STATUS EPILEPTICUS INDUCED BY HYPONATREMIA AS AN ADVERSE REACTION TO OXCARBAZEPINE – CASE REPORT

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ABSTRACT

We present a case of status epilepticus induced by hyponatremia as an adverse reaction to an antiepileptic drug. A 60 years old female was admitted to our department for partial seizures cluster activity with secondary generalization. The patient had a history of surgery for cerebral cavernoma with symptomatic epilepsy on treatment with levetiracetam and oxcarbazepine daily. Laboratory results revealed severe hyponatremia and hypokalemia. Thiopental induced coma under EEG monitoring stopped the seizure clusters. Metabolic disorders were taking in consideration and were excluded by appropriate investigations. As there were no other causes of hyponatremia, we concluded that it was an adverse event to oxcarbazepine. After the withdrawal of oxcarbazepine, the neurological status improved, with no seizures and normalization of electrolytes values confirming the hypothesis. This report illustrates a relatively uncommon adverse effect to oxcarbazepine as confirmed in the literature.

Key words: status epilepticus; hyponatremia; oxcarbazepine

INTRODUCTION

Epilepsy is considered to be the third most common disorder, after stroke and dementia, affecting old adults (1). Due to this fact, the presence of physiological changes, co-morbidities, concomitant treatments in the elderly increase the risk of drug interaction and adverse events, especially for the old antiepileptic drugs.

CASE REPORT

We present the case of a 60 years old woman, admitted in the Neurology Department for repeated focal seizures with secondary generalization resembling a cluster seizures activity. The patient had a history of operated right frontal cavernoma (Fig. 3) from which she developed a focal epilepsy with secondary generalized seizures. She was treated with levetiracetam 1,000 mg daily and oxcarbazepine 900 mg daily. The general examination showed an obese patient with a BMI of 36.5 kg/sqm, hirsutism, Cushing facies and right frontotemporal scar. There were no abnormal clinical features in the examination of the cardiorespiratory systems (BP – 140/70 mmHg; HR-70bpm, sinus rhythm). The neurological examination at admission showed a stuporous state with partial cluster seizures sometimes complicated with secondary generalization, left hemiplegia with left central facial palsy; brisk reflexes on the left side with plantar extension sign. Just after the after admission, the patient entered in *status epilepticus* refractory to treatment which implied for general anesthesia with Thiopental 20 mg/kg bolus followed by 5 mg/kg/h for 24 hours in continuous perfusion; valproic acid i.v. bolus of 25 mg/kgc/30 min, followed by 100 mg/h for 24 hours;

