Dermatology Reports
https://www.pagepress.org/journals/index.php/dr/index

eISSN 2036-7406

Please cite this article as: Aljehani F, Alqahtani S, Alharbi S, Alsulami S. Nightmares caused by isotretinoin in treating hidradenitis suppurativa: a case report and clinical insights. *Dermatol Rep 2024 [Epub Ahead of Print] doi: 10.4081/dr.2024.10171*

Submitted 16/10/24 - Accepted 24/11/24

Nightmares caused by isotretinoin in treating hidradenitis suppurativa: a case report and clinical insights

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Key words: isotretinoin; hidradenitis suppurativa; nightmares.

Contributions: FA, conceptualization of the study, analysis of clinical data, drafting of the case report, responsibility for patient treatment and management, and manuscript revision; ShA, data collection, literature review, initial drafting of the manuscript, contribution in clinical analysis and editing the final manuscript; SaA, assistance in patient follow-up, contribution to the literature review, and critical revision the manuscript for intellectual content; SeA, expert dermatological insights, contribution to the interpretation of the data, and revision of the manuscript for final approval.

Conflict of interest: the authors declare no potential conflict of interest.

Availability of data and materials: data and materials are available upon request from the corresponding author.

Ethics approval and consent to participate: the authors confirm that they have followed the Journal's ethical guidelines and that this report is consistent with them.

Consent for publication: the patient has provided written consent for the publication of personal data and any accompanying images.

Abstract

Isotretinoin, widely used for treating severe acne, has also been prescribed off-label for hidradenitis suppurativa (HS). While effective in some cases, isotretinoin is known to cause psychiatric side effects. This case report discusses a 24-year-old male with HS who developed severe nightmares after isotretinoin dosage was increased. Initially prescribed to manage his HS symptoms, the drug led to vivid, distressing nightmares that significantly disrupted his sleep, resulting in the discontinuation of treatment. The symptoms resolved upon cessation of isotretinoin, and a probable association was confirmed using the Naranjo algorithm. The patient was later transitioned to adalimumab, a biologic therapy for HS. This case highlights the need for careful psychiatric monitoring during isotretinoin therapy and emphasizes the importance of considering alternative treatments in cases of intolerable side effects. Further research is necessary to understand better the psychiatric implications of isotretinoin, including sleep disturbances like nightmares.

Introduction

Hidradenitis suppurativa (HS) is a chronic, recurrent inflammatory disorder that affects apocrine gland-bearing areas, including the axillae, inguinal, anogenital, and inframammary regions and is characterized by painful abscesses, deep-seated nodules, and fistulas.[1] HS significantly impacts patients' quality of life due to its recurrent nature and the often severe physical and psychological burden associated with it. The pathophysiology of HS remains poorly understood, though it is currently thought to be an inflammatory immune-mediated disease (IMID).[2] Effective management of HS is essential, and treatment selection is crucial given the disease's profound impact on physical and emotional well-being.[2]

While isotretinoin is the gold-standard treatment for severe acne, it has been used off-label in the management of HS due to its anti-inflammatory properties and potential to reduce lesion formation.[3] However, its efficacy in HS has been mixed, with some studies suggesting improvement in symptoms, while others highlight its limitations in treating this condition, particularly in more advanced stages.[4] Despite this, isotretinoin continues to be considered in the treatment arsenal for HS, particularly in patients who have not responded to standard therapies.[3]

Recent evidence suggests that while isotretinoin may be effective for some patients with HS, particularly those with a history of acne, its overall use in HS is still controversial.[5] The HS ALLIANCE working group has advised against using isotretinoin as a primary treatment option for HS, citing concerns about both its efficacy and safety profile in this population.[5] Some studies have shown that isotretinoin might help reduce lesion formation in certain HS patients, especially those with milder forms of the disease, but these findings are inconsistent.[6] In fact, some reports indicate that isotretinoin can exacerbate HS in certain cases, raising safety concerns about its use.[7] As a result, biologic therapies, particularly tumor necrosis factor inhibitors such as adalimumab, are increasingly favored due to their demonstrated ability to reduce symptom severity and prevent recurrence, particularly in more advanced cases of HS.[8]

