Minocycline-induced transient depersonalization: A case report

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Abstract
Minocycline is a medication commonly used for the treatment of acne vulgaris. The central nervous system-induced side effects of minocycline include headaches, pseudotumor cerebri, ataxia, and vestibular dysfunction. Many minocycline-related side effects have been presented in the literature, however, reports of depersonalization symptoms induced by the medication are rare. We present the case of a 37-year-old female diagnosed with perioral dermatitis treated with minocycline, who within 1 week suffered from severe depersonalization symptoms. The pathophysiologic mechanism of depersonalization induced by minocycline is unclear but various hypotheses include hypersensitivity of the serotonin system, drug-related metabolic encephalopathy, substance-induced temporal disintegration, and panic-disorder-related etiology. Depersonalization is a potentially severe and important side effect of minocycline that should be documented, further investigated, and recognized by clinicians.

Keywords
Minocycline, depersonalization

Introduction
Minocycline is a second-generation semi-synthetic tetracycline derivative that is commonly used for the treatment of acne vulgaris due to its excellent lipophilic properties and penetration into the sebum. More recently, it has been studied for its use beyond its antimicrobial activity. Its anti-inflammatory and anti-apoptotic properties make it a potentially effective treatment for various conditions such as bullous dermatoses, rheumatoid arthritis, and inflammatory bowel disease. Its liposolubility and ability to cross the blood–brain barrier, in addition to newly recognized neuroprotection properties, have made it a topic of study in animal models for treatment of certain CNS diseases.¹ Furthermore, minocycline is being studied as an adjunctive treatment in psychiatric conditions such as mood disorders, schizophrenia, and addiction, which are mediated by oxidative stress, inflammation, and changes in glutamatergic pathways.²

As minocycline becomes more widely used, its side effects are being increasingly studied and reported in the literature. A double-blinded study by Fanning et al.³ discussed the incidence and types of side effects associated with minocycline. The most common side effects of minocycline were light-headedness, nausea, and vestibular symptoms (ataxia, vertigo, and dizziness). A review of literature by Somech et al.⁴ describe the severe adverse effects reported with minocycline use. These include drug-related lupus, serum sickness, hepatitis, pseudotumor cerebri (when used together with isotretinoin), hyperpigmentation, pulmonary side effects, and chronic interstitial nephritis. Depersonalization symptoms, however, were only seldom described in the literature in relation to the use of minocycline and are not well recognized by dermatologists, who prescribe this medication. Depersonalization is a disruption of self-awareness, characterized by feelings of disembodiment, emotional numbness, subjective recall, and derealization.³ The pathophysiologic mechanism of depersonalization induced by minocycline is not clear but involves various hypotheses including hypersensitivity of the serotonin system, drug-related metabolic encephalopathy, substance-induced temporal disintegration, and panic-disorder-related etiology.⁶ This case report is intended to describe a woman who experienced depersonalization symptoms when taking minocycline. As clinicians, it is important to recognize the signs of minocycline-induced depersonalization because it

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is documented in the literature as a strong harbinger for multiple suicide attempts in the affected individual.  

**Case report**

A 37-year-old female diagnosed with periorificial dermatitis was prescribed minocycline and topical metronidazole cream. At the time, her past medical history was only significant for asthma. The only other medications she was taking were Advair and Ventolin puffers. She had no documented or reported personal or family history of any psychiatric disorders, including depersonalization, depression, psychosis, and substance abuse.

Two days after starting minocycline, she started to experience depersonalization symptoms. She felt extremely disconnected and lost. She did not care about the matters that were normally important to her. She described feeling ‘out of this world’ and ‘out of her body’. She felt as though she was ‘floating’ and looking down on herself from above. She knew that these symptoms weren’t normal and so she refrained from telling her family or friends. She even described thinking that she could cut her finger off and not feel it. Her family noticed a significant change in her personality.

She took the medication for a total of 3 weeks. She read forums online describing a similar experience with minocycline and decided to stop the medication. She felt her normal self within 2–3 days of stopping minocycline. She returned to our clinic, where her physical exam, including a complete neurological exam and vital signs were normal. She was provided with an alternative treatment of topical tacrolimus for her dermatitis, which nearly resolved. The patient was offered to undergo a thorough psychiatric evaluation to further confirm the diagnosis and to exclude other comorbidities, but unfortunately, she declined a referral to a psychiatrist. A follow-up phone call confirmed the depersonalization symptoms have not returned, 1 month after the discontinuation of minocycline.

**Discussion**

The DSM-5’s fourth criteria that the ‘disturbance is not attributable to the physiological effects of a substance’ limits the diagnosis of depersonalization disorder in this patient. However, the patient successfully meets the other four criteria of the disorder, which include the following:

1. The presence of persistent or recurrent experiences of depersonalization: experience of unreality, detachment, or being an outside observer with respect to one’s thoughts, feelings, sensations, body, or actions.
2. During the depersonalization experiences, reality testing remains intact.
3. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
4. The disturbance is not better explained by another mental disorder.

Unfortunately, a drug screening and a psychiatric consult were not done as the patient felt it was not necessary since the symptoms resolved by the time we saw her in clinic. However, the patient’s reliability as a historian and the clear correlation between beginning and stopping the medication with the presence of the symptoms is highly suggestive that minocycline is related to the depersonalization symptoms of this patient.

One case of depersonalization induced by minocycline similar to the case described has been reported in the literature. A case report by Cohen et al. recounts the depersonalization symptoms experienced by a 24-year-old female after beginning treatment of minocycline for acne vulgaris. The symptoms began when she started the medication, disappeared when she stopped it, and reappeared when she tried it again.

Simeon et al. briefly list minocycline as a potential exacerbating factor of depersonalization disorder. Gump et al. report feelings of dissociation in a study of side effects associated with different dosage regimens of minocycline. However, depersonalization is not described as a side effect of minocycline in most medical references, including *Up to Date*.

The most common precipitants of depersonalization disorder are severe stress, depression, panic, marijuana, and hallucinogen use. Mood, anxiety, and personality disorders are frequently comorbid, but depersonalization can occur in the absence of another psychiatric disorder. Neurochemical findings have suggested a potential involvement of serotonergic, endogenous opioid, and glutamatergic NMDA pathways in the development of depersonalization disorder. Suppression of the fronto-limbic system, specifically the anterior insula, has also been proposed as an underlying mechanism of the disorder; however, the pathophysiology of dissociative disorder is still poorly understood and the mechanism by which minocycline may induce dissociative symptoms has not yet been established.

Dissociative symptoms are often troubling and can lead to serious consequences, such as suicide. Herein, it is important to continue to document the cases of minocycline-induced dissociative symptoms. More research is necessary in order to prove the relationship between minocycline and depersonalization symptoms and we hope that this case report will serve as a first step in the recognition of a possible serious side effect of this widely used drug.

**Informed consent**

The patient provided written consent for publication of the case report.

**Declaration of conflicting interests**

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