Non-Recurrence of Carbamazepine Induced Vitiligo after Rechallenge with Carbamazepine

Masoomeh Saeedloo, MD [1]
Seyed Vahid Shariat, MD[2]

1 Mental Health Research Center and Faculty of Medicine, Iran University of Medical Sciences, Tehran, Iran
2 Mental Health Research Center and Department of Psychiatry, Tehran Institute of Psychiatry-Faculty of Behavioral Sciences and Mental Health, Iran University of Medical Sciences, Tehran, Iran

Corresponding author:
Seyed Vahid Shariat, MD
Mental Health Research Center, Tehran Institute of Psychiatry-Faculty of Behavioral Sciences and Mental Health, Mansouri Lane, Niayesh Street, Sattarkhan Avenue, Tehran, Iran
Tel & fax: +982166506862
Email: vshariat@tums.ac.ir, vahid.shariat@gmail.com

Objective: Vitiligo is a rare side effect of carbamazepine whose exact mechanism is unknown. The aim of this report is to describe a single case of vitiligo induced by carbamazepine .
Methods: The case was a patient with Bipolar I disorder whose medications were changed from valproate to carbamazepine and who developed vitiligo after a short while. We followed the case for about four years when he was rechallenged with carbamazepine .
Results: When depigmentation occurred, we immediately discontinued carbamazepine after which the depigmented areas improved gradually. About three years later, he received carbamazepine again, but depigmentation did not recur.
Conclusion: Carbamazepine-induced vitiligo is not an absolute contraindication for the prescription of carbamazepine if other choices fail to respond or are not tolerated. The case has implications for the mechanism of medication induced vitiligo.

Key words: *vitiligo, carbamazepine, bipolar disorder*

Iran J Psychiatry 2013; 8:4: 201-203

Vitiligo is a psychologically disturbing skin disease that affects approximately 0.5% of the general population(1). Although the exact etiology of the illness is unknown, several hypotheses have been proposed for its pathogenesis, including autoimmune mechanisms and neural hypothesis(2). Drug-induced vitiligo is a rare side effect of several medications from different chemical and pharmacological classes(3). Carbamazepine is one of the medications associated with induction of vitiligo in few cases(3, 4). Carbamazepine is an antiepileptic drug frequently used in psychiatry as a mood stabilizer(5). It has been shown to have both antimanic and antidepressant effects in patients with bipolar disorder, and it is also able to prevent affective episodes in these patients(6). Carbamazepine may show a variety of side effects from milder and more common side effects like dizziness and ataxia to the rare occurrence of agranulocytosis and aplastic anemia(7). Vitiligo is one of the rare side effects of carbamazepine that has only been reported in a number of case reports. However, few data exists on the course of carbamazepine-induced vitiligo, and it is not known if it recurs after re-challenging the medication. Here, we report a patient with carbamazepine-induced vitiligo whose skin condition did not recur after re-challenge of carbamazepine three years later.

Case Report

The patient was a 34 -year -old male with a diagnosis of bipolar I disorder who was admitted to Iran Psychiatric Hospital with a manic episode with psychotic features in September 2007, and this was his first manic episode. He received sodium valproate as well as antipsychotic medications for the active phase treatment and was stabilized on 600 mg of valproate. In the post-discharge follow up, his manic symptoms were under control, but he complained of a debilitating tremor. The tremor was mainly of a postural type and was so severe that made eating, drinking and shaving very difficult for the patient. Propranolol was added and titrated up to 120 mg, but was not successful in controlling the tremor. Therefore, valproate was tapered and replaced with carbamazepine to a total dose of 800 mg/d.
Nearly one month later, areas of depigmentation appeared on the patient's face (Figure 1).