Despite its therapeutic benefits, isotretinoin is known to cause a range of adverse effects, including psychiatric symptoms. Research indicates that psychiatric side effects are not uncommon among isotretinoin users. A study by Wysowski *et al.* (2001) found that approximately 10% of patients reported symptoms such as insomnia and minor depression during treatment.[9] Furthermore, there have been significant reports of psychiatric adverse events, including suicides and suicide attempts, among isotretinoin users compared to those treated with antibiotics for acne. Suuberg (2019) highlighted that about 25.16% of reported adverse effects from isotretinoin were psychiatric, with a notable incidence of depression and suicidal thoughts.[10] This aligns with a review by Kontaxakis *et al.* (2009), which found that mood changes could occur as early as one day after initiating treatment and persist for up to four months.[11] The underlying mechanisms of isotretinoin-induced psychiatric symptoms remain poorly understood.

While various psychiatric side effects of isotretinoin, such as depression and suicidal ideation, are well-documented, nightmares have been rarely reported. This case report presents a 24-year-old patient with HS who developed nightmares after increasing the isotretinoin dosage, shedding light on this rare but clinically significant psychiatric side effect.

Case Report

A 24-year-old male, obese, with a medical history of controlled asthma (on medication) and irritable bowel syndrome (not on medication), presented to the dermatology clinic with a seven-year history of multiple painful abscesses in both underarms and the lower abdomen. These

abscesses were accompanied by sinus tracts leaking pus and blood with a foul-smelling discharge. Despite visiting multiple hospitals over the years, the patient had been misdiagnosed as a case of recurrent abscesses. One year prior to this presentation, he was diagnosed clinically with hidradenitis suppurativa (HS) at our facility (Table 1 provides a summary of the clinical case and treatment course).

The patient was initially treated with topical clindamycin solution and oral doxycycline, but this led to no significant improvement. As a next step, isotretinoin 20 mg once daily was prescribed to manage the symptoms of HS. After one month with no improvement, the dose was increased to 20 mg twice daily. The patient began to experience marked improvement in the abscesses and sinus tracts but developed notable side effects after the dose escalation.

The patient reported new-onset joint pain, constipation, dryness, fatigue, headaches, low mood, sleep disturbances, and, most notably, nightmares. He described the nightmares as vivid, recurring almost nightly, and involving distressing themes that interrupted his sleep. These nightmares were long and intense, causing significant emotional distress and contributing to the overall disturbance in his sleep pattern. Despite these symptoms, the patient had no previous personal or family history of psychiatric illness. A basic psychological evaluation using the Beck Depression Inventory showed mild depressive symptoms, likely related to the side effects of isotretinoin. A sleep quality assessment revealed significant impairment in sleep, predominantly due to vivid nightmares.

The patient found the side effects, especially the nightmares and sleep disturbances, intolerable and decided to discontinue isotretinoin after two months. Following cessation of the medication, all side effects, including nightmares and sleep disturbances, resolved.

The adverse drug reaction was evaluated using the Naranjo algorithm, with a score of 6, indicating a probable association between isotretinoin and psychiatric symptoms (Table 2). Given the failure of isotretinoin and previous antibiotic treatments and the severity of the patient's HS (Hurley stage III), a biologic therapy was considered. The patient was started on adalimumab, the first and only FDA-approved biologic for HS, based on evidence that biologics targeting TNF-alpha can significantly reduce the severity and recurrence of symptoms in advanced HS. This decision was supported by clinical guidelines and the patient's lack of response to other therapies.

Investigations, including a complete blood count, renal function test, liver function test, lipid profile, and serology, were all within normal limits.

