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Myoclonus relieved by carbamazepine in subacute sclerosing panencephalitis

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ABSTRACT – A 20-year-old woman with subacute sclerosing panencephalitis, bedridden because of dystonic posturing and very frequent myoclonic involuntary movements, improved dramatically with carbamazepine. The favorable effect of the carbamazepine on myoclonus was demonstrated by discontinuing and reintroducing carbamazepine, and videoing the consequent reappearance and disappearance of the myoclonus.
[Published with video sequences]

Key words: SSPE, myoclonus, carbamazepine, measles, subacute sclerosing panancephalitis

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Subacute sclerosing panencephalitis (SSPE) is a rare neurological disorder, caused by persistent, defective measles virus. The diagnosis is based upon characteristic clinical and electroencephalographic (EEG) findings, and the presence of elevated antibody titers against measles in the serum and cerebrospinal fluid. The prognosis of the disease is usually poor, with a gradual, progressive course leading to death in a few years, but patients with a very slowly progressing course have also been observed (Garg 2002). Oral inosiplex (isoprinosine) combined with intraventricular alfa-interferon has been recommended as the best treatment (Gascon *et al.* 1993), although not confirmed by a randomized treatment study (Gascon 2003). Beta-interferon might also be combined with inosiplex in some patients (Anlar *et al.* 1998).

Patients with SSPE are usually disabled by myoclonic involuntary movements, which interfere with gait and cause falls. Myoclonus may be controlled by sodium valproate and clonazepam, but are often refractory to treatment. Trihexyphenidyl, combined with isoprinosine (Nunes *et al.* 1995), ketogenic diet (Bautista 2003), carbamazepine (Hayashi *et al.* 1996, Vela *et al.* 1997, Ondo and Verma 2002), and topiramate (Duman *et al.* 2004) have been shown to relieve temporarily myoclonus in a few patients. We report a patient with SSPE, in whom severely disabling dystonic and myoclonic involuntary movements disappeared on treatment with carbamazepine.

Case report

A 20-year-old woman presented with a three-year history of frequent falls, forgetfulness and behavioral changes. A progressive decline in the school performance obliged her to quit high school. She became bedridden because of abnormal posturing and very frequent involuntary movements disturbing ambulation.

The EEG showed a normal background activity, interspersed with periodic, bilateral, high voltage polyphasic sharp and slow wave complexes (*figure 1*). An MRI scan of the brain disclosed posteriorly predominant, white matter involvement *(figure 2)*. SSPE was diagnosed, based on elevated serum and cerebrospinal IgG measles titers, 5.1 RU/mL (normal: 0-1.1 RU/mL) and 7.1 RU/mL (normal: 0-1.1 RU/mL), respectively.

The patient was placed on treatment with interferon beta, inosiplex and clonazepam, without any improvement.

