the absence of onconeuronal antibodies, since this does not rule out the diagnosis.[6]

Although cases of PNS with no known associated autoantibodies have been described, cases with such complex clinical symptoms are rare. The clinical heterogeneity of our case represents a contribution to the existing knowledge on atypical PNS. Furthermore, it demonstrates the need for studies revealing improvement, which is mandatory in the absence of autoimmune markers.

Author contributions

Study design, drafting, and approval of the final version: E. Casas Peña.

Approval of the final version: M.A. Martín Santidrián and J. González Fernández.

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Status dissociatus: the most extreme expression of state dissociation☆

Status dissociatus: la expresión más extrema de los estados de disociación

Dear Editor,

Status dissociatus (SD) was first described by Mahowald and Schenck[1] in 1991 and is currently considered the most extreme form of state dissociation.[2] Healthy individuals present 3 states, wakefulness, non-REM (NREM) sleep, and REM sleep,[3] each with its own neuroanatomical, neurophysiological, and neurochemical characteristics. In this context, state dissociations result from errors in the normal process of dynamic changes in the central nervous system as it shifts between states, where one state is interrupted by another (for example, in cataplexy, where the characteristic atonia of the REM sleep appears during wakefulness) or elements of one state persist into the next (for example, sleep paralysis, where wakefulness appears while atonia from the REM sleep state persists).[4] These errors may occur spontaneously, or as a result of a neurological dysfunction or the use/withdrawal of substances or drugs. These state dissociations should not be confused with dissociative disorders, which are defined in the DSM-V as a group of psychiatric disorders characterised by disruption and/or discontinuation of the normal integration between consciousness, memory, awareness of identity, emotions, perception, body representation, motor control, and behaviour.[5] The third edition of the International Classification of Sleep Disorders of the American Academy of Sleep Medicine[6] classifies SD as a subtype of REM sleep behaviour disorder (RSBD).

SD is associated with direct thalamic lesions or lesions to structures related to the thalamus, which cause a thalamolimbic GABAergic dysfunction. It is therefore associated with neurodegenerative diseases (Parkinson's disease or multiple system atrophy), rapidly progressive neurodegenerative diseases (fatal familial insomnia or Creutzfeldt-Jakob disease), autoimmune diseases (autoimmune encephalitis

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