



## Case Report

# Carbamazepine induced central hypothyroidism in a patient of focal seizures due to underlying porencephaly left frontal lobe and hippocampal atrophy

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## ABSTRACT

A case of central hypothyroidism, following controlled-release carbamazepine (CBZ-CR) monotherapy for focal seizure prophylaxis. A 19 years old woman, presented to the neurology department with history of three episodes of sudden onset, abnormal body movements during sleep. Patient was diagnosed as a case of focal seizures with secondary generalization and was prescribed tablet CBZ-CR 300 mg twice a day for seizure prophylaxis. 3 months later patient presented with complaints of facial hair growth and menstrual irregularities. The patient was seizure free and was continuing with the treatment. Blood biochemistry parameters indicated central hypothyroidism. According to World Health Organization Uppsala monitoring Centre (WHO-UMC) causality assessment, she was classified as 'possible' for carbamazepine-induced central hypothyroidism. Carbamazepine was discontinued. She was switched to tablet levetiracetam 500 mg twice daily, thyroxine 25 microgram once daily and clobazam 10 mg at bedtime.

**Conclusion:** Thyroid function tests should be monitored in patients receiving carbamazepine therapy.

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## 1. Introduction

'Seizure' denotes brief alteration of behavior due to the abnormal, synchronous and rhythmic firing of brain neurons. Antiseizure drugs are administered orally for prevention of seizure recurrence.<sup>1</sup>

Carbamazepine is widely used for focal, focal with secondary generalization tonic-clonic seizures.<sup>2</sup> It blocks voltage-gated sodium channels, responsible for the rising phase of neuronal action potentials.<sup>2</sup> Common adverse effects are drowsiness, vertigo, diplopia, blurred vision, increased seizure frequency, nausea, vomiting, aplastic anemia, agranulocytosis, hypersensitivity reactions and water retention.<sup>1</sup>

This is a case of carbamazepine induced central hypothyroidism. Central hypothyroidism is defined as reduced thyroid hormone production resulting from deficient stimulation of a normal thyroid gland by

thyrotropin (TSH).<sup>3,4</sup>

Carbamazepine has been reported to decrease the serum concentration of thyroid hormones.<sup>5</sup> Antiepileptic medications cause subclinical hypothyroidism.<sup>6</sup>

Carbamazepine leads to low T4, normal T3 and TSH, due to its hepatic microsomal enzyme induction leading to increased metabolism of thyroid hormones.<sup>3,7,8</sup>

## 2. Case

A 19 years old woman, study participant for post-graduate academic thesis. The patient visited neurology OPD with complaints of three episodes of abnormal body movements with teeth clenching and loss of consciousness. Each episode lasted for 3 to 5 minutes. There was postictal confusion. All the episodes occurred during sleep without any aura. No family history of seizures was there. In MRI of brain left hippocampal atrophy and porencephaly left frontal lobe was seen (Figure 1). The EEG showed abnormal awake pattern, indicating structural lesion in the brain.

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**Fig. 1:** MRI showing porencephaly left frontal lobe and left hippocampal atrophy.

Routine blood investigations were within normal limits. The patient was diagnosed as a case of focal seizures with secondary generalization. Patient had no history of drug or food allergy. She was randomly allocated to CBZ-CR 300 mg orally twice daily arm. Next morning, somnolence with dizziness was reported. She was advised to continue the treatment.

At 1<sup>st</sup> month follow-up she was seizure free, without any complaints. Blood biochemistry revealed normal results.

At 3<sup>rd</sup> month follow up she complained about facial hair growth and oligomenorrhea. Uniform hair growth on both the cheeks and under the chin was seen (Figure 2).

Thyroid function tests; serum total T3 level was low normal 95.53 nanogram/dl (normal range 86-192 ng/dl) serum total T4 was low 4.30 microgram/dl (normal range 5.5-11.1  $\mu$ g/dl)

TSH was normal 3.25  $\mu$ IU/ml (normal range 0.51-4.94 $\mu$ IU/ml).

Other pituitary hormones viz. prolactin (7.3 ng/ml), FSH (4.9 mIU/ml), LH (4.31 mIU/ml) and cortisol (12.65 microgram/dl) were within normal limits.

Liver and kidney function tests were within normal limits.

The patient was diagnosed as a case of central hypothyroidism secondary to carbamazepine therapy.

She was switched to;

Tablet levetiracetam 500 mg twice daily.

Tablet clobazam 10 mg once at bedtime.

Tablet ethinyl estradiol 0.035 mg + cyproterone acetate 2 mg once daily cyclic therapy (21/30 days).

Tablet spironolactone 100 mg once daily.



**Fig. 2:** Facial hair growth due to carbamazepine induced central hypothyroidism.

Tablet thyroxine 25  $\mu$ g once daily morning.

According to the World Health Organization Uppsala monitoring Centre (WHO-UMC) causality assessment system the case was classified as 'possible' for carbamazepine-induced central hypothyroidism. Although it is a rare adverse effect, but it is imperative to continuously monitor the patients, so that adverse events may be reported.

### 3. Discussion

The literature shows cases of subclinical hypothyroidism due to carbamazepine use. In this case a 19 years old female having new onset focal seizures with secondary generalization have developed abnormal facial hair growth and irregular menses. Our case was classified as drug induced central hypothyroidism.

Aanderud et al.<sup>7</sup> reported that serum T4 and T3 concentrations were significantly reduced after 3 weeks of CBZ intake as compared to those at baseline. Serum TSH concentrations were unchanged.<sup>7</sup>

Isojärvi et al.<sup>8</sup> reported that serum T4 and T3 concentrations were significantly lower ( $p < 0.001$ ) in the CBZ group compared to control group. No statistically significant differences were found in the serum TSH concentrations between these two groups. All the patients remained clinically euthyroid.<sup>8</sup>

Miller et al.<sup>3</sup> reported three children (2 female and 1 male) receiving oxcarbazepine developed central hypothyroidism. They had low free T4 levels but normal TSH levels.<sup>3</sup>

Simko et al.<sup>5</sup> reported that there was a significant ( $p < 0.001$ ) decrease in total T4, starting from the first week of treatment and remained stable afterwards. During CBZ

treatment, mild increase in TSH was reported ( $p=0.073$ ) but it never surpassed the normal range. They recommended that, CBZ may be substituted by an anticonvulsant without enzyme-inducing property.<sup>5</sup>

Meta-analysis by Zhang et al.<sup>9</sup> suggested that use of CBZ was associated with decrease of T4 and increase of TSH levels among patients with epilepsy.<sup>9</sup>

#### 4. Conclusion

It is necessary to carefully monitor as well as educate the patient for adverse events after initiating therapy with any drug. Considering the possibility of drug induced hypothyroidism, it is pertinent to investigate thyroid functions before initiating CBZ therapy and follow-up regularly. Patients with subclinical hypothyroidism should not be treated with CBZ.

#### 5. Conflicts of Interest

All contributing authors declare no conflicts of interest.

#### 6. Source of Funding

None.

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