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## Depression Secondary to Isotretinoin – a Case Report

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### Abstract

Depression is one of the leading causes of morbidity in the world and significantly affects the lives of people suffering from it. The exact cause of depression has not been established and it is believed to be a complex play between various social, biological, environmental, personal factors. A relatively rare but distinct cause includes pharmacological agents.

In this case report, we describe the case of a 17-year-old girl who developed depression with psychotic symptoms on two occasions, both preceded by a history of Isotretinoin use. She was admitted and treated with anti-psychotics and psychotherapy with significant improvement in her mental state.

There is no global consensus and direct scientific evidence establishing causality but many case reports are present in medical literature showing association between depression and Isotretinoin use. Therefore, it is important for clinicians to exercise caution when prescribing Isotretinoin to vulnerable groups.

### Keywords

Adverse Drug Reaction, Depression, Isotretinoin, Psychosis, Psychiatry

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### Cover Page Footnote

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### Consent

Consent was obtained from the parents as patient is a minor. Assent was also obtained from the patient.

### Introduction

Depression is one of the most common mental health condition affecting patients of all ages. About a quarter billion people are estimated to be suffering from it with women affected more frequently than men. It is a serious condition, severely affecting the quality of life of the patient and of those around them. A study finds that Depression accounts for nearly half of all psychiatric consultations and approximately 12% of all admissions [1]. Access to help continues to be limited which explains the fact that nearly 700,000 people die to suicide every year. About 75% people suffering with depression in low- and middle-income countries do not have access to any form of medical help. Even when available, help is difficult to access due to social stigma, guilt, fear, financial condition, limited resources etc.

Depression is diagnosed with the help of criterion established by International Statistical Classification of Diseases (ICD), edition 10. Depressive disorder is covered under chapter V, section F32 [2].

Symptoms include – low mood, loss of interest in pleasurable activities, significant weight loss/gain or appetite increase/decrease, sleep disturbance, tiredness/ low energy, worthlessness/guilt, impaired concentration, suicidal ideation, etc. The symptoms should be causing significant impairment to psycho-social functioning and must not be explained by other medical conditions or use of drugs. Some patients also develop somatic manifestations in the form of myalgia, abdominal pains, headaches etc.

Depression is caused by a complex interplay between many social, personal, environmental, psychological and biological factors. Most experts believe that the cause is multifactorial. The involvement of brain neurotransmitters like Serotonin, Dopamine, Norepinephrine and regions like Amygdala and Hippocampus have been established before [3]. A relatively less known cause includes drugs. Some of these drugs include Beta Blockers, Calcium Channel Blockers, Oral Contraceptive Pills, Testosterone, Anti-Epileptics, ACE inhibitors, Angiotensin Receptor Blockers, Corticosteroids, Alpha and Beta interferons [4].

Another drug known to cause depression is Isotretinoin, being described in a few hundred case reports. It has been approved by FDA for treatment of nodulo-cystic acne and is found to be highly efficacious. In 1998, the FDA issued a warning about the potential association between Isotretinoin and Depression however it also admitted that there was no hard evidence for the same. Currently, the only evidence of possible link between Isotretinoin and Depression comes from case reports with the association still being controversial in clinical practice.

In this case report, we describe a case of a 17-year-old girl diagnosed with Depression secondary to Isotretinoin use.

## **Case presentation**

A 17-year-old girl, only child from 3<sup>rd</sup> degree consanguineous parents presented to the Psychiatry OPD with complaints of sadness, crying spells, irritability, suspiciousness and decreased sleep for 2 days. The parents also report violent behavior without warning/reason including slapping and pushing. The patient reported stress of examinations as the precipitating factor. She expressed frustration with her parents and attributed their lack of education for their apparent inability to understand her. Further history elicited suicidal ideation, delusion of grandiosity, delusion of persecution, delusion of reference and jealousy. On interviewing, patient was found to be short tempered, irritable and sensitive to criticism. Patient also showed high levels of Neuroticism, Mood lability and Conscientiousness.