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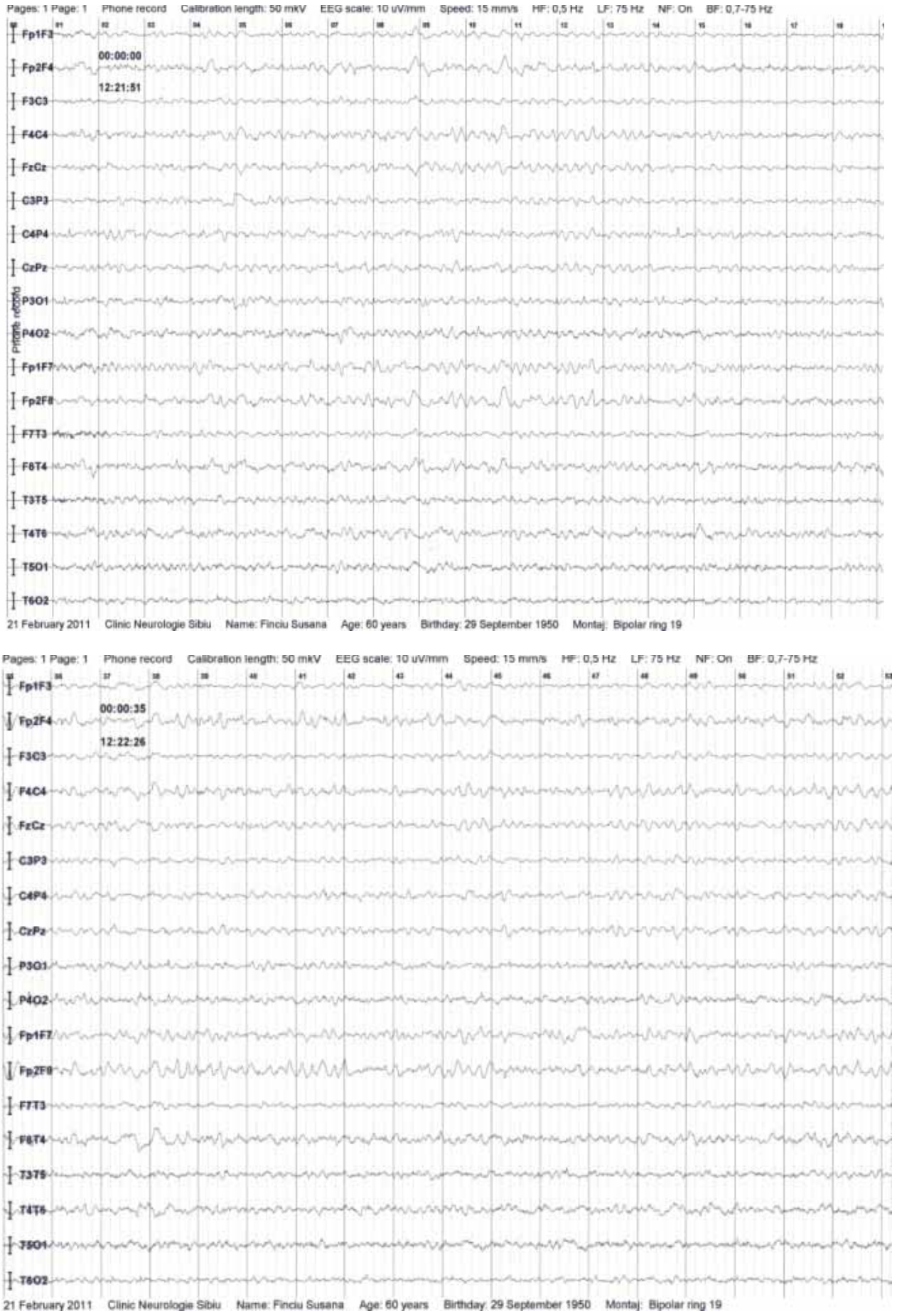


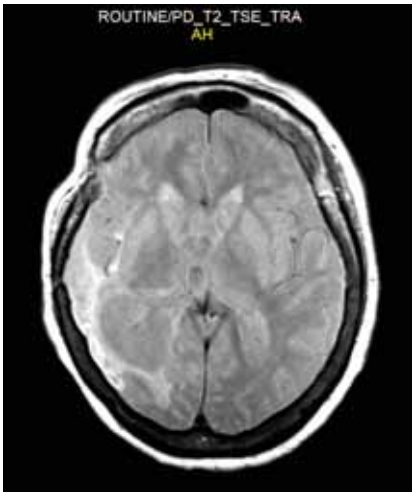
FIGURE 1, 2. **Interictal EEG** *Theta activity (5-6 Hz) with hyper voltage waves on right frontal derivations*

After status epilepticus was resolved, the antiepileptic drugs given were valproic acid i.v. 1 mg/kgc/h associated with levetiracetam 2 x 500 mg on nasogastric tube. Associated medication was continued with Midazolam, Mannitol, Glucose, KCl and NaCl perfusions, B1 and B6 vitamins.

The laboratory findings showed a low serum sodium of 125 mmol/L, low potassium of 2.3 mEq/L, serum glucose – 69 mg/dL, all endocrine markers (TSH, FT4, ADH, Cortisole) were found within normal ranges and a diuresis of 3500 ml/24h.

