Case Report

SAGE Open Medical Case Reports

SAGE Open Medical Case Reports
Volume 8: 1–3

DOI: 10.1177/2050313X20931342
journals.sagepub.com/home/sco
SAGE

Isotretinoin-induced psychotic episode in a 17-year-old adolescent male

Bushra Elhusein, Walid Elkhaled, Mohamed Adil Shah Khoodoruth, Rajeev Kumar and Majid Al Abdulla

Abstract

Isotretinoin, a synthetic vitamin A derivative, is primarily used in the management of severe nodulocystic acne. Since its introduction, isotretinoin has been linked with various psychiatric side effects. In particular, depression and suicidality have been extensively reported as side effects. This case report features a young male who developed a first psychotic episode within 3 months of starting isotretinoin therapy. The patient was hospitalized, and organic pathologies and use of psychoactive substances that could explain his presentation were ruled out. After stopping isotretinoin and starting olanzapine 10 mg, the psychotic symptoms remitted completely within 2 weeks. This case highlights the need for increased vigilance toward psychiatric manifestations of isotretinoin. In addition, it suggests that secondary psychosis should be considered as a differential diagnosis by clinicians, especially in patients with no past psychiatric history or family history of mental illness.

Keywords

Acne, isotretinoin, vitamin A, psychosis, drug-related side effects, adverse reactions

Date received: 27 November 2019; accepted: 11 May 2020

Introduction

Isotretinoin (13-cis-retinoic acid) belongs to the retinoid family, which includes endogenous molecules derived from vitamin A (retinol) that are essential in regulating the cell cycle in multiple organ systems.[1] Being the only anti-acne drug to affect all major pathologic factors implicated in acne rendered isotretinoin superior to other conventional treatments; it prevents comedogenesis, decreases sebum production, inhibits *Propionibacterium acnes* growth, and reduces the inflammation associated with acne.[2]

Following the approval of isotretinoin by the US Food and Drug Administration (FDA) in 1982 to be used for severe and treatment-resistant nodulocystic acne, multiple studies have denoted a possible link between the drug and psychiatric side effects, which were increasing in prevalence. This warranted the FDA in 2005 to place a black box warning for suicide, depression, aggression, and psychosis as possible side effects associated with isotretinoin use.[3]

Depression and suicidality have been extensively addressed in the literature, with some studies suggesting a relationship with isotretinoin, whereas a link with psychosis is rarely reported in the literature.[4] We report a case of an adolescent male with no previous psychiatric history who presented with a psychotic episode while on isotretinoin therapy for acne vulgaris.

Case presentation

We present a 17-year-old adolescent male (weight, 54 kg), pre-university student, who presented to the Accident and Emergency department with a 2-day history of decreased need for sleep (sleeps for short hours and feels invigorated upon awakening), mood swings, and disorganized erratic behavior (dispatching laptop batteries, destroying cell phones, and foraging garbage bins). The patient's mental status examination revealed a young man who looked scared and suspicious, mood was irritable with labile affect. He had irrelevant speech and disorganized thoughts with signs of dissociation. The patient experienced persecutory delusions (indicated that his room was being filled by toxic gases) and

Mental Health Services-Consultation Liaison Psychiatry-Hamad Medical Corporation, Doha, Qatar

Corresponding Author:
Walid Elkhaled, Mental Health Services-Consultation Liaison Psychiatry-Hamad Medical Corporation, P.O. Box 3050, Doha, Qatar.
Email: w.elkhaled.92@gmail.com

third-person auditory hallucinations (He reported hearing voices of unseen people talking about him). He denied any episode of visual hallucinations and other abnormal perceptions. The patient denied experiencing death wishes or suicidal ideation.

On admission, the patient lived with both parents, and was described by his mother as "the best student with the highest grades." He had no psychiatric or medical history, no family history of psychiatric or medical illnesses, and did not take any medications routinely, except isotretinoin (30 mg/day) for severe nodulocystic acne on the forehead and cheeks, which was started 3 months before his psychiatric presentation.