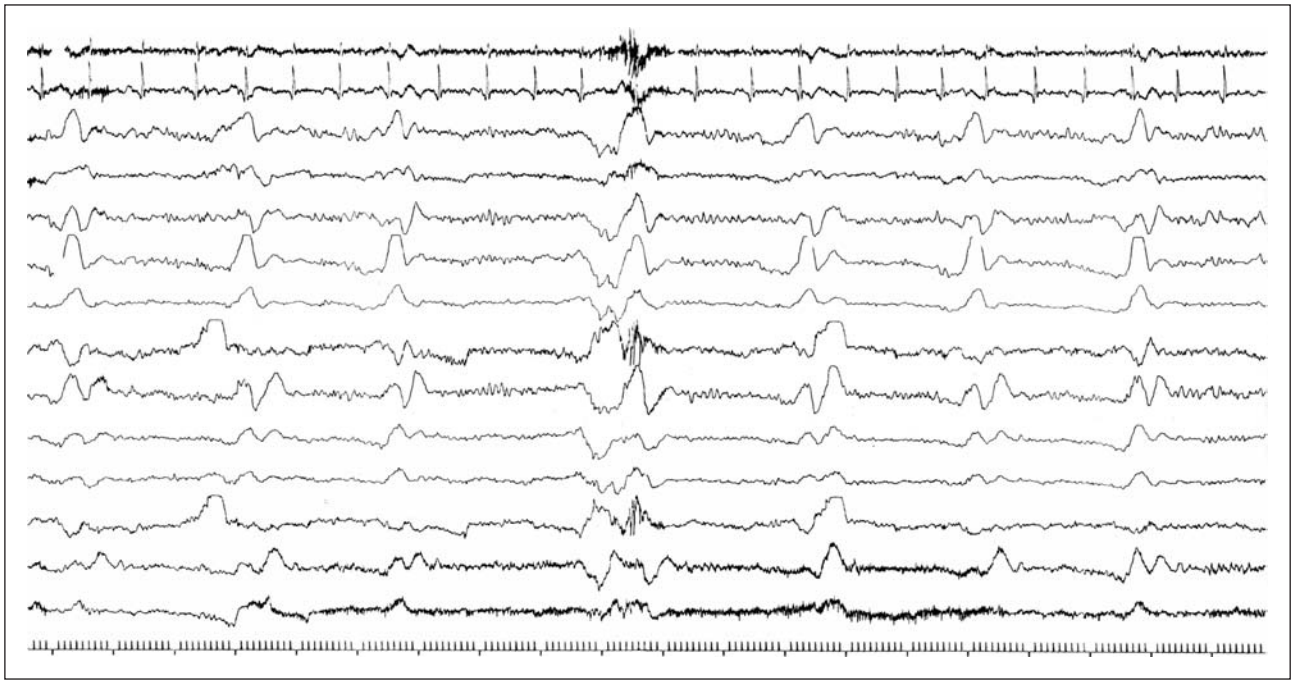

Figure 1. EEG showing a normal background activity, interspersed with periodic, bilateral, high voltage polyphasic sharp and slow wave complexes.

