We report a patient diagnosed with primary biliary cirrhosis well-controlled with treatment, who developed bilateral LE with a good therapeutic response to intravenous corticosteroids.

**Case Report**

The patient was a 45-year-old nonsmoking woman with a previous history of fibromyalgia. She was diagnosed 2 years ago with primary biliary cirrhosis by liver biopsy, and was treated with ursodeoxycholic acid, with good control. She had been examined by the Internal Medicine Department because of a 6-month history of recent memory impairment of remote memory, and antiepileptic drugs has been recom-
Routine CSF analysis showed 4 leukocytes/mm³, glucose 72 mg/dl, and protein 31.9 mg/dl. PCR for herpes simplex virus types 1 and 2, Epstein-Barr virus, and cytomegalovirus, serologic studies for Borrelia and Brucella, and cytological studies in the CSF were negative.

A diagnosis of idiopathic LE was made, and the patient was treated with valproic acid 900 mg/day, thiamine 100 mg/8 h, acyclovir 750 mg/8 h, and 3 cycles of intravenous methylprednisolone (1 g/day for 5 days) at the diagnosis and after 2 and 4 months. Recent and remote memory impairment improved slightly, while attentional deficit and temporal disorientation did not improve. A brain MRI performed 7 months after diagnosis showed bilateral hippocampal atrophy (fig. 1b).

Discussion
Paraneoplastic LE has been reported in association with various tumors. Approximately 50% of paraneoplastic LE are associated with lung carcinoma, both oat cell and other histological types, 20% are associated with testicular carcinoma and 8% with breast cancer [4]. Cases associated with immature ovarian teratoma [8], Hodgkin’s lymphoma [9, 10] and malignant thymoma [11, 12] have also been reported. Most of these patients, up to 60%, showed positivity of onconeural antibodies [4]. The following antibodies were most frequently positive: anti-Hu antibodies [4, 7], with positivity rates up to 50% in cases with LE associated with lung carcinoma of the oat cell type [13], antibodies against P/Q-type voltage-dependent calcium channels [14], anti-Tr antibodies in patients with Hodgkin’s disease associated with cerebellar degeneration or LE [9], and anti-Ta or anti-Ma2 antibodies in a patient with LE and breast cancer [15] and in patients with testicular tumors [4]. Onconeural antibodies were frequently negative in patients with LE and lung cancer other than oat cell type [13].

Currently, anti-VGKC antibodies are considered to be important to differentiate ‘pure’ autoimmune LE from paraneoplastic LE. These antibodies have been detected in the serum of patients with neuromyotonia – which frequently coexists with thymoma or autoimmune diseases such as myasthenia gravis – and in such patients, the risk for development of LE seems to be higher [16–19], but with a better prognosis [17]. In addition, in the serum and CSF of patients with ataxia, LE and some types of epilepsy, the existence of antibodies against calcium channels and glutamate receptors has been described. The presence of these antibodies, together with the good therapeutic response to immunotherapy, could suggest that they might have a pathogenetic role [20].

Primary biliary cirrhosis is a liver autoimmune disease of unknown etiology. Autoimmune attack is organ specific despite the presence of mitochondrial autoantigens, which are the main target of autoimmunity in this disease in all nucleated cells [20]. Primary biliary cirrhosis has been reported to be associated with Sjögren’s syndrome and transverse myelitis [21, 22], with mitochondrial encephalomyopathy [23] and with sensory neuropathy [24, 25].

In our patient, the diagnosis of autoimmune LE was made after a reasonable exclusion of possible infectious or paraneoplastic etiologies of LE syndrome. However, despite the patient being a nonsmoker, the short time of follow-up does not allow ruling out the possibility of a paraneoplastic LE, because the tumor may appear 2–3 years after the diagnosis of LE [4, 26]. Although, to our knowledge, there are no previous reports of primary biliary cirrhosis associated with LE, the coincidence of two diseases of possible autoimmune origin in the same patient would suggest the existence of a relationship between them.

To date, only a few patients have been reported with LE associated with autoimmune diseases after excluding a paraneoplastic origin. The autoimmune disease most frequently reported in association with LE (MRI was usually normal) is Hashimoto’s thyroiditis [27–30]. Nakajima et al. [31] reported a patient with left mesial temporal encephalitis including hippocampal affection with increased titers of antinuclear and anti-SSA/Ro antibodies and increased CSF IgG levels and IgG index. Morita et al. [11] described LE, opsoclonus myoclonus and sensorimotor and autonomic neuropathy in a patient with Addison disease and malignant thymoma. The association of LE with malignant thymoma has also been reported by Evoli et al. [12]. Finally, Stubgen [32] described a patient with LE and increased CSF titers of antireibo-P antibodies, suggesting its association with CNS lupus erythematosus.

Most authors suggest that, in the absence of evidence of neoplastic or infectious disease, treatment with a combination of plasmapheresis and intravenous immunoglobulins improves the clinical outcome and decreases the MRI abnormalities [33]. Other authors recommend the use of intravenous steroid boluses (methylprednisolone 1 g/day for 5 days) repeated monthly for 3 months and, in refractory cases, intravenous immunoglobulins and plasmapheresis [7].
References