



Letter to Editor

Carbamazepine-Induced Peripheral Angioedema: Case Report of a Rare Adverse Drug Reaction

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Dear Editor,

Carbamazepine is used for the treatment of epilepsy, neuralgias, and mood disorders. It acts by blocking voltage-dependent sodium channels, thus inhibiting repetitive neuronal firing.^[1] It is known to cause cutaneous drug reactions like exanthems, rashes, petechiae, or erythema.^[2] The prevalence of carbamazepine-induced cutaneous drug reactions has been estimated to be up to 3%.^[3] Although it can cause a plethora of cutaneous drug reactions, angioedema has been rarely reported.^[2,4] Angioedema involves vascular leakage in the dermis and subcutis mediated by immunoglobulin-E and bradykinins.^[2] In severe cases, angioedema involving the laryngeal mucosa can be life-threatening due to respiratory obstruction. Here, we present a rare case of carbamazepine-induced peripheral angioedema.

A 28-year-old female was brought to the psychiatry outpatient department with complaints of aggressive, abusive behavior, increased talks, tall claims, and decreased sleep for the past several months. She had numerous episodes of similar complaints in the past 12 years. She had no prior history of any dermatological, hematological, or immunological disorder. Considering her presentation and illness history, the diagnosis was made as bipolar type I disorder, current episode manic, with psychotic symptoms as per the International Classification of Diseases 11th Revision (ICD-11). In the recent episode, the symptoms were exacerbated due to poor treatment adherence. In view of a significant documented leukocytosis with lithium in the past treatment history, she was started on carbamazepine at 400 mg dose. Along with mood stabilizer, aripiprazole was started at 10mg and gradually optimized to 15 mg. Considering the initial good tolerability, the dose of carbamazepine was hiked to 600 mg on the fourth day. From the fifth day onwards, the patient started complaining of swelling of both legs and mild swelling of hands, which significantly increased on the sixth day [Image 1]. On physical examination, bilateral pitting pedal and hand edema were noted. All vital parameters were found normal. There were no signs of laryngeal edema. Blood investigations were sent that showed alanine aminotransferase 99 U/L, albumin 4 g/dL, bilirubin total 0.53 mg/dL, urea 25.3 mg/dL, creatinine 0.73 mg/dL, albumin globulin ratio 1.28, and sodium 140.4 mmol/L. Ultrasound abdomen was done to rule out any systemic cause of the edema which turned out to be normal. Thus, the systemic causes were ruled out. Considering the temporal relation with carbamazepine initiation and optimization and lack of any significant contributory physical cause, carbamazepine-induced angioedema was suspected. Carbamazepine was immediately stopped on the seventh day and the patient's vitals were regularly monitored, which were stable. The swelling gradually subsided on stopping carbamazepine and completely resolved after three days of stopping the medication [Image 2]. Aripiprazole was continued and was optimized to 30 mg. Considering persistent affective symptoms, lithium was restarted at 750

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Image 1: The swelling of the hand noted with carbamazepine.



Image 2: Resolution of swelling after stopping carbamazepine.

mg under close monitoring of leucocyte count. The patient started showing gradual improvement with no significant increase in leucocyte count this time.

Angioedema is a clinical condition that is characterized by localized swelling in the deeper layers of the skin and mucosa, generally acute in onset and lasting for several days. The condition is known to be caused by bradykinin and/or mast cell mediators, including histamine. Angioedema results from an increased permeability of blood vessels in the affected area leading to tissue swelling.^[5] Complications of acute laryngeal angioedema include dysphagia, respiratory distress, and death. In our case, fortunately, any of the severe symptoms of angioedema did not occur. As it developed abruptly after carbamazepine optimization, we could identify and withhold the offending agent quickly. Our patient was also tried on lithium and aripiprazole prior to starting carbamazepine. Applying Naranjo's algorithm for detecting adverse drug reactions, we could see that the event was temporally connected with carbamazepine optimization.^[6] The symptoms started when lithium had already been stopped for more than five days, thereby minimizing the risk of lithium exposure. Furthermore, while rare cases of angioedema have been reported previously with carbamazepine, it has not been reported with aripiprazole previously. Last, the symptoms gradually improved when carbamazepine was stopped. She

had no previous history of dermatological or immunological disorder. Hence, according to the World Health Organization causality monitoring system, we could grade this adverse effect as “probably/likely” caused by carbamazepine.^[7]

Angioedema can be life-threatening if not identified and managed quickly. Carbamazepine is commonly used in treatment-naïve bipolar and epilepsy patients even on an outpatient basis, which can lead to such devastating consequences if not identified early. This case report emphasizes this rare but life-threatening side effect of carbamazepine, which needs to be kept in mind while prescribing.

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