Received: 20 February 2020 | Revised: 28 May 2020 | Accepted: 31 May 2020

DOI: 10.1002/ccr3.3055

CASE REPORT

Clinical Case Reports Open Access WILEY

Naltrexone-induced drug eruption

Johannes Heck[1,2] | **Katharina Burda**[2,3] | **Thomas Hillemacher**[2,4] | **Stefan Bleich**[2] | **Dirk O. Stichtenoth**[1] | **Adrian Groh**[2]

[1]Institute for Clinical Pharmacology, Hannover Medical School, Hannover, Germany

[2]Center for Addiction Research (CARe), Department of Psychiatry, Social Psychiatry and Psychotherapy, Hannover Medical School, Hannover, Germany

[3]KRH Psychiatry Langenhagen, Langenhagen, Germany

[4]Department of Psychiatry and Psychotherapy, Paracelsus Medical University, Nuremberg, Germany

Correspondence
Johannes Heck, Institute for Clinical Pharmacology, Hannover Medical School, Carl-Neuberg-Str. 1, 30625 Hannover, Germany.
Email: heck.johannes@mh-hannover.de

Abstract

Treatment of alcohol dependence with oral naltrexone may elicit an urticarial rash and angioedema. Acute spontaneous urticaria and an allergic reaction to an excipient represent important differential diagnoses.

KEYWORDS

dermatology, pharmacology, psychiatry

1 | INTRODUCTION

A variety of substances are used for relapse prevention and to suppress craving in alcohol dependence. Naltrexone is a competitive μ-opioid receptor antagonist originally used to prevent relapse with opioids after detoxification.[1] Randomized controlled trials have also shown its positive effects on reducing alcohol consumption through inhibition of dopamine discharge in the mesocortical reward system.[2] Well-known adverse drug reactions of naltrexone include nausea, vomiting, irritability, and reversible elevation of serum liver transaminases.[3,4] A drug eruption is an immunologically mediated dose-independent reaction of the skin toward a certain drug.[5]

2 | CASE PRESENTATION

A 53-year-old woman admitted herself to our psychiatric day care unit with alcohol dependence (International Classification of Diseases 10th revision (ICD-10): F10.2) and a moderately severe episode of a recurrent depressive disorder (ICD-10: F33.1). Additionally, she suffered from nicotine dependence (ICD-10: F17.2), arterial hypertension (ICD-10: I10.90), and an Achilles tendinitis (ICD-10: M76.6). She was treated with venlafaxine SR (slow release) 75 mg/d, ibuprofen 600 mg/d, and a combined oral contraceptive containing ethinylestradiol. Oral naltrexone 50 mg/d was prescribed due to persistent craving toward alcohol. Six days after the initiation of treatment with naltrexone, the patient displayed a

sudden onset of wheals on her trunk, which were accompanied by intense pruritus. Furthermore, the patient developed an angioedema which involved both her upper and lower lip. Other parts of her body such as pharynx, larynx, eyelids, or digits were not affected by angioedema. Consequently, the patient was referred to the emergency department of an external hospital, where she was treated with prednisolone 30 mg/d and a topical H_1 antihistamine for three consecutive days. Importantly, naltrexone was stopped immediately. The comedication (venlafaxine, ibuprofen, oral contraceptive) was continued. The urticarial rash as well as the angioedema resolved entirely within four days and did not recur during follow-up.

3 | DISCUSSION

To the best of our knowledge, this is the first description of a serious cutaneous reaction following administration of oral naltrexone. In general, naltrexone is well tolerated under the standard dosage of 50 mg/d for achieving alcohol abstinence.[6] Yet, we observed a severe urticarial rash including angioedema, a complication which can be potentially life-threatening due to asphyxiation. Therefore, an immediate emergency treatment was initiated, which, in conjunction with cessation of naltrexone, led to a complete resolution of the cutaneous symptoms within four days. A comprehensive medication analysis using an electronic interaction database did not reveal clinically relevant pharmacokinetic or pharmacodynamic interactions between naltrexone and the other drugs our patient was treated with.[7] Thus, an unintentional intoxication appears unlikely. The time course observed indicates a causal relationship between the intake of naltrexone and the eruption of the urticarial rash and angioedema. To evaluate the likelihood of each drug administered to our patient with regard to her cutaneous symptoms, we applied the Naranjo adverse drug reaction probability scale (scale ranging from –4 to + 13, with higher scores indicating a higher probability).[8] The score for naltrexone was + 3, for ibuprofen was –1, for the oral contraceptive was –1, and for venlafaxine was –2, suggesting naltrexone as the primary offending agent. An alternative explanation for the cutaneous symptoms of our patient might be acute spontaneous urticaria, precipitated by the combined intake of alcohol, a non-steroidal antiinflammatory drug (ibuprofen) and an oral contraceptive.[9]

The clear temporal relationship between the start of treatment with naltrexone and the development of the cutaneous symptoms as well as the positive dechallenge reaction upon cessation of naltrexone lead us to the conclusion that our patient experienced a naltrexone-induced drug eruption. However, we cannot rule out an allergic reaction to an excipient of the naltrexone tablet such as iron oxide/oxide-hydroxide (E172).

ACKNOWLEDGMENTS

Published with written consent of the patient.

CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

JH and AG: writing the first draft of manuscript. KB, TH, SB, and DOS: commented on previous versions of the manuscript. All authors: read and approved the final manuscript.

ORCID

Johannes Heck https://orcid.org/0000-0002-5382-3014

REFERENCES

1. Gonzalez JP, Brogden RN. Naltrexone. A review of its pharmacodynamic and pharmacokinetic properties and therapeutic efficacy in the management of opioid dependence. *Drugs*. 1988;35:192-213.
2. Rösner S, Hackl-Herrwerth A, Leucht S, et al. Opioid antagonists for alcohol dependence. Cochrane Database of Systematic Reviews 2010, Issue 12. Art. No.: CD001867.
3. Park TW, Friedmann PD. Medications for addiction treatment: an opportunity for prescribing clinicians to facilitate remission from alcohol and opioid use disorders. *R I Med J*. 2014;97:20-24.
4. Adepend® (Naltrexone) [Summary of product characteristics] 2018. Amomed Pharma GmbH, Vienna, Austria.
5. Chung WH, Wang CW, Dao RL. Severe cutaneous adverse drug reactions. *J Dermatol*. 2016;43:758-766.
6. Garbutt JC. Efficacy and tolerability of naltrexone in the management of alcohol dependence. *Curr Pharm Des*. 2010;16:2091-2097.
7. AiDKlinik® Release 3.7.1 Revision 494ed1df (V2) - © 2019. Dosing GmbH, Heidelberg, Germany.
8. Naranjo CA, Busto U, Sellers EM, et al. A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther*. 1981;30:239-245.
9. Guo C, Saltoun C. Urticaria and angioedema. *Allergy Asthma Proc*. 2019;40:437-440.

How to cite this article: Heck J, Burda K, Hillemacher T, Bleich S, Stichtenoth DO, Groh A. Naltrexone-induced drug eruption. *Clin Case Rep*. 2020;8:2049–2050. https://doi.org/10.1002/ccr3.3055