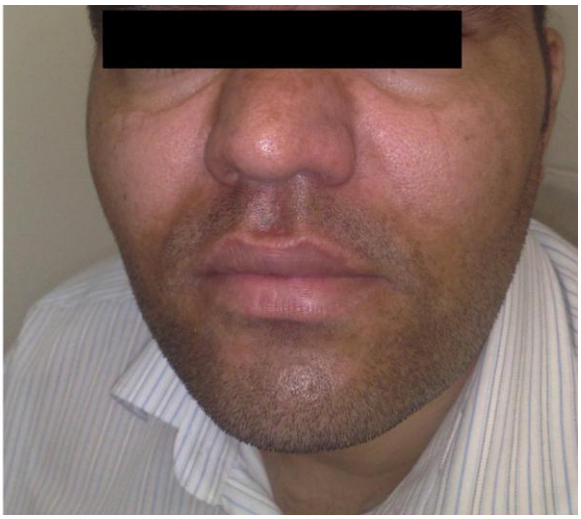

Figure 1: Depigmented areas on the face of the patient after carbamazepine use

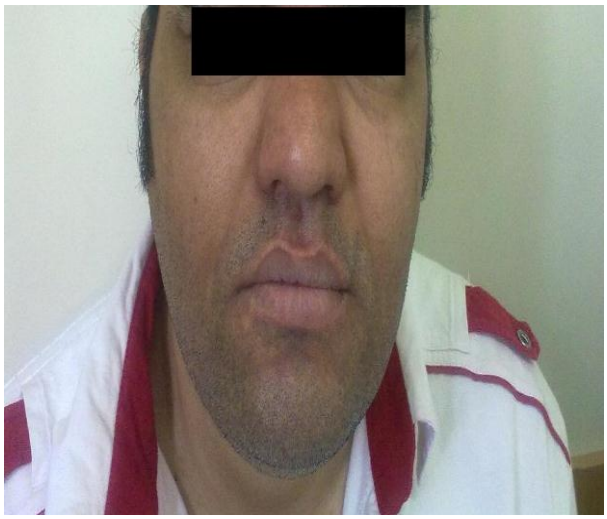

Figure 2: Reversal of the normal pigmentation after discontinuation of carbamazepine

Carbamazepine was discontinued and replaced with lithium. Although depigmentation decreased gradually in the next two months, it could still be observed in an attenuated form in a close inspection. However, an incapacitating and unmanageable tremor reappeared with lithium. Then, lithium was tapered to discontinuation and a combination of lamotrigine (up to 100 mg/d) and olanzapine (10 mg/d) was the next treatment choice. Despite a mild tremor, the patient remained well for the following 18 months when he was admitted for one week in March 2011 for an episode of methamphetamine-induced psychotic disorder.

After discharge, the patient was visited by a physician unaware of his history of vitiligo who decided to change the medications from lamotrigine and olanzapine to carbamazepine and aripiprazole. It seemed that the decision had been made to decrease the side effects of the drugs (weakness, dryness of mouth, and tremor). The patient continued to improve and vitiligo did not recur (or was not aggravated) after re-challenging the patient with carbamazepine for the following 6 months. Currently, the patient is receiving carbamazepine (800 mg/d) and aripiprazole (20 mg/d) and remains in remission and is trying to get a job (Figure 2).

Figure 1: Depigmented areas on the face of the patient after carbamazepine use

Figure 2: Reversal of the normal pigmentation after discontinuation of carbamazepine

Discussion

Few case reports of medication-induced vitiligo have reported the following mechanisms for this condition: Activation of T CD8+ cells against melanocytes, apoptosis of melanocytes as a direct effect of the drugs, and damage to sympathetic nerves(3). Although a single case cannot prove or rule out any of the proposed mechanisms, reviewing the history of this case could be informative. The reversibility of vitiligo in this case shows that the involved mechanism should not be a totally irreversible cellular change like apoptosis of melanocytes or permanent damage in sympathetic nerves at least in the early stages of medication-induced vitiligo. On the other hand, non-recurrence of vitiligo with re-challenge of carbamazepine suggests that some kind of immunity or desensitization has developed. The latter point is against the direct cytotoxic effects of medications on induction of vitiligo. Further studies are needed to elucidate the exact mechanism of medication-induced vitiligo.

We would like to emphasize that the patient also used other medications when the skin condition appeared. Therefore, it is theoretically possible that these medications (such as propranolol or antipsychotic drugs) would be related to vitiligo. However, the temporal relationship of vitiligo appearance and the used medication suggests that carbamazepine is the most probable culprit for inducing vitiligo. The other limitation of the current report is that we did not use additional methods to confirm the diagnosis, like skin biopsy or Wood's lamp examination. Because the patient did not show any other signs or symptoms of other autoimmune diseases, we did not perform the lab test to rule them out. Finally, we would like to suggest that the appearance of carbamazepine-induced vitiligo is not an absolute contraindication for the prescription of carbamazepine if other choices fail to respond or are not tolerated.

Acknowledgment

We would like to thank the patient that allowed us to report his case.

References

1. Taieb A, Picardo M. Clinical Practice. Vitiligo. N Engl J Med 2009; 360: 160-169.
2. Namazi MR. Phenytoin as a Novel Anti-Vitiligo Weapon. J Autoimmune Dis 2005; 2: 11.
3. Curzytek K, Pietowska J, Spiewak R. Drug-induced vitiligo: A meta-analysis of reported cases. J Physiol Pharmacol. 2007; 58 (Suppl 4: First International Conference "Medical Biology and Human Life"):66.
4. Yazidi A, Belagnaoui F Z, Benzekri L, K. S, Hassam B. Vitiligo au décours d'une érythrodermie induite par la carbamazépine (Tégrétol®). Les Nouvelles dermatologiques 1999; 18: 514-515.
5. Gitlin M, Frye MA. Maintenance Therapies in Bipolar Disorders. Bipolar disorders 2012; 14 Suppl 2: 51-65.
6. Ceron-Litvoc D, Soares BG, Geddes J, Litvoc J, de Lima MS. Comparison of Carbamazepine and Lithium in Treatment of Bipolar Disorder: A Systematic Review of Randomized Controlled Trials. Hum Psychopharmacol 2009; 24: 19-28.
7. Sadock BJ, Sadock VA, Ruiz P, Kaplan HI. Kaplan and Sadock's Comprehensive Textbook of Psychiatry. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2009.