On clinical examination, the patient had painful, erythematous nodules in the axillary and groin areas, accompanied by scars, multiple sinus tracts with purulent discharge, and hyperpigmented macules, consistent with Hurley stage III HS (Figures 1 A, B; Figure 2).

Discussion

Isotretinoin is a well-established treatment for severe acne, and its anti-inflammatory properties have made it an off-label option for various other dermatological conditions, including hidradenitis suppurativa. However, the drug is associated with a wide range of adverse effects, including psychiatric symptoms such as depression, suicidal ideation, and, as highlighted in this case, sleep disturbances and nightmares.

While depression and suicidal ideation are the most reported psychiatric symptoms associated with isotretinoin use, nightmares are rarely documented.[9,10] In this case, the patient experienced vivid, distressing nightmares that began after the isotretinoin dose was increased. These nightmares were so severe that they caused significant emotional distress and sleep disturbances, ultimately leading the patient to discontinue the medication. Upon cessation, the nightmares resolved, suggesting a probable causative link between isotretinoin and sleep disturbances, as supported by the Naranjo algorithm score of 6.

The underlying mechanisms of isotretinoin-induced psychiatric symptoms are not fully understood, though some studies suggest alterations in neurotransmitter systems, particularly serotonin [12]. Retinoic acid receptors in the brain may affect pathways involved in mood and sleep regulation, which could explain the occurrence of nightmares.[13] This aligns with existing literature that suggests isotretinoin can influence serotonin and dopamine levels, potentially disrupting REM sleep and leading to vivid dreams or nightmares.[14,15]

Despite these potential mechanisms, psychiatric side effects like nightmares are not commonly recognized in clinical practice.[13] This case underscores the importance of monitoring not only mood but also sleep quality in patients receiving isotretinoin, even in those with no prior

psychiatric history. Given those psychiatric symptoms, particularly sleep disturbances, can profoundly affect patients' well-being, routine psychiatric screening and sleep assessments should be considered essential components of the care plan for patients receiving isotretinoin.[16] This may involve regular use of standardized tools, such as the Beck Depression Inventory, and targeted sleep assessments to detect early signs of sleep disruption.[17]

Additionally, this case highlights the clinical need for psychiatric vigilance in patients on isotretinoin therapy, where routine mental health evaluations, including sleep quality assessments, could help identify rare but severe side effects, such as nightmares. Clinicians must ensure they thoroughly monitor psychiatric health, particularly given isotretinoin's known association with depression and suicidal ideation. In cases of intolerable psychiatric side effects, transitioning to alternative therapies, such as biologics, should be considered.

Given the severity of the patient's hidradenitis suppurativa and the intolerable side effects of isotretinoin, discontinuation was necessary. Transitioning to biologic therapy, specifically adalimumab, offered an alternative treatment without the psychiatric risk profile associated with isotretinoin.[18] In clinical practice, this case reinforces the importance of balancing the therapeutic benefits of isotretinoin against its potential psychiatric side effects, ensuring that appropriate psychological support and alternative treatment options are readily available for affected patients.

Limitations

This case report is inherently limited by its focus on a single patient, which restricts the generalizability of the findings. As a single-case report, it is difficult to draw broader conclusions about the psychiatric side effects of isotretinoin. Furthermore, the reporting of nightmares and sleep disturbances is subjective, relying on the patient's self-reported experiences without objective verification. This subjectivity limits the ability to fully assess the frequency and intensity of the nightmares or determine if other factors may have contributed to the patient's sleep disturbances. Additionally, this study did not include detailed psychiatric evaluations, such as standardized psychiatric interviews or objective sleep studies (*e.g.,* polysomnography) that could have provided more robust data on the nature and impact of sleep disturbances. While the temporal relationship between isotretinoin usage and the onset of nightmares strongly suggests

causality, the absence of objective sleep assessments makes it difficult to definitively attribute these symptoms to isotretinoin.

