1	SUBMITTED 10 JUN 24
2	REVISION REQ. 4 AUG 24; REVISION RECD. 14 AUG 24
3	ACCEPTED 5 SEP 24
4	ONLINE-FIRST: OCTOBER 2024
5	DOI: https://doi.org/10.18295/squmj.10.2024.065
6	
7	Acute Self-Harm Ideation as Presenting Adverse Event Associated with
8	Adalimumab Treatment of Severe Scalp Psoriasis
9	*Julian Cortes,¹ Reid Oldenburg¹,²
10	
11	¹ Department of Dermatology, University of California San Diego Health, La Jolla, USA;
12	² Department of Dermatology, VA San Diego Healthcare System, San Diego, USA.
13	*Corresponding Author's E-mail: jcortes21311@gmail.com
14	
15	Abstract
16	We present a case of a 34-year-old woman with severe scalp psoriasis who developed acute self-
17	harm ideations and major depressive symptoms shortly after initiating adalimumab treatment.
18	The patient had a history of major depressive disorder, post-traumatic stress disorder, and
19	anxiety, all well-controlled with multiple medications. Following the administration of
20	adalimumab, she experienced intrusive thoughts of self-harm and exacerbation of depressive
21	symptoms, prompting immediate discontinuation of the drug. The patient's symptoms resolved
22	completely three weeks after discontinuation. This case highlights the potential psychiatric risks
23	associated with adalimumab therapy for psoriasis, especially in patients with preexisting mental
24	health conditions. Dermatologists should carefully evaluate patients for psychiatric disorders and
25	suicide risk factors before initiating treatment and be vigilant in monitoring for adverse
26	psychiatric events during therapy. Proper counseling and prompt identification of adverse events
27	are crucial to prevent serious outcomes.
28	Keywords: Adalimumab-Associated Self-Harm Ideation, Drug-Induced Lupus Erythematosus,
29	Systemic Lupus Erythematosus, Adverse Drug Event.
30	

31 Introduction 32 Psoriasis is a chronic, inflammatory skin disease with an estimated prevalence of 3% in the 33 United States. It has been associated with elevated rates of depression, anxiety, and suicidality, especially in patients with severe psoriatic disease. Here we report a case of acute self-harm 34 ideation and major depressive symptoms as a presenting complaint related to recent adalimumab 35 36 treatment initiation for psoriasis. 37 38 Case Report A 34-year-old woman presented to the dermatology clinic for follow up of chronic, severe scalp 39 40 psoriasis, with about 60% involvement of her scalp and around 10% body surface area involvement. She had nearly a decade-long history of progressively worsening cutaneous 41 42 psoriasis and was previously treated with topical high potency corticosteroids and intralesional 43 triamcinolone injections. The patient also had a prior history of major depressive disorder 44 (MDD) complicated by suicidal ideation with no suicide attempts, post-traumatic stress disorder 45 (PTSD), and anxiety well controlled with multiple neurotropic medications (escitalopram 15mg 46 daily, lamotrigine 75 mg daily, gabapentin 300 mg daily, and clonazepam 0.5 mg). In addition to her topical regimen, treatment with adalimumab was started (80 mg loading dose, followed by 47 48 maintenance dosing of 40 mg every 2 weeks). At the time of adalimumab administration, the patient was not on any additional concurrent oral medications (e.g., apremilast) for treatment of 49 50 her scalp psoriasis. 51 Approximately one week after administration of 80 mg of adalimumab, the patient developed 52 deeply intrusive thoughts of self-harm and exacerbation of depressive symptoms. She described 53 54 constant, intrusive thoughts of detailed images of her hurting herself. She denied active suicidal 55 ideation or an active plan for suicide. Review of systems revealed onset of generalized fatigue, 56 arthralgias, and aphthous ulcer like lesions in her mouth. Adalimumab was discontinued

immediately, and she was advised to immediately seek urgent psychiatric care. Given her absence of suicidal intent, high insight into her condition and close follow up with mental health staff, her psychiatry team did not recommend hospitalization and no specific severity scores for depression or suicidality were performed. Return precautions were provided to the patient to report to the Emergency Department if she developed any active suicidal ideation. Her acute

57

58

59

60

61

depressive symptoms and suicidal ideations completely resolved 3 weeks after discontinuation of adalimumab. Given the abrupt onset of generalized fatigue, arthralgias, and oral aphthous ulcers following administration of adalimumab, a diagnosis of Drug-induced lupus Erythematosus (DILE) was considered. Laboratory testing of C-reactive protein and thyroid stimulating hormone levels were within normal limits. Antinuclear and anti-histone antibody serum testing were negative. Complete blood count with differential was unremarkable and without leukopenia or lymphopenia. Adalimumab was added to her list of allergy/adverse events list to prevent future administration of adalimumab and other tumor necrosis factor (TNF) blocking agents. She was continued on topical and intralesional treatment of her scalp psoriasis and Tyk2 inhibitor therapy was initiated due to its favorable side effect profile relatively short half-life. The patient has provided informed consent for the publication of her case.