A 19 derivation video-EEG was performed showing a theta activity (5-6 c/sec) on right frontal derivations corresponding to the lesion site (Fig. 1 and 2). The cranial CT scan showed no acute intracranial pathology, right frontal and temporal postoperative area. The head MRI revealed a temporal postoperative scar, enlarged, asymmetrical lateral ventricles with cortical atrophy (Fig. 3 and 4). Chest radiography showed a transversally enlarged heart, bilateral diminished pulmonary transparency. Diagnosis: Refractory status epilepticus; right frontal cavernoma operated with left hemiplegia, hyponatremia, hypokalemia, possible syndrome of inappropriate antidiuretic hormone secretion (SIADH). Later SIADH was ruled out on biochemical and clinical grounds (normal osmolarity, euvolemia, no edema or natriuresis). The suggested etiology of hyponatremia, which in our opinion caused and maintained the cluster seizures and later the status epilepticus could have been the oxcarbazepine therapy.

After oxcarbazepine was withdrawn from the therapy scheme, the evolution was favorable, with no seizures activities and discharge after 10 days with normal electrolyte values. Control biochemistry was normal and the EEG showed intermittent theta pattern in the frontal and temporal derivation. The patient continued the oral therapy with levetiracetam and valproic acid, free of seizures.



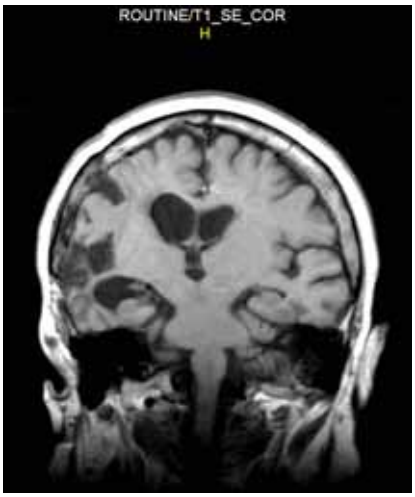


FIGURE 3, 4*. T2 axial and T1 coronal MRI showing a postoperative scar for right fronto-temporal cavernoma, enlarged asymmetrical lateral ventricles and cortical atrophy*

DISCUSSIONS

Recent studies showed that carbamazepine can lead to hyponatremia in patients with neurological disorders with a frequency varying from 4.8 to 40% (2). Oxcarbazepine, which is structurally related to carbamazepine, has shown similar hyponatremic effects, but whether hyponatremia occurs more often than with carbamazepine is not yet clear (3). A study of 97 oxcarbazepine – treated and 451 carbamazepine – treated patients with epilepsy using cross – section and follow-up studies (4) showed that the frequency of hyponatremia (Na^+<< 134 mEq/L) was 29.9% among oxcarbazepine – treated patients and 13.5% among carbamazepine – treated patients. Hyponatremia (Na^+ << 128 mEq/L) was severe in 12.4% of those treated with oxcarbazepine and 2.8% of the patients under carbamazepine therapy. In our case report the hyponatremia was severe, but maintained a seizure cluster activity which led to status epilepticus necessitating induced coma. Age is suspected to be a risk factor in developing hyponatremia during oxcarbazepine treatment and the elderly patients are more prone to develop this side effect, but this is still controversial (4). Paliwal (5) finds that hyponatremia was induced in 0.4% of children with less than 17 years comparative with 3.8% of older patients (aged 18 – 64 years). Other risk factors include the multiple association of antiepileptic drugs (5), high doses of oxcarbazepine and association with loop diuretics and selective serotonin reuptake inhibitors (1,2).

CONCLUSION

The treatment with oxcarbazepine should be considered with caution in elderly patients with

epilepsy, who are more susceptible to hyponatremia because of the impaired ability of maintaining the homeostasis of water and sodium. Although hepatically metabolized, oxcarbazepine is not a major inducer of hepatic enzymes as carbamazepine is, but hyponatremia is seen more frequent particularly in older adults with co-morbidities and concomitant medication.

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