Conclusions

This case highlights isotretinoin's potential to cause rare but severe psychiatric side effects, specifically vivid nightmares that significantly disrupt sleep. While isotretinoin remains an effective treatment for hidradenitis suppurativa, clinicians should remain vigilant in monitoring for psychiatric symptoms, even in patients without a prior mental health history. Regular psychiatric screening and sleep assessments are recommended during isotretinoin therapy. In cases of intolerable psychiatric side effects, discontinuation, or transition to alternative treatments, such as biologics, should be considered. Further research is needed to better understand the mechanisms behind isotretinoin’s effects on sleep and mental health.

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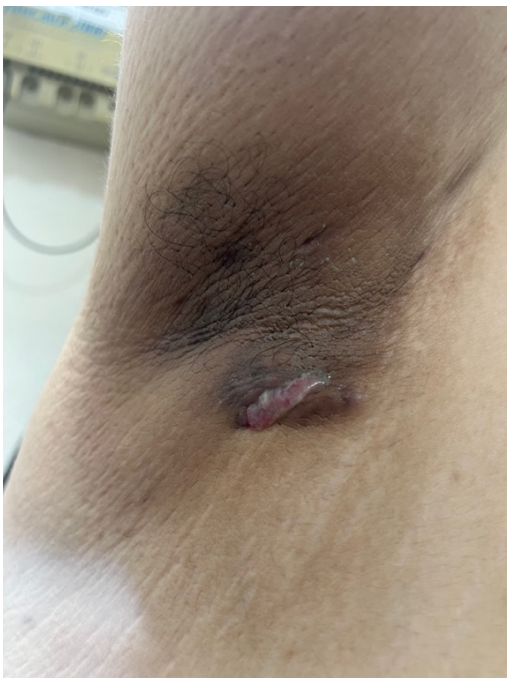

Figure 1. A) Multiple nodules and draining sinus tracts in the right axilla, characteristic of severe hidradenitis suppurativa (Hurley stage III).

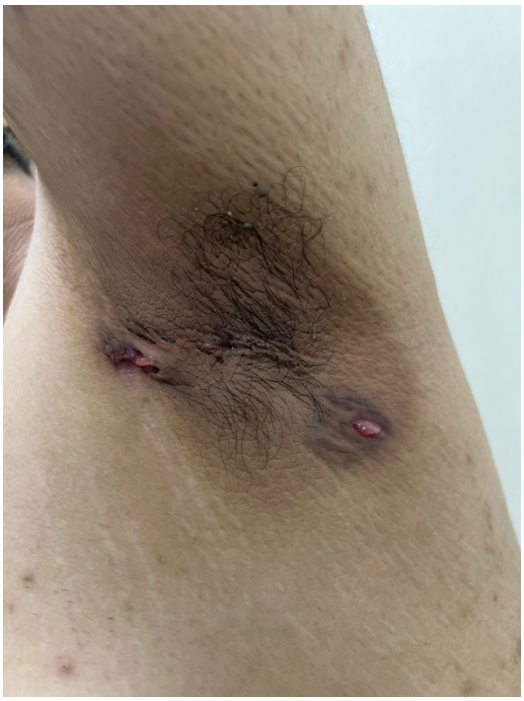

Figure 1. B) Painful abscess with erythema and sinus tract formation in the left axilla of a patient with Hurley stage III hidradenitis suppurativa.