Patient had a previous episode with similar complaints in February of 2022. She also had flight of speech, hyperhidrosis, decreased need for sleep, harsh and abusive speech, anger, decreased appetite and increased activity levels. At that time, she was admitted and treated

with Olanzapine, Amisulpride and Trihexyphenidyl. She discontinued medicines 3 months back due to weight gain and feeling symptomatically better. Patient also has menstrual irregularities and was diagnosed with PCOS earlier.

Patient expressed low self-esteem with respect to her weight and acne that started several years ago. The patient started taking Isotretinoin for the same about 1 year ago. The consumption of Isotretinoin seems to be temporally associated with her episodes. The timeline of events is shown in figure 1.



**Figure 1 – Timeline of events**

Kirby's examination was done as the patient was uncooperative and it was normal except spontaneous episodes of crying and distressed facial expressions.

General and systemic examination was found to be normal. Laboratory investigations were also found to be normal.

Patient was initiated with Psychotherapy and treated with oral Olanzapine 10 mg once a day and oral Amisulpride 100 mg twice a day with gradual improvement in symptoms. She and her parents were counselled regarding future use of Isotretinoin.

## Discussion

Depression is a serious and common illness, affecting millions of people. It can lead to suicide which is one of the most common causes of death, particularly in the young-adult population.

Patients can develop symptoms like sadness, guilt, alterations in sleep cycle, alterations in appetite, suicidal ideation etc. In some cases, patients may develop even more serious symptoms, like Psychosis characterized by delusions, hallucinations, disconnect with reality etc. Patients who have Depression with Mania (flight of ideas, pressured speech, hyperarousal, anger, lack of need for sleep etc.) are diagnosed with bipolar disorder. This condition is treated slightly differently than depression alone as use of anti-depressants can precipitate an episode of mania.

In this particular case, we explore Depression with psychotic symptoms secondary to the use of Isotretinoin. The patient reported displeasure over acne on her face, for which she started taking Isotretinoin. As seen in the timeline in figure 1, the patient developed an episode of Depression with psychosis within a few days of stopping Isotretinoin. This is

noted to have happened twice. It is interesting to note that the 'stoppage' of the drug and not its introduction seemed to have precipitated these episodes.

Naranjo et al [5] established a simple guide for classifying such drug – score of >9 implies definite ADR and <2 implies unlikely ADR. We used this scale and got a score of 5 (Probable). The same can be seen in figure 2.

**RESULT** 2022-11-07 20:16

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**Score 5**

**Based on the following parameters:**

1. Are there previous conclusive reports on this reaction?	Yes +1
2. Did adverse event appear after the suspected drug was given?	Yes +2
3. Did the adverse reaction improve when the drug was discontinued or a specific antagonist was given?	No
4. Did the adverse reaction appear when the drug was readministered?	Yes +2
5. Are there alternative causes that could have caused the reaction?	Yes -1
6. Did the reaction reappear when a placebo was given?	Not known or not done
7. Was the drug detected in any body fluid in toxic concentrations?	Not known or not done
8. Was the reaction more severe when the dose was increased, or less severe when the dose was decreased?	Not known or not done
9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	Not known or not done
10. Was the adverse event confirmed by any objective evidence?	Yes +1

Disclaimer: This model is provided for educational, training and information purposes. It must not be used to support medical decision making, or to provide medical or diagnostic services.

**Figure 2 – Our results from the Modified Naranjo scale for ADR – Sourced from Evidencio™**  
 from <https://www.evidencio.com/models/show/661>

Isotretinoin (13-cis-retinoic acid) has been successfully used for the treatment of acne for over 30 years but the association between Isotretinoin and Depression has been a cause of concern for a while and there is contradicting information in the literature. While the FDA has issued a warning suggesting that the Isotretinoin may be associated with Depression, a systematic review by Li et al [6] showed improvement of symptoms of Depression in those who were actually taking Isotretinoin. Another paper by Bremner [7] showed that neuro-psychiatric side effects, including depression are strongly associated with Isotretinoin and that caution needs to be exercised while prescribing to vulnerable groups.

Clinicians need to be careful while prescribing Isotretinoin to vulnerable groups and counsel patients about the risk of neuro-psychiatric adverse events until any association is conclusively disproven through well designed studies.

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