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Case Report

Hereditary Hemochromatosis and Exacerbation of Psychiatric Manifestations Following Therapeutic Phlebotomy Sessions: A Case Report

Aditi Sarker [1], Josephine Chiu [2], Raheel I. Memon [3]
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Abstract:

Background: Hereditary hemochromatosis, characterized by iron overload, is well known for its systemic effects; however, psychiatric clinical manifestations are underreported. Previous research articles discussed the link between excessive iron accumulation and mood disorders that were resolved following therapeutic phlebotomy treatment. In this case study, we presented a unique case that revealed the emergence of mood disorders following phlebotomy sessions. Our aim is to explore the relationship between them.

This case report describes a 24-year-old Caucasian male who was admitted to the hospital with severe depression and suicidal ideations along with poor insight and tangential thought process following a financial trauma. He was diagnosed with a Major Depressive Disorder based on the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-V). The patient reported a diagnosis of hereditary hemochromatosis in 2023 and has received two phlebotomy treatments since then. After the second phlebotomy session, he experienced worsening depressive symptoms (passive suicidal ideations); his blood tests revealed normal iron and ferritin levels on the 5th day of admission. He had been taking Escitalopram and Lamotrigine over the past six months.

Methods: We developed and searched keywords in multiple databases (PubMed, Google Scholar, etc.) after obtaining informed written consent from the patient. We then reviewed the literature thoroughly to identify cases of psychiatric exacerbation associated with hemochromatosis and phlebotomy.

Results: Our case report highlights a possible linkage between phlebotomy sessions for hemochromatosis and worsening depressive symptoms despite iron normalization.

Conclusion: This study stresses the need for routine mental health screening and iron profile checking following phlebotomy sessions and a multidisciplinary approach.

Background: In hemochromatosis, iron accumulates excessively in many organs, such as the liver, pancreas, heart, and joints, and rarely in the brain, leading to neuropsychiatric manifestations such as anxiety, depression, mood swings, autism, and movement disorders [1, 2, 3, 4, 5, 6, 7]. Iron dysregulation can result in mood disorders, psychosis, anxiety, and neurodevelopmental problems [8]. A study showed an increased risk of psychiatric manifestations in patients with hemochromatosis, with a prevalence of 79% and 65% for depression and anxiety, respectively [9]. Although patients with hemochromatosis show a higher incidence of mental illness, specific psychiatric disorders that significantly impact quality of life are rarely reported [3, 7, 10]. Over one billion people globally are living with a mental disorder, causing increased disability and premature mortality [11]. Previous existing studies have reviewed iron dysregulation on brain function; however, the correlation between hemochromatosis with or without therapeutic phlebotomy and manifestations of psychiatric disorders still requires further research to understand better [7, 8, 12]. In this case report, we aim to explore the link between hemochromatosis and increased psychiatric manifestations following successive therapeutic phlebotomies.

Keywords: Hemochromatosis, iron dysregulation, iron homeostasis, oxidative stress, brain, neuroinflammation, phlebotomy, psychiatric disorders, mental health.

Methods: Informed written consent was obtained from the patient before writing this case study. We generated the keywords and used three databases, such as PubMed, PubMed Central, ScienceDirect, and two journals, to extract some peer-reviewed research articles related to the patient case. We then thoroughly reviewed the literature, aiming to explore the linkage between therapeutic post-phlebotomy for hemochromatosis and the worsening of psychiatric symptoms.

Case Presentation:

Introduction to the Patient Case:

This is a case report of a 24-year-old Caucasian male with a past psychiatric history of anxiety, depression, attention deficit and hyperactivity disorder (ADHD), autism spectrum disorder (ASD) who was admitted to

the hospital in March 2025 for severe depression and recurrent suicidal thoughts with a plan to cut his wrist following involvement in an online scam and resulting in financial trauma. He also complained about a history of frequent mood swings that last for a couple of hours. The patient did not have any past hospitalizations. During psychiatric assessment, the patient denied any history of mania, psychosis, post-traumatic stress disorder, or use of illicit substances. There was no history of previous suicidal attempts.

Patient Background:
The patient's highest level of education is high school. He lives with his grandmother and is financially dependent upon her. The patient's attachment relationship with his parents is limited.