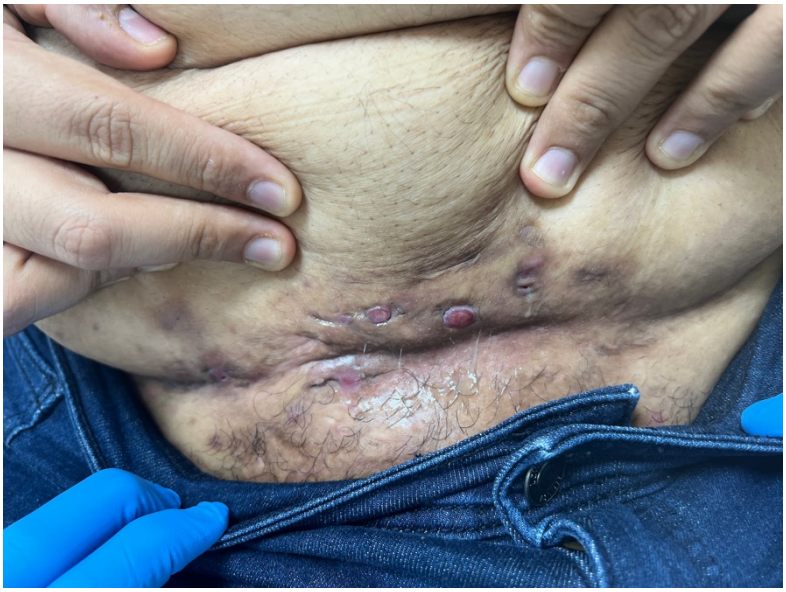

Figure 2. Erythematous nodules in the groin region, accompanied by scars, multiple draining sinuses with purulent discharge, and hyperpigmented macules in a patient with Hurley stage III hidradenitis suppurativa.

Table 1. Summary of clinical case and treatment course.

Parameter	Details
Patient Demographics	24-year-old male, obese
Relevant Medical History	Controlled asthma (on medication), Irritable bowel syndrome (not on medication)
HS Diagnosis	Hidradenitis suppurativa (Hurley stage III), diagnosed one year prior to presentation
Previous Treatments	Topical clindamycin, oral doxycycline (no significant improvement)
Initial Isotretinoin Treatment	Isotretinoin 20 mg once daily, increased to 20 mg twice daily after one month
Isotretinoin Efficacy	Marked improvement in abscesses and sinus tracts
Isotretinoin Side Effects	Joint pain, constipation, dryness, fatigue, headaches, low mood, sleep disturbances, vivid and distressing nightmares
Psychiatric Assessment	No prior psychiatric history; mild depressive symptoms on Beck Depression Inventory (related to isotretinoin)
Sleep Assessment	Impaired sleep quality due to vivid nightmares
Response to Isotretinoin Cessation	Complete resolution of side effects, including nightmares and sleep disturbances
Naranjo Algorithm Score	6 (probable isotretinoin-induced adverse psychiatric effects)
Alternative Treatment	Adalimumab (TNF-alpha inhibitor) initiated following cessation of isotretinoin, in line with clinical guidelines for severe HS
Laboratory Investigations	Complete blood count, renal function test, liver function test, lipid profile, and serology: All within normal limits

Clinical Findings	Painful erythematous nodules, multiple sinus tracts with purulent discharge, scarring, and hyperpigmented macules in the axillary and groin areas
Outcome	Successful transition to biologic therapy (adalimumab) after discontinuation of isotretinoin

HS, hidradenitis suppurativa; Naranjo Algorithm, scale used to assess the likelihood of adverse drug reactions being related to the drug.

Table 2. Naranjo adverse drug reaction probability scale applied to isotretinoin-induced nightmares.

Question	Answer	Score
1. Are there previous conclusive reports on this reaction?	Yes	+1
2. Did the adverse event appear after the suspected drug was administered?	Yes	+2
3. Did the adverse reaction improve when the drug was discontinued?	Yes	+1
4. Did the adverse reaction reappear when the drug was readministered?	Not applicable	0
5. Are there alternative causes (other than the drug) that could have caused the reaction?	No	+2
6. Did the reaction reappear when a placebo was given?	Not applicable	0
7. Was the drug detected in any body fluids in toxic concentrations?	No	0
8. Was the reaction more severe when the dose was increased, or less severe when the dose was decreased?	Yes	+1
9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	No	0
10. Was the adverse event confirmed by any objective evidence?	No	0
Total Score		**6**