The next day, the patient experienced an episode of seizure with convulsion of the whole-body, including the head, whereas his eyes were open with a central gaze. The seizure lasted 10 min without postictal symptoms besides confusion, and one instance of fever (38.2°C). He was admitted under observation of the medical team; antibiotics were initiated and he was investigated thoroughly for systemic diseases because of the high suspicion of meningoencephalitis.

Physical examination was unremarkable; his seizures continued with a fluctuating course, and he developed a total of three episodes of seizure during his hospital stay. Eventually, these events were considered psychogenic non-epileptic seizures (PNES) based on the following characteristics: asynchronous motor movements with a waxing and waning pattern, prolonged duration of seizures, no upward rolling of the eyes, absence of urinary incontinence, and normal electroencephalogram (EEG) spikes with unremarkable prolactin levels. The results of pertinent investigations, including head computed tomography (CT), magnetic resonance imaging (MRI), and lumbar puncture, were within normal limits; his vitamin A level was 1.746 μmol/L (normal: 1.047–2.094 μmol/L).

The patient continued to experience mood swings and psychotic symptoms; eventually, antibiotics were stopped, and isotretinoin was discontinued. A provisional diagnosis of drug-induced psychotic episode was made.

Olanzapine (10 mg) was initiated on day 6 of admission by the psychiatry team. Thereafter, the patient started showing progressive improvement in his mental status, and within 1 week, his psychotic symptoms were almost in complete remission. The patient was followed up 1 week after discharge in the outpatient clinic; his psychotic symptoms were in complete remission and he was preparing for medical school.

Discussion

Isotretinoin is the only non-psychotropic drug that ranks among the list of top 10 drugs in the FDA's database in terms of the number of reports on depression and suicidal attempts, whereas psychosis, obsessive-compulsive disorder, and anxiety have been rarely reported.[5]

Some reports imply that isotretinoin is contraindicated in psychosis as it complicates the course of the disease. For example, Kępska et al.[6] described worsening of positive symptoms in a 35-year-old lady with schizophrenia who was taking isotretinoin, and they have recommended close cooperation between dermatologists and psychiatrists in patients with schizophrenia presenting with dermatological concerns. In Table 1, we charted individual cases of isotretinoin-related psychosis reported in the literature.

Goodman has put forward three lines of evidence proposing retinoid dysregulation as a possible cause of schizophrenia: (1) the similarity of symptomatology and clinical features, for example, thought disorder, intellectual disability, enlarged ventricles, microcephaly, and congenital malformations; (2) specific gene loci linked to schizophrenia are also known gene loci within the retinoid signaling system, namely RAR and RXR; and (3) retinoid regulation targets schizophrenia genes, in particular, genes of dopamine and serotonin.[11] More recently, isotretinoin treatment, schizophrenia, and depression have each been associated with elevated homocysteine levels, indicating the possibility that isotretinoin-induced homocysteine elevation may contribute to psychiatric side effects.[1]

Furthermore, a series of cases of manic psychosis that developed in 1 year (2003) in association with isotretinoin treatment and resulted in suicidality and progression to long-standing psychosis was reported; these cases were selected from among 500 soldiers who had been evaluated in a military specialist's dermatology clinic for severe acne.[12] However, nearly all of them had either a personal psychiatric history or a family history of mental illness. In contrast, in the case we presented here, the patient had no predisposing personal or family psychiatric history.

In this case, we were looking to formulate the following research question: "Is there an association between the use of isotretinoin and the development of new emerging psychosis?" we conducted an extensive literature review using databases such as PubMed and Google scholar, where we evaluated similar cases using keywords such as acne, isotretinoin, vitamin A, psychosis, drug-related side effects, and adverse reactions. Eventually, we concluded that there is a lot of controversy regarding this topic; however, in our case, with no previous psychiatric history and with the temporal association between the appearance of psychosis and use of isotretinoin, we deemed the association as non-coincidental; therefore our report may promote more awareness among clinicians regarding the possibility of the existence of such associations.

Conclusion

Numerous studies have reported psychiatric adverse events associated with isotretinoin use, and this should prompt clinicians to have a higher index of suspicion for potential psychiatric events other than depression and suicidality related to

Table 1. Summary of data reported on isotretinoin-related psychosis.

