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LETTER TO THE EDITORS

Lithium neurotoxicity mimicking rapidly progressive dementia

Andrea Mignarri · Elena Chini · Alessandra Rufa · Raffaele Rocchi · Antonio Federico · Maria Teresa Dotti

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Dear Sirs,

Lithium is currently used in the prophylaxis and treatment of depression and bipolar disorders. It is rapidly assimilated by gastrointestinal tract and mainly eliminated by the kidney. The narrow therapeutic range and the well-known adverse effects represent two important limits to its utilization in clinical practice: serum levels of lithium should be assessed every 3–6 months, since intoxication may determine renal failure, thyroid dysfunction, cardiac arrhythmias and neurotoxicity including tremor, nystagmus, ataxia, seizures and even coma [1]. Here we describe a case of insidious-onset lithium intoxication resembling a progressive neurodegenerative dementia and requiring differential diagnosis with Creutzfeldt-Jacob disease (CJD).

A 60-year-old Italian woman was recently referred to our Unit. She had been affected by bipolar disorder since adolescence, and had been receiving treatment with lithium carbonate (600 mg/day) for 15 years and olanzapine (5 mg/day) for 5 years. Serum lithium concentration had been regularly assessed and never revealed abnormalities. Moreover, there had been no recent variation of lithium dose. Apart of the psychiatric illness, her clinical history was unremarkable. In the last 2 months, the patient was noted to have decreased cognitive function associated with worsening ataxia and involuntary movements. Also, relatives referred that the patient had become distractible, dysphoric and irritable. On admission, neuropsychological evaluation revealed she was deeply demented, almost speechless, giving erratic or delayed verbal responses to questions. She displayed poverty of thought, disorganization, and attentional impairment. No signs of psychosis were present. Neurological examination revealed ideomotor apraxia, gait ataxia, limb dysmetria and hand myoclonic movements. Routine blood tests were normal, including renal and thyroid function. Electrocardiogram did not reveal alterations. Electroencephalography (EEG) uncovered a significant background slowing with intrusion of biphasic and triphasic slow waves, compatible with cortical and subcortical dysfunction due to toxic/metabolic encephalopathy (Fig. 1a). Brain magnetic resonance imaging showed a chronic vascular encephalopathy with multiple post-ischemic gliotic changes in the periventricular and subcortical white matter. Cerebrospinal fluid analysis did not reveal abnormalities except for mildly increased levels of total-tau protein (347 pg/ml; normal <275) and phosphorylated-tau protein (65 pg/ml; normal <50). Assessment of serum lithium concentration revealed a marked increase at 2.45 mmol/l (therapeutic range 0.6–1.2). Subsequent lithium discontinuation led to a sharp normalization of serum lithium levels and a rapid improvement of cognitive function and ataxia, as well as disappearance of myoclonic jerks. The EEG performed 5 days after drug withdrawal showed partial recovery of background activity and marked decrease of the slow waves (Fig. 1b). On day 10, the patient was discharged with a normal neurological examination.

The evaluation of patients with rapidly progressive dementia represents one of the most binding challenges for neurologists [2]. In these patients, taking a drug history is at least as important as performing instrumental and invasive exams. As a matter of fact, a number of medications that are currently used to treat psychiatric and neurological diseases, such as lithium, sodium valproate, carbamazepine

A. Mignarri · E. Chini · A. Rufa · R. Rocchi · A. Federico · M. T. Dotti (✉)
Department of Medicine, Surgery and Neurosciences, University of Siena, Viale Bracci 2, 53100 Siena, Italy
e-mail: dotti@unisi.it