Patient Diagnosis:
In the hospital, the patient met the criteria for a Major Depressive Disorder based on the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-V).

The patient's severity of depression was measured using the Patient Health Questionnaire-9 (PHQ-9), and the patient scored 21 out of 27 points, indicating severe depression.

Home Medications:
The patient used to take Concerta 40 mg for ADHD, diagnosed in 2023, Escitalopram (Lexapro) 20 mg for depression, and Lamotrigine (Lamictal) 200 mg for stabilizing his mood over the past six months before hospital admission.

Past Medical History and Diagnosis of Hemochromatosis:
The patient was having recurrent syncopal episodes after taking Concerta. He was referred to a cardiologist and found to have abnormal lab results. Later, the patient was referred to a hematologist and diagnosed with hemochromatosis after confirmation by genetic testing in 2023. The patient received therapeutic phlebotomy treatments twice in the past year (2024). The patient and his grandma could not recall the exact date of the phlebotomies. However, the grandma mentioned that the patient's depressive symptoms got worse following the second phlebotomy, possibly in November 2024.

Exacerbation of Psychiatric Manifestations:
Following the second phlebotomy, the patient began experiencing concentration difficulties, memory impairment, trouble making logical decisions, anxiety, anhedonia, insomnia, poor appetite, hopelessness, and feelings of guilt—symptoms that escalated after becoming a victim of an online scam—ultimately leading to severe depression and recurrent suicidal ideation. The patient reported feeling stable before his second phlebotomy treatment. His grandmother was contacted to verify the patient's history and safety discharge.

Hospital Lab Results:
After hospitalization, routine laboratory testing was done. Aspartate aminotransferase (34 U/L; reference range 15–46 U/L) and alanine aminotransferase (41 U/L; reference range 13-69U/L) were normal. Complete blood count revealed (elevated red blood cell: 5.79 cells/mcL; reference range 4.00-5.00 cells/mcL; and elevated white blood cell: 12.8 cells/mcL; reference range 3.5-10.9. Iron profile study of serum iron (54 mcg/dl; reference range 49-181 mcg/dl), iron saturation (21%; reference range, 20-45), serum ferritin (34 ng/ml; reference range 18-465 ng/ml), and total iron binding capacity (261 mcg/dl; reference range 261-462 mcg/dl) all returned within normal limits. Urinalysis and urine drug screen were both negative as well.

Hospital Treatment and Patient Outcome:
The patient was prescribed Prozac in the hospital with continuation of Lamictal only. Lexapro and Concerta were discontinued in the hospital. With this medication adjustment, the patient's symptoms continued to improve, and his mood became stabilized.

Discussion: In our case report, we initially diagnosed the patient with Major Depressive Disorder—severe, recurrent, without psychosis—and Panic Disorder based on DSM-V [13, 14]. However, after confirming the patient's history through collateral information, we planned to investigate the possibility of exaggerated psychiatric symptoms associated with hemochromatosis treatment.

Previous Case Studies Related to Hemochromatosis and Psychiatric Disorders:
A previous case study examined the causal relationship between hereditary hemochromatosis and bipolar disorder and the complete recovery of psychiatric symptoms following phlebotomy treatment [7]. Another case report previously demonstrated an increased risk of non-suicidal self-injurious behavior following cessation of therapeutic phlebotomy sessions in a patient with hemochromatosis [12].

Iron Dysregulation and Mental Health:
Iron is essential in synthesizing neurotransmitters in the brain, such as dopamine, norepinephrine, and serotonin, which affect emotional liability, reward functioning, movement, and many other functions [8, 15]. Several previous human and animal studies discussed brain iron homeostasis, regulation, neurophysiological role of iron, and their potential link to psychiatric manifestations [2, 11, 16, 17, 18, 19].

Few research studies have illustrated brain iron overload with hemochromatosis, associated oxidative damage, and its connection to cognitive impairment [20,21]. Figure 1 below shows the association between iron dysregulation, oxidative damage, and mental disorders [8].

