Valproate-induced acute encephalopathy
Encefalopatía aguda induzida pelo valproato

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ABSTRACT
We report a case of an acute encephalopathy induced by valproate used as antiepileptic drug and the clinical improvement after withdrawal of valproate.

Keywords: Brain diseases/chemically induced; Valproic acid/adverse effects; Epilepsy/drug therapy

INTRODUCTION
Many medications can cause acute encephalopathy. It is considered a rare condition when valproate, used in monotherapy to control epileptic seizures, is the culprit of brain involvement(¹).

CASE REPORT
A 11-year-old male patient, with no prior relevant abnormality, was admitted to Hospital Israelita Albert Einstein (HIAE) in August 2004, for having had a generalized grand mal seizure minutes before. Upon examination, he was torpid, with no other alterations in neurological examination.

Blood test results (CBC, electrolytes, transaminases, glycemia, urea and creatinin) were all within normal range. The cerebrospinal fluid presented lymphomononuclear hypercytosis. The electroencephalogram revealed tracing compatible with diffuse brain involvement, associated with bilateral frontotemporal irritative activity. Brain computed tomography (CT scan) showed signs of cerebral edema in the frontotemporal and parasagittal regions bilaterally.

Immune tests for herpes were negative, both in blood and cerebrospinal fluid. After a satisfactory clinical progression, he was discharged in the tenth day, although he still had mild time and space disorientation. Upon discharge, he was on phenytoin, which was kept on regular use. After two weeks, he underwent a brain magnetic resonance imaging that, in flair images, showed a hyperintense signal in the frontal, parasagittal and parietal regions, bilaterally. Since the clinical picture evolved in a clearly favorable manner, the patient went back to his school and sports activities with no difficulties.

After 12 months, he presented no abnormality and remained symptomless, so that he slowly and progressively discontinued phenytoin; in November 2005, he was no longer on any medication. In March 2006, he started to complain of dizziness, a feeling that the objects were moving, vomits and headache. The electroencephalogram revealed signs of diffuse irritative activity, when phenytoin was reinitiated. In June 2006, he was admitted because of a generalized grand mal seizure. Laboratory tests did not reveal abnormalities, and the MRI yielded similar results to those found in September 2005.

Since it was difficult to control seizures with phenytoin at hospital, we decided to replace it with valproate. The patient then had sporadic vomiting and dizziness, which worsened, and later presented mental confusion.

The electroencephalogram showed important slowing of cerebral electrical activity, which was compatible with acute encephalopathy. Blood tests to dose ammonia, valproate, liver function, electrolytes, as well as cerebrospinal fluid were normal. The brain MRI did not show any alteration different from the...
previous tests. Based on the results, we diagnosed as acute encephalopathy triggered by valproate.

When valproate was discontinued, the patient presented progressive and fast improvement in his confusion status. After five days, there was a clear improvement in his electroencephalographic tracing, since the slowing in cerebral electrical rhythm was mild; however, there were still signs of epileptiform discharges (paroxysmal spikes). The electroencephalogram was repeated two months later and did not show any abnormalities.

His school performance was absolutely normal, as well as his physical activities.

**DISCUSSION**

Valproate is a broad spectrum anticonvulsant agent, which is considered as first-line therapy for epilepsy. In Brazil, valproate has been used since 1979, although in other countries it has been available for more than 40 years. Numerous adverse effects have been noticed during this period, and the most frequent are nausea, vomiting, vertigo, diplopia, asthenia, diarrhea, sleepiness, tremor, abdominal pain, hepatitis, pancreatitis, anorexia, alopecia, weight gain and thrombocytopenia.

Currently, valproate has been also recommended to treat some psychiatric disorders (bipolar disorder and depressive symptoms) and migraine. Valproate rarely causes acute encephalopathy, especially in monotherapy. The clinical picture presented is similar to reversible acute encephalopathy or dementia. Encephalopathy usually develops in association with hyperammonemia or liver failure. Our patient did not present high ammonia levels, and liver function tests were within normal limits. Besides the clinical picture, the EEG revealed signs of brain involvement, which regressed after discontinuation of valproate. Moreover, the neurological symptoms improved at the same time. These data agree with those presented by Panda.

**CONCLUSION**

It was the case of a patient presenting a clinical and electroencephalographic picture of acute encephalopathy when in use of valproate that presented complete remission after discontinuing the medication.

**REFERÊNCIAS**