

Letter to the Editor (Case report)

A successful outcome with valproic acid in a case of mania secondary to stroke of the right frontal lobe

Dear editor,

Despite a steady decline in its incidence over the last 50 years due to improvement in the treatment of diseases such as hypertension, diabetes mellitus and hypercholesterolemia, stroke continues to represent a major health problem. Stroke is the second leading cause of death worldwide (Lavados et al., 2007).

While depression is the most frequently occurring psychiatric disorder after stroke, secondary mania is considered an uncommon consequence and it is only reported anecdotally. Since the results published in the literature comprise only case reports and open label trials, there is no clear evidence regarding the most effective treatment for post-stroke mania at present (Wijeratne and Malhi, 2007).

In the present report, we describe a woman with post-stroke mania with successful outcome with valproic acid.

1. Case report

A 47-year-old Caucasian woman presented to our emergency department with a history of abnormal behavior during the last two weeks. She developed elated mood, irritability, motor excitement, increased rate of speech with racing thoughts and grandiose delusions. She also displayed insomnia, distractibility and had no insight into her illness.

She was evaluated with a structured clinical interview and no previous history of any psychiatric disorder, including mood or substance use disorders, could be evidenced. Her family psychiatric history was also unremarkable. Of relevance, the patient had a stroke three weeks before the onset of psychiatric symptoms. At the time of the stroke, she presented paresis of left limbs, but no behavioral symptom. She had a seven year history of chronic hypertension treated with enalapril (10 mg/day) and smoked 20 cigarettes per day. No other predisposing factor for stroke was noticed.

At admission, neurological examination revealed a mild left-sided limb weakness. She scored 27 out of 30 in the Folstein Mini-Mental State Examination. Laboratory work-up, including complete blood count, creatine kinase level, electrolytes, renal, liver and thyroid function tests, serology for syphilis and HIV, echocardiography, hemoculture and X-ray of thorax were unrevealing. Magnetic resonance scan showed an area at the right medial frontal lobe (1.2–1.8 cm) compatible with the recent stroke and few chronic ischemic lesions widespread throughout the white matter.

As she fulfilled clinical criteria for a manic episode according to DSM-IV-TR, and based on her clinical history and symptoms, the diagnosis of mania secondary to the stroke was hypothesized. She scored 39 out of 60 in the Young Mania Rating Scale (YMRS).

She was started on carbamazepine and the dose gradually increased up to 1200 mg/day (serum level of carbamazepine was 8.7 mg/ml). Haloperidol 2.0 mg/day was also introduced due to the presence of grandiose delusions and extreme hyperactivity. As after one month of treatment no significant clinical improvement was noticed, carbamazepine and haloperidol were withdrawn and valproic acid initiated. After two weeks of treatment with valproic acid 1500 mg/daily (serum level of valproic acid was 92.0 µg/ml), she improved notably, and the YMRS score dropped from 36 to 9.

During the follow-up period of twelve months, the patient maintained asymptomatic on a daily dose of 1500 mg of valproic acid with YMRS scoring five. Subsequent liver panels and ammonia were normal.

2. Discussion

The present case refers to an interesting condition that has been rarely reported after stroke events. Four reviews have analyzed the prevalence of post-stroke mania. Starkstein et al. (1988) and Dunne et al. (1986) identified only three cases among, respectively, series of 700 and 661 consecutive stroke patients. In a large community studies that investigated the prevalence of neuropsychiatric disorders after stroke, secondary mania was not observed. (House et al., 1991).

As a consequence of the paucity of post-stroke mania, it is difficult to determine precisely the clinical, demographic and prognostic features. Nevertheless, family history of mood disorders seems to be correlated with post-stroke mania (Wijeratne and Malhi, 2007). Furthermore it has been demonstrated significant correlation between post-stroke mania and right hemispheric lesions, especially involving right orbitofrontal and basotemporal cortices, the dorsomedial thalamic nucleus, and the head of the caudate nucleus, leading to dysfunction of the ventral limbic circuit (Chemerinski and Levine, 2006; Goyal et al., 2006; Wijeratne and Malhi, 2007).

A hypothesis that may explain the low prevalence of post-stroke mania is that dysfunction in more than one area of the right hemisphere is required for its development, in contrast with post-stroke depression. Imaging studies evidenced that the majority of patients with secondary mania demonstrated complicated mixed artery infarctions with lesions in the basal ganglia, frontal lobe, and temporal lobes (Goyal et al., 2006;

Wijeratne and Malhi, 2007). In line with these findings, our patient presented white-matter lesions besides the right frontal lobe lesion.

Furthermore, biochemical response of the two hemispheres to stroke may be different, as has been demonstrated by PET scan findings. Right hemisphere stroke produces an increase in serotonin receptor binding, which is not found following comparable left hemisphere strokes. If mania could be related to increased levels of serotonin in brain synapses, what it seems to occur in antidepressant-induced mania, this biochemical dysfunction secondary to right hemisphere stroke probably contributes to the development of manic episodes (Robinson, 1997; Goyal et al., 2006). Thus the pharmacological action on the serotonin system could explain why mood stabilizing drugs can be effective in this clinical context.

For the treatment of this condition, some drugs including olanzapine, lithium, carbamazepine and acid valproic have been tried with variable or no response (Robinson, 1997; Goyal et al., 2006; Wijeratne and Malhi, 2007). In our case, a successful outcome was achieved with valproic acid.

Concluding, anticonvulsant mood stabilizers may be superior to lithium or atypical antipsychotics in the treatment of secondary mania, and given the propensity for seizures in the post-stroke period, mood stabilizing anticonvulsants may be the agents of choice.

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