Discussion

To our knowledge, this is the second case of suicidality reported in association with adalimumab therapy for psoriasis.³ While the previous patient reported a history of multiple suicide attempts and completed suicide following a several-month course of adalimumab, our patient presented with acute transient self-harm ideation following a single 80 mg injection. Not only so, but the resolution of psychiatric symptoms within 3 weeks of adalimumab discontinuation is concordant with the drug's half-life (approximately 2 weeks).⁴ This case report further supports the association between adalimumab and the development of psychiatric adverse events, specifically addressing the unique clinical scenario of drug-induced lupus erythematosus following treatment of psoriasis.

DILE should be considered in patients with abrupt onset of systemic symptoms, including arthralgias, myalgias, fever, rash, fatigue, aphthous ulcers, or others, following an initial trial of medication.⁵ TNF-blockade has been associated with DILE, which has been found to be associated with acute exacerbation of psychiatric symptoms, including acute onset suicidal ideation.⁶⁻⁷ Although the prevalence of psychiatric symptoms in DILE is unclear, approximately 21% of patients with systemic lupus erythematosus suffer from comorbid mood disorders.⁸ In patients prescribed anti-TNF medications, a recent systematic review by Jain et al. found the incidence of psychiatric and anxiety disorders to be less than 1% in most studies with some

variation between specific agents. In fact, this study did not find a significant association between TNF blockade and depressive adverse events. Surprisingly, increased levels of TNF-alpha and other pro-inflammatory cytokines have been associated with the development of MDD via a potential reduction in serotonergic activity, and blockade of these markers has been proposed as a treatment for MDD. Overall, immunopathogenesis of TNF blockade associated DILE and acute exacerbation of psychiatric disorders is poorly understood, but may involve the formation of autoantibodies.

Given adalimumab's association with DILE, a thorough evaluation for psychiatric illness and suicide completion risk factors may be indicated while considering its use for patients with moderate to severe psoriasis, especially if the patient presents with a pertinent prior history of suicidality. The risk of suicide with MDD and PTSD has been well established and patients with such comorbidities should be appropriately monitored. This is doubly true for patients who concurrently suffer from psoriasis given its association with an increased risk for completed suicide. Moreover, psoriasis patients frequently see dermatologists, putting dermatologists in a strategic position to promptly identify patients during crises. Proper counseling prior to medication initiation and prompt identification of adverse events related to medication use are critical to prevent catastrophic adverse events.

Conclusion

Adalimumab therapy for psoriasis may be associated with severe acute self-harm that may pose an immediate threat to patients. As dermatologists consider pursuing TNF-blockade, they should be aware of rare adverse events of drug-induced lupus erythematosus and acute self-harm and suicidal ideations to permit rapid identification, medication discontinuation and treatment.

Authors' Contribution

Both authors contributed equally to the literature review, drafting and revising the manuscript.

RO directly managed the case and cared for the patient. Both authors approved the final version

of the manuscript.

123 Acknowledgement

We'd like to thank our patient for agreeing to the publication of her case.

