

Carbamazepine-induced hypertension: A rare case

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ABSTRACT

A 74-year-old female with trigeminal neuralgia developed hypertension after the initiation of carbamazepine therapy. The time sequence of start of the suspected drug and onset of hypertension are consistent with the diagnosis. The hypertension did not resolve with antihypertensive therapy or dose reduction of carbamazepine. Patient recovered after the carbamazepine therapy was discontinued. The positive rechallenge and positive dechallenge showed association of carbamazepine therapy with hypertension as its adverse effect. This is a rare case that we report of carbamazepine-induced hypertension and this report may act as alerting mechanism to the health care professionals especially neurologists.

Key words: Carbamazepine, hypertension, trigeminal neuralgia

INTRODUCTION

The trigeminal neuralgia is defined as sudden, usually unilateral, severe, brief, stabbing, recurrent episodes of pain in the distribution of one or more branches of the trigeminal nerve (fifth cranial nerve).^[1] In 80-90% of cases, it is thought to be caused by compression of the trigeminal nerve by a loop of artery or vein.^[2] The annual incidence worldwide is 4 to 5 in 100,000.^[3] Women are affected twice than men. The incidence increases with age and is rare in people younger than 40 years of age.^[2]

The drug of choice for trigeminal neuralgia is carbamazepine.^[2,4] Most common adverse effects observed with carbamazepine are drowsiness, unsteadiness, constipation, nausea, and

vomiting. There are various side effects related to different systems.^[4] It is also reported to cause hypertension;^[4,5] however, the frequency of occurrence is rare ($\geq 1/10,000$ to $< 1/1,000$).^[5]

CASE REPORT

A 74-year-old female presented to a private practitioner with complaint of facial pain on the left side. On examination her blood pressure (B.P) was 117/80 mmHg. Her dental examination was normal and based on the symptoms a provisional diagnosis of trigeminal neuralgia was made. She had no significant past medical or family history of similar condition. The patient was prescribed tablet carbamazepine 300 mg tablet OD. After 2 days, she complained of headache, restlessness and on examination B.P was found to be 290/110 mmHg. There was no previous history of hypertension. The drug was discontinued and the B.P. returned to 120/78 mmHg.

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As the pain was persisting, she presented to the neurology OPD of the institute with complaint of left side facial pain and the diagnosis was confirmed as trigeminal neuralgia. The baseline B.P. was 118/80 mmHg. The patient was started with carbamazepine 50 mg tablet BD and was gradually titrated to 200 mg BD. The MRI findings confirmed the diagnosis of trigeminal neuralgia. On examination, her B.P. was 180/100 mmHg and there were no features suggestive of hypertensive encephalopathy. She was started with tablet telmisartan/hydrochlorothiazide and carbamazepine was continued. She was advised to get thyroid profile, random blood sugar and lipid profile done, all of which were within normal range. She presented after 4 days with severe nausea, vomiting and dizziness with persisting constipation. Home B.P. records were not done. Her facial pain had recovered. The B.P. was 146/80 mmHg. The dose of carbamazepine was reduced to 100 mg BD and rest all the medicines were continuing. She was also prescribed tablet betahistine. The ECG and fundus examination were normal, biochemistry reports revealed low uric acid 2.3 (2.5-6.2 mg/dl); low serum sodium 119 mg/dl (135-155); low chloride 96 mmol/l (98-107); high total protein 9.3 g/dl (6.3-8.2); and high serum globulin 4.3 g/dl (2.5-3.5).

Next day the patient was admitted to a private hospital with complaints of severe headache, epigastric pain and vomiting. On examination B.P. was 180/99 mmHg. All her medicines were stopped and she was managed symptomatically. The patient was discharged in satisfactory condition. The B.P. records were normal and the patient is off all the antihypertensive treatment. The patient is stable now [Table 1]. The trigeminal neuralgia resolved after the carbamazepine was stopped. No other treatment modality was used.

Meanwhile, based on literature search and detailed review of the patient's medical and family history, carbamazepine was suspected to be the causal agent for this adverse reaction as there was no underlying cardiovascular disease. Sudden shoot

of B.P. after oral carbamazepine high dose; and non-resolution of hypertension despite anti-hypertensive therapy confirmed that hypertension was induced by oral carbamazepine therapy as it resolved only after carbamazepine discontinuation.

A causal association between hypertension and carbamazepine was assessed by World Health Organization (WHO) probability method and Naranjo's adverse drug reaction probability scale.^[6,7] The WHO probability method and Naranjo's Adverse Drug Reaction Probability Scale showed "certain" and "definite" (Naranjo's score 10) association, respectively. As per modified Hartwig and Siegel scale, the severity of the reaction was "moderate: Level 4b".^[8]

DISCUSSION

Literature search was conducted which showed six reports on carbamazepine-induced hypertension from various countries.^[9-14] All the cases had patients who developed hypertension during carbamazepine treatment which resolved on discontinuation. To the best of our knowledge, this is the first report of carbamazepine-induced hypertension from India.

Bo *et al.* discussed the possible role of anti-diuretic hormone in the production of this infrequent side effect.^[9] The possible mechanism as to why the antihypertensive therapy is unresponsive as explained by Downey *et al.* is that antiepileptic agents could induce drug-metabolizing system and thus reduce the effects of antihypertensive medications.^[10] Another author stated that carbamazepine induces the cytochrome P450, which catalyze the metabolism of most of the antihypertensive used.^[13]

The time sequence of start of the suspected drug and onset of hypertension are consistent with the diagnosis. The rechallenge by another physician led to raised blood pressure, not successfully managed by the appropriate treatment. The

Table 1: Sequence of events summary

| Day | Events | B.P Records | Management |
|-------------|--|------------------------|--|
| Day 1 | Left facial pain | Baseline: 117/80 mm Hg | (presented at clinic) Carbamazepine 300 mg OD started |
| Day 3 | Headache, restlessness | 290/110 mm Hg | Ongoing Carbamazepine 300 mg OD |
| Day 4 | For follow-up | 120/78 mm Hg | After drug withdrawal |
| Rechallenge | | | |
| Day 7 | Left facial pain | Baseline: 118/80 mm Hg | (presented at institute OPD) Carbamazepine started at 50 mg and titrated to 200 mg BD |
| Day 18 | For follow-up: Headache, restlessness | 180/100 mm Hg | Ongoing Carbamazepine 200 mg BD |
| Day 23 | For follow-up: With test reports | 146/80 mm Hg | Ongoing Carbamazepine 100 mg BD + Telmisartan and hydrochlorothiazide combination 40/12.5 mg |
| Day 24 | At emergency ward: Restlessness, shooting headache vomiting, nausea, heartburn | 180/99 mm Hg | (at private hospital emergency ward) Drug withdrawn and symptomatic management |
| Day 25 | Before discharge | 122/80 mm Hg | After drug withdrawal |

OD=Once a day, OPD=Out patient department

symptoms recovered after withdrawal of the suspected drug and the patient did not develop hypertension further owing to cessation of carbamazepine which is suggestive of possible association between carbamazepine and hypertension.

CONCLUSION

Carbamazepine-induced hypertension is rare and this report may act as alerting mechanism to the health care professionals. Neurologists, doctors and experts in various fields, pharmacist and patients need to be aware of the potential of carbamazepine-induced hypertension.

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Conflicts of interest

There are no conflicts of interest.

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