

sidered a typical sign of demyelination processes. These features were detected in every patient in the series.

The main parameter to assess disease activity is the occurrence of clinical relapses. The time to recovery is shorter in children, but the frequency of relapse in the first year is greater than in adults, which suggests a course of disease with a stronger inflammatory component.<sup>5</sup> Our findings support this hypothesis.

Management with first-line treatments authorised in adults has proven safe and effective in reducing the frequency of relapse by 30%–40% in children, similar to the effectiveness observed in adults. In the adult population, up to 30% of patients do not respond to first-line treatment.<sup>6</sup> In our series, 4 patients (44%) required second-line treatment with hardly any side effects, which corroborates the efficacy of these treatments in the paediatric population.

Juvenile multiple sclerosis, while having a slower and more benign course, may eventually cause a level of disability comparable to adult-onset multiple sclerosis due to its earlier onset. Given the high incidence of optic neuritis in paediatric patients, optical coherence computed tomography of the optic nerve may be a useful non-invasive assessment tool in the follow-up of these patients.

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2341-2879/ © 2021 Published by Elsevier España, S.L.U. on behalf of Asociación Española de Pediatría. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

## Tick-borne encephalitis. Description of the first imported case in Spain in a paediatric patient<sup>☆</sup>

### Encefalitis centroeuropea. Descripción del primer caso importado en España en un paciente pediátrico

Dear Editor:

Acute encephalitis is an infrequent neurologic emergency that can have devastating consequences.<sup>1</sup> It is an illness characterised by neurologic impairment due to the inflammation of the cerebral parenchyma, which may be due to various causes. In the paediatric population, it is usually caused by viral infection, although the aetiology is not estab-



lished in up to 62% of cases.<sup>1</sup> We present the case of a toddler that received a diagnosis of tick-borne encephalitis (TBE, also known as Central European encephalitis). We emphasise the need to include this disease in the differential diagnosis, especially in children from endemic regions.

The patient was a boy aged 2 years that was unvaccinated due to parental refusal, brought to the emergency department on account of somnolence and fever of 7 days' duration associated with headache and light and sound sensitivity with onset 5 days after returning to Spain from a 2-month trip to a rural area in north-east Austria. The patient had experienced a few tick bites during the trip and a self-limited episode of fever without source a month before the current episode, after which he had been asymptomatic for 3 weeks. At admission, he exhibited somnolence (12 points in the Glasgow comma scale) accompanied by irritability, nuchal rigidity and ataxic gait. Blood tests revealed leucocytosis (21 200 cells/mm<sup>3</sup>) with neutrophilia (18 000 neutrophils/mm<sup>3</sup>), lymphopenia (1900 lymphocytes/mm<sup>3</sup>) and normal C-reactive protein and procalcitonin levels. The findings of neuroimaging (TC y RM) normal. The cerebrospinal fluid (CSF) analysis evinced lymphocytic pleocytosis (125 lymphocytes/mm<sup>3</sup>, 95% mononuclear cells) and increased protein levels in

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CSF (47 mg/dL) with normal glucose levels. A meningitis/encephalitis panel, FilmArray™ (bioMérieux, Madrid, Spain), ruled out the main bacterial, viral and fungal agents involved in central nervous system infections. Suspicion of aseptic encephalitis of possible viral aetiology led to initiation of empirical treatment with acyclovir until a negative polymerase chain reaction (PCR) test ruled out the presence of herpes simplex virus. The enterovirus PCR test was negative for the rectal swab and nasopharyngeal samples, as were serologic tests for *Borrelia burgdorferi* and *Rickettsia conorii*. The SARS-CoV-2 antibody test was positive for IgG and negative for IgM. Due to the epidemiological history and the biphasic course of illness, compatible with TBE, tests were ordered to assess for this disease. The immunohistochemical analysis of CSF (EUROIMMUN, Lübeck, Germany) did not detect antibodies against the virus, and a generic real-time PCR test for detection of Flavivirus species was also negative.<sup>2</sup> However, we found a four-fold increase of TBE-specific IgG antibodies compared to paired serum samples, with positive IgM antibodies and no cross-reactivity to other flaviviruses, such as West Nile virus or Japanese encephalitis virus, which fulfilled the laboratory criteria for a confirmed case according to European guidelines.<sup>3</sup> In the first 48 h of the hospital stay, the patient continued to be lethargic and ataxic, with no other focal neurologic deficits. At 72 h from admission, the patient started to exhibit progressive improvement, achieving full neurologic recovery by day 5. The patient did not receive steroids or immunoglobulin therapy. In the follow-up after discharge, he remained asymptomatic and the neurologic examination was normal.

Tick-borne encephalitis is an infectious disease caused by a virus of the Flaviviridae family, transmitted through the bite of ticks of species in the *Ixodes* genus, of which 4 subtypes are known: European, Far-Eastern and Siberian.<sup>4</sup> It is an important cause of encephalitis in Eastern and Central European countries, northern China, Mongolia and Russia. However, in recent years it has become an international public health problem due to the increase of travel to endemic areas, with trips to high-risk rural areas in the Spring and Summer, although there have also been reports of cases of secondary infection through the consumption of unpasteurised milk of infected goats, sheep or cows.<sup>4</sup> Although ticks of *Ixodes* species are distributed throughout Europe, including Spain, there have been no reports of cases of TBE in Spain until April 2020, when the first case of imported TBE due to consumption of contaminated milk was reported in a patient aged 18 years after a trip to Estonia.<sup>5</sup>

The typical course of disease is biphasic. After an incubation period of approximately 8 days, the initial phase manifests with nonspecific symptoms such as fever, asthenia or myalgia. After 1–3 weeks of absent symptoms, a third of infected individuals develop neurologic manifestations compatible with meningoencephalitis or encephalomyelitis.<sup>4</sup> Disease severity increases with age, and the Far-Eastern subtype is associated with the poorest outcomes, with a mortality of 20%–40% compared to 1%–2% for

the European subtype.<sup>6</sup> At present, there is no specific treatment for TBE, and management consists of supportive care. Vaccination is the most effective method of prevention, and has been recommended in Spain since 2008 for individuals that travel to endemic regions for outdoor activities.<sup>6</sup> Here, we describe the second known case of imported TBE in Spain, which highlights the importance of epidemiological surveillance of emerging endemic infectious diseases and the need of vaccination as highly effective tools for the prevention of diseases like TBE.

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