125

126

References

- Armstrong AW, Mehta MD, Schupp CW, Gondo GC, Bell SJ, Griffiths CEM. Psoriasis
 Prevalence in Adults in the United States. JAMA Dermatol. 2021;157(8):940-946.
- doi:10.1001/jamadermatol.2021.2007
- 2. Kurd SK, Troxel AB, Crits-Christoph P, Gelfand JM. The risk of depression, anxiety, and suicidality in patients with psoriasis: a population-based cohort study. Arch Dermatol.
- 2010;146(8):891-895. doi:10.1001/archdermatol.2010.186
- 3. Ellard R, Ahmed A, Shah R, Bewley A. Suicide and depression in a patient with psoriasis
 receiving adalimumab: the role of the dermatologist. Clin Exp Dermatol. 2014;39(5):624 627. doi:10.1111/ced.12351
- 4. Croom KF, McCormack PL. Adalimumab: in plaque psoriasis. *Am J Clin Dermatol*.
 2009;10(1):43-50. doi:10.2165/0128071-200910010-00008
- 5. Solhjoo M, Goyal A, Chauhan K. Drug-Induced Lupus Erythematosus. In: *StatPearls*.
 Treasure Island (FL): StatPearls Publishing; April 3, 2023.
- Vaglio A, Grayson PC, Fenaroli P, et al. Drug-induced lupus: Traditional and new
 concepts. Autoimmun Rev. 2018;17(9):912-918. doi:10.1016/j.autrev.2018.03.016
- 7. Pego-Reigosa JM, Isenberg DA. Psychosis due to systemic lupus erythematosus: characteristics and long-term outcome of this rare manifestation of the disease.
- Rheumatology (Oxford). 2008;47(10):1498-1502. doi:10.1093/rheumatology/ken260
- Unterman A, Nolte JE, Boaz M, Abady M, Shoenfeld Y, Zandman-Goddard G.
 Neuropsychiatric syndromes in systemic lupus erythematosus: a meta-analysis. *Semin Arthritis Rheum.* 2011;41(1):1-11. doi:10.1016/j.semarthrit.2010.08.001
- Jain A, Marrie RA, Shafer LA, et al. Incidence of Adverse Psychiatric Events During
 Treatment of Inflammatory Bowel Disease With Biologic Therapies: A Systematic
 Review. Crohns Colitis 360. 2020;2(1):otz053. doi:10.1093/crocol/otz053
- 10. Ma K, Zhang H, Baloch Z. Pathogenetic and Therapeutic Applications of Tumor
 Necrosis Factor-α (TNF-α) in Major Depressive Disorder: A Systematic Review. *Int J Mol Sci.* 2016;17(5):733. Published 2016 May 14. doi:10.3390/ijms17050733

. Aringer M, Smolen JS. The role of tumor necrosis factor-alpha in systemic lupus erythematosus. <i>Arthritis Res Ther</i> . 2008;10(1):202. doi:10.1186/ar2341 . Li X, Mu F, Liu D, et al. Predictors of suicidal ideation, suicide attempt and suicide death among people with major depressive disorder: A systematic review and meta-analysis of cohort studies. J Affect Disord. 2022;302:332-351. doi:10.1016/j.jad.2022.01.103 . Stanley IH, Rogers ML, Hanson JE, Gutierrez PM, Joiner TE. PTSD symptom clusters and suicide attempts among high-risk military service members: A three-month prospective investigation. J Consult Clin Psychol. 2019;87(1):67-78. doi:10.1037/ccp0000350
Li X, Mu F, Liu D, et al. Predictors of suicidal ideation, suicide attempt and suicide death among people with major depressive disorder: A systematic review and meta-analysis of cohort studies. J Affect Disord. 2022;302:332-351. doi:10.1016/j.jad.2022.01.103 Stanley IH, Rogers ML, Hanson JE, Gutierrez PM, Joiner TE. PTSD symptom clusters and suicide attempts among high-risk military service members: A three-month prospective investigation. J Consult Clin Psychol. 2019;87(1):67-78.
among people with major depressive disorder: A systematic review and meta-analysis of cohort studies. J Affect Disord. 2022;302:332-351. doi:10.1016/j.jad.2022.01.103 . Stanley IH, Rogers ML, Hanson JE, Gutierrez PM, Joiner TE. PTSD symptom clusters and suicide attempts among high-risk military service members: A three-month prospective investigation. J Consult Clin Psychol. 2019;87(1):67-78.
cohort studies. J Affect Disord. 2022;302:332-351. doi:10.1016/j.jad.2022.01.103 . Stanley IH, Rogers ML, Hanson JE, Gutierrez PM, Joiner TE. PTSD symptom clusters and suicide attempts among high-risk military service members: A three-month prospective investigation. J Consult Clin Psychol. 2019;87(1):67-78.
. Stanley IH, Rogers ML, Hanson JE, Gutierrez PM, Joiner TE. PTSD symptom clusters and suicide attempts among high-risk military service members: A three-month prospective investigation. J Consult Clin Psychol. 2019;87(1):67-78.
and suicide attempts among high-risk military service members: A three-month prospective investigation. J Consult Clin Psychol. 2019;87(1):67-78.
prospective investigation. J Consult Clin Psychol. 2019;87(1):67-78.
doi:10.1037/ccp0000350