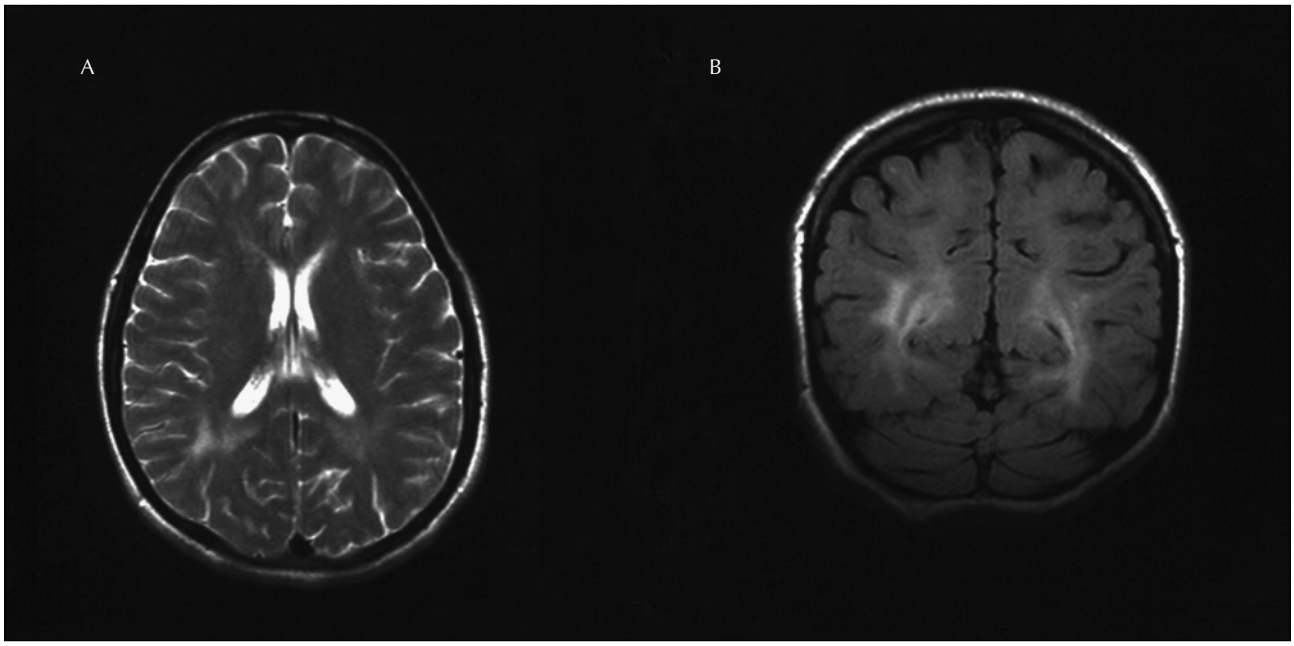

Figure 2. MRI scan of the brain, showing white matter involvement.

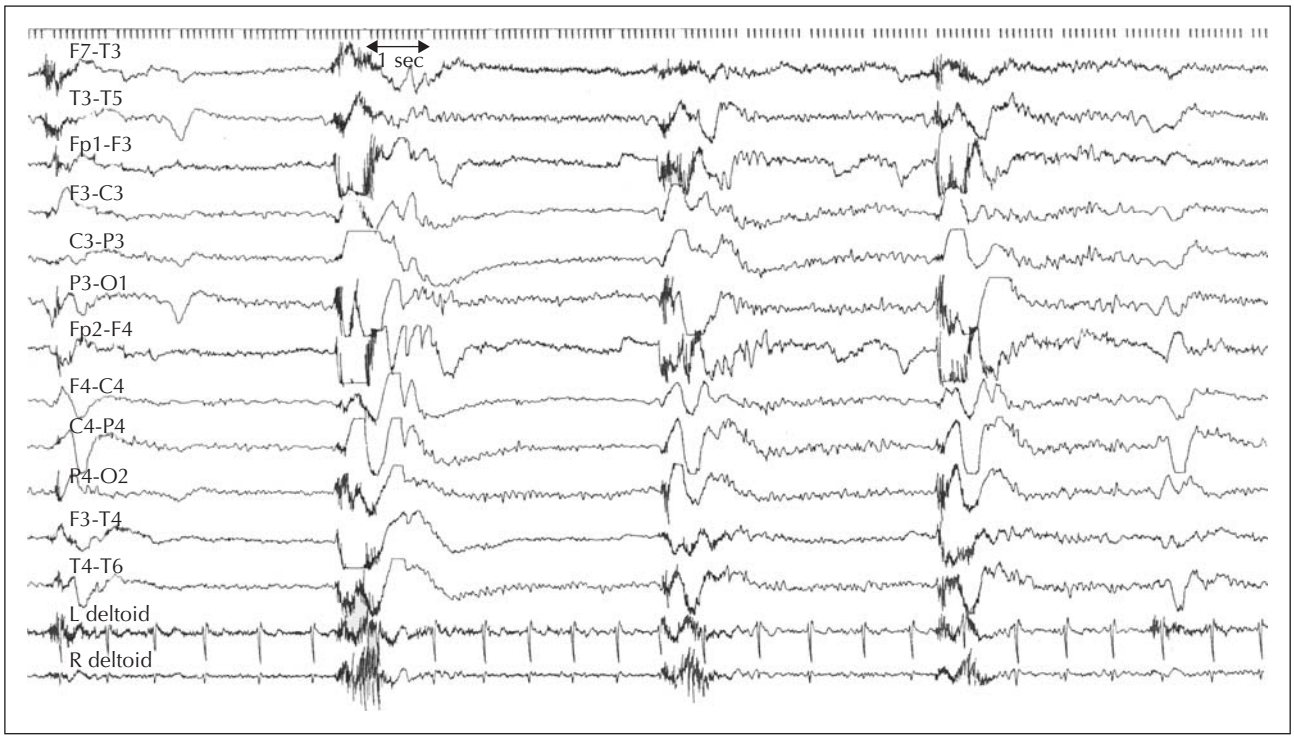

Figure 3. EMG recording of involuntary movements associated with periodic EEG complexes (L: left, R: right).