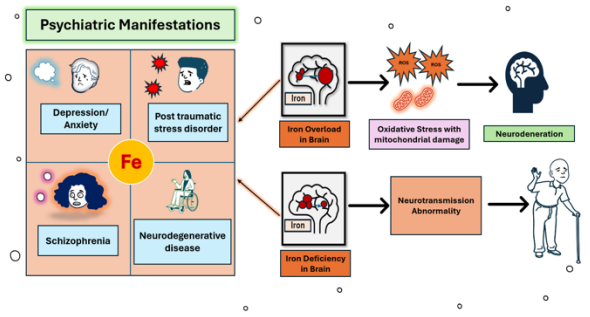

Figure 1: The relationship between iron dysregulation, oxidative damage, and mental disorders

Neuroinflammation, Oxidative Damage, and Psychiatric Manifestations:

Iron dysregulation can disrupt iron homeostasis-related protein via inflammatory mediators through the iron regulatory element/iron regulatory protein (IRE/IRP), leading to severe neuroinflammation and oxidative damage [22]. Progressive neuroinflammation can cause mood disorders and many neurodegenerative diseases [23]. Previous studies from decades discussed the mechanism of iron overload in the brain and its impact on neuroinflammation, followed by the emergence of mood disorders and neurodegenerative diseases [22, 23]. Figure 2 below reveals the pathophysiology of neuroinflammation and mood disorders [23].

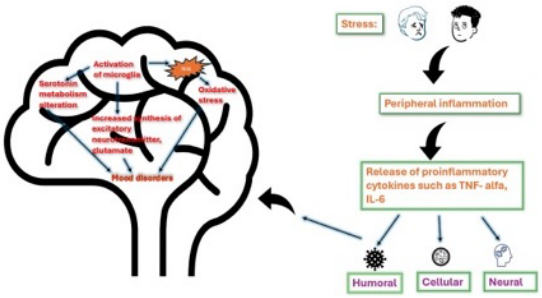

Figure 2: The pathophysiology of neuroinflammation and mood disorders; TNF: Tumor Necrosis Factor, IL: Interleukin

Although existing literature has discussed the linkage between hereditary hemochromatosis and psychiatric manifestations and their treatment modality, there is minimal research on the manifestation of psychiatric disorders and cognitive impairment in hemochromatosis patients following therapeutic phlebotomy. Unlike previous cases where psychiatric symptoms improved with iron removal, our patient deteriorated.

In our case, the patient came to the hospital with active suicidal ideation following successive phlebotomy sessions despite taking a mood stabilizer and antidepressant for the previous six months. This raises the question of a possible correlation between post-therapeutic phlebotomy for hemochromatosis and psychiatric manifestations, along with concerns regarding patient safety.

Limitation: This case report has some limitations. Although it revealed the possible link between worsening depressive symptoms and post-phlebotomy symptoms, this study cannot establish a causal relationship between them. In this case study, it should be taken into consideration that depression could act as a confounding factor. There is a possibility that depression started to worsen due to iron overload, which impacted the brain before phlebotomy started, followed by iron dysregulation after phlebotomy. Therefore, worsening depression could be related to both hemochromatosis and phlebotomy, making it hard to know which one is causing the mood changes. Also, in our case report, the patient was involved in an online scam with financial strain around the time of depression due to difficulty in making logical decisions following the second phlebotomy, which worsened his depression further. The study's findings are not generalizable to all patient populations.

Conclusion: This case report bridged the potential relationship between worsening psychiatric symptoms following post-phlebotomy sessions for hemochromatosis. This raises concerns about iron dysregulation as a possible contributing factor. We recommend routine psychiatric screening, monitoring, and iron profile study, especially in vulnerable psychiatric patients undergoing therapeutic phlebotomy sessions. Consider individualized phlebotomy sessions if any neuropsychiatry symptoms emerge. More research is needed in the future to investigate the role of iron dysregulation, altering neurotransmitter balance in hemochromatosis patients undergoing therapeutic phlebotomy treatment, and the development of psychiatric disorders. We also recommend long-term follow-up to monitor for new developments and advise a multidisciplinary approach to patient care to enhance outcomes.

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Authors: Aditi Sarker [1], Josephine Chiu [2], Raheel I. Memon [3]

1 Psychiatry Residency Program, Baptist Hospitals of Southeast Texas, Beaumont, TX. 2 Sam Houston State University College of Osteopathic Medicine, Conroe, TX. 3 Associate Program Director, Psychiatry Residency Program, Baptist Hospitals of Southeast Texas, Beaumont, TX.

Email address of Primary Author: aditixavier14@gmail.com