Case number	Author(s)	Year	Age	Gender	Dosage	Remarks
1	Segmiller et al.[7]	2013	25	F	20 mg/day for 3 weeks	Improved within 10 days after discontinuation of isotretinoin, and quetiapine titrated up to 400 mg daily
2	Rajagopal[8]	2014	27	M	Not reported	Psychiatric symptoms started 5 days after starting isotretinoin. Symptoms resolved 3 days after discontinuation of isotretinoin, and risperidone 1 mg daily
3	Lucca et al.[9]	2016	20	F	20 mg/day for 45 days, then increased to 60 mg/day for 15 days	Manic and psychotic features resolved after 6 days of discontinuation of isotretinoin, and addition of quetiapine 100 mg bedtime, oxcarbamazepine 300 mg daily, and risperidone 2 mg bedtime
4	Valderrama et al.[10]	2017	13	M	20 mg/day for 2 months	Complete remission of symptoms after 2 weeks of stopping isotretinoin, and olanzapine 10 mg daily

isotretinoin use. Although no causal relationship has been established, the increase in reported studies describing psychiatric events associated with isotretinoin indicates a link between the medication and psychopathology. This case serves as a reminder to psychiatrists that history-taking, including medication history, remains the pillar of a proper psychiatric assessment because it will affect the diagnosis, management, and subsequently, the long-term treatment plan.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

Ethical approval to report this case series was obtained from "ABHATH" (APPROVAL NUMBER/ID: MRC-04-19-471).

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: The publication of this article was funded by the Qatar National Library.

Informed consent

Written informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article. A general consent form to publish patient information was obtained from the legal guardians (both parents).

ORCID iDs

Bushra Elhusein https://orcid.org/0000-0003-0803-1138
Walid Elkhaled https://orcid.org/0000-0002-3188-4545
Mohamed Adil Shah Khoodoruth https://orcid.org/0000-0003-3104-7525

References

1. Suuberg A. Psychiatric and developmental effects of isotretinoin (Retinoid) treatment for acne vulgaris. *Curr Ther Res* 2019; 90: 27–31.
2. Layton A. The use of isotretinoin in acne. *Dermatoendocrinol* 2009; 1: 162–169.
3. Ludot M, Mouchabac S and Ferreri F. Inter-relationships between isotretinoin treatment and psychiatric disorders: depression, bipolar disorder, anxiety, psychosis and suicide risks. *World J Psychiatry* 2015; 5: 222–227.
4. Bremner JD, Shearer KD and McCaffery PJ. Retinoic acid and affective disorders. *J Clin Psychiatry* 2012; 73: 37–50.
5. Wysowski DK, Pitts M and Beitz J. Depression and suicide in patients treated with isotretinoin. *N Engl J Med* 2001; 344: 460–460.
6. Kępska A, Majtyka M, Kowman M, et al. Dermatitis artefacta as a symptom of schizophrenia? *Adv Dermatology Allergol* 2014; 4: 277–279.
7. Segmiller FM, Rüther T, Linhardt A, et al. Psychosis during treatment with isotretinoin. *Ther Adv Psychopharmacol* 2013; 3: 244–245.
8. Rajagopal S. Acute psychosis induced by isotretinoin. *Indian J Psychiatry* 2014; 56: 295–297.
9. Lucca J, Varghese N, Ramesh M, et al. A case report of isotretinoin-induced manic psychosis. *Indian J Dermatol* 2016; 61: 120.
10. Valderrama F, Gomez A and Restrepo D. Isotretinoin therapy for acne vulgaris and first episode psychosis in an adolescent patient. *Rev Colomb Psiquiatr* 2017; 46(1): 50–54.
11. Goodman AB. Chromosomal locations and modes of action of genes of the retinoid (vitamin A) system support their involvement in the etiology of schizophrenia. *Am J Med Genet* 1995; 60: 335–348.
12. Barak Y, Wohl Y, Greenberg Y, et al. Affective psychosis following Accutane (isotretinoin) treatment. *Int Clin Psychopharmacol* 2005; 20(1): 39–41.