She decided to discontinue this treatment and to try carbamazepine, 200 mg twice daily, on the advice of a patient with epilepsy. The abnormal posturing and involuntary movements disappeared dramatically and she could walk without assistance. The plasma carbamazepine concentration was 7.79 mg/mL.

The patient was first seen in our outpatient clinic three years after the initial diagnosis. She had tapered carbamazepine in order to demonstrate her disability. The neurological examination revealed infrequent involuntary movements of the neck and arms, a mild hypertonia and hyperreflexia. The patient had a score of 17/30 points on mini-mental state examination (MMSE), suggesting a mild cognitive decline. A repeat EEG confirmed the periodic, bilateral, high voltage polyphasic sharp and slow wave complexes; simultaneous electromyographic recording on deltoids showed involuntary muscle contractions associated with periodic EEG complexes lasting 0.5 to 1 second *(figure 3)*.

To test the beneficial effect of carbamazepine on the involuntary movements, we hospitalized the patient and obtained informed consent for discontinuing carbamazepine and videoing her for the demonstration of the involuntary movements. Carbamazepine was discontinued by tapering over three days. Involuntary movements reappeared when the plasma concentration fell to 1.96 mg/mL; no withdrawal seizure was anticipated. The movements disappeared four days after the reintroduction of carbamazepine, when the plasma concentration had reached 7.01 mg/mL.

Discussion

The diagnosis of SSPE can be reliably established if three of the following criteria are met: (1) progressive, subacute mental deterioration with typical signs such as myoclonus, (2) periodic, stereotyped, high voltage discharges on EEG, (3) raised gammaglobulin or oligoclonal patterns in cerebrospinal fluid, (4) raised titers of measles antibodies in serum and/or cerebrospinal fluid, and (5) brain biopsy suggestive of panencephalitis (Garg 2002). Our patient met the first four diagnostic criteria for SSPE, so brain biopsy was not required for diagnosis. The condition of the patient before the administration of carbamazepine was considered as stage II, with mental-behavioral deterioration, frequent myoclonic contractions, and drop spells rendering her unable to walk independently (Gascon 1993).

The involuntary movements are the prominent disabling symptom of patients with SSPE. They have been usually described as myoclonus, but other descriptive terms are also proposed, based on phenomenological and electrophysiological investigations. Westmoreland *et al.* (1979) described the involuntary movements of their two patients as "motor spasms". Oga *et al.* (2000) reported a patient with abrupt onset, stereotyped, dystonic posturing, which

they classified as "periodic dystonic myoclonus". Ondo and Verma (2002) described a patient with frequent "paroxysmal dystonic posturing", which improved markedly when she was placed on carbamazepine. The involuntary movements of our patient lasted about 0.5 to 1 second, a duration which can be considered very long for typical forms of myoclonus. So, we could describe them more accurately as "dystonic myoclonus".

The effect of carbamazepine on the myoclonus in SSPE is anecdotally reported and controversial. The treatment with carbamazepine was accompanied by a dramatic improvement in three patients with myoclonus as reported by Hayashi *et al.* (1996), in a patient with craniocervical myoclonus as reported by Vela *et al.* (1997), and in a patient with paroxysmal dystonia as reported by Ondo and Verma (2002). On the other hand, the patients decribed by Duman *et al.* (2004) and Berker *et al.* (2004) did not improve on carbamazepine.

Our patient with SSPE had disabling involuntary movements and treatment with interferon beta, isoprinosine and clonazepam did not control them. The beneficial effect of carbamazepine on the involuntary movements, discovered by chance by the patient herself, was demonstrated by the discontinuation and reintroduction of the drug. We suggest that carbamazepine is very effective in the symptomatic treatment of the involuntary movements in SSPE, although any beneficial effect in the long-term prognosis of SSPE is unlikely. □

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