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A potential case of refeeding syndrome in a patient with severe mental illness

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Abstract

Refeeding syndrome (RFS) occurs when previously malnourished patients are reintroduced to nutritional support, triggering a metabolic response that often results in electrolyte abnormalities, vitamin deficiencies, and potential end organ disturbance. Whereas RFS has been well documented in patients with eating disorders, its presentation in those with severe mental illness (SMI), such as schizophrenia, is less commonly reported. This report highlights a case of schizophrenia-induced starvation and the potential development of RFS during an inpatient psychiatric hospitalization. RFS may not always be identified in patients, especially when its presentation deviates from classic signs and symptoms. Increased awareness of the signs, symptoms, and at-risk populations, including individuals with SMI, may aid in the prevention and management of RFS.

Keywords: refeeding syndrome, severe mental illness, psychosis

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Background

Refeeding syndrome (RFS) is a potentially life-threatening condition that occurs when nutritional support is reintroduced after prolonged starvation or severe malnutrition.[1] First described in the 1940s among starved prisoners of war, RFS is characterized by a profound metabolic response as the body transitions from a catabolic, starved state to an anabolic, fed state.[2-5] This shift triggers insulin secretion, leading to cellular uptake of glucose, potassium, magnesium, and phosphate, often resulting in electrolyte imbalances and metabolic derangements.[1] Despite its clinical significance, RFS has lacked a standardized definition, and its presentation can vary widely, complicating diagnosis and management. Historically, a distinguishing feature of RFS has been hypophosphatemia, being documented in up to 96% of cases.[1-3,5-9] However, the 2020 American Society for Parenteral and Enteral Nutrition (ASPEN) consensus recommendations propose diagnostic criteria as a decrease in serum phosphorous, potassium, and/or magnesium levels (at least a 10% to 20% change), and/or organ dysfunction resulting from a decrease in any of these and/or due to thiamine deficiency all occurring within 5 days of reintroduction of calories.[10] Signs and symptoms of severe RFS that may signify end-organ disturbance include respiratory failure, cardiac arrythmias, cardiac decompensation including fluid overload, and seizures. Early in the refeeding process, liver enzyme elevations may also occur, reflecting hepatocellular stress.[5,6,11] Symptoms typically emerge within 1 to 3 days after the initiation of refeeding although onset can be delayed for up to 5 days in some cases.[1]

The National Institute for Health and Clinical Excellence (NICE) 2006 guidelines provide general criteria for identifying

individuals at higher risk of developing RFS.[12] The criteria for high-risk include 2 of the following: body mass index (BMI)<18.5 kg/m^2, unintentional weight loss exceeding 10% over the past 3 to 6 months, little to no oral intake for more than 5 days, or a history of alcohol or drug misuse. According to other literature, high-risk populations include individuals with chronic malnutrition, malabsorptive syndromes, malignancy, chronic medical conditions, older adults, and certain postoperative patients.[1-3,9] Additionally, several psychiatric conditions, including eating disorders, depression, catatonia, and severe mental illness (SMI) such as schizophrenia, have been linked to an increased risk of RFS.[10,13,14] In these cases, malnutrition—whether resulting from self-imposed starvation, food refusal related to a lack of motivation, emotional distress, immobilization and withdrawal, or neglect due to psychosis—may contribute to the development of RFS.[10,13,14] Whereas there are multiple cases describing anorexia nervosa and RFS, reports of RFS in SMI remains limited.[2,5,9,11] This report describes a patient with schizophrenia-induced starvation, highlighting a potential presentation of RFS during inpatient psychiatric stabilization at a Veterans Affairs Medical Center (VAMC). An internal institutional review was completed and approved for publication.

Case

A 28-year-old male was transferred to a VAMC inpatient psychiatric unit after less than 24 hours at an outside hospital (OSH) due to altered mental status and suicidal ideation. His past psychiatric history was significant for unspecified psychosis with no notable past medical or social history. Per collateral, he had recently been becoming more paranoid and was only drinking bottled water and eating prepacked foods due to fear of being poisoned. It was unknown at the time how much oral intake the patient had prior to admission; however, his recorded weight at the OSH was 59.1 kg (BMI 18.2 kg/m^2), which was 16 kg lower than his last recorded weight 2 years prior. Historical medications included olanzapine and bupropion; however, no medications were filled by the patient in over a year.

Labs from the OSH were remarkable for sodium 149 mmol/L, creatine kinase 657 U/L, serum creatinine 1.4 mg/dL, magnesium (Mg) 1.6 mg/dL, carbon dioxide 12.7 mmol/L, and an electrocardiogram (EKG) displaying sinus tachycardia at 117 beats per minute with ST segment depression. Before his transfer to the VAMC, he had received 2000 mL of normal saline intravenously (IV) and a 1-time dose of haloperidol 5 mg intramuscularly (IM).

Upon arrival to the VAMC inpatient psychiatric unit (hospital day [HD] 1), the patient continued to appear confused and paranoid. He denied auditory or visual hallucinations; however, during his initial intake interview, he appeared to be responding to internal stimuli. On HD 3 haloperidol 5 mg by mouth at bedtime was ordered; however, the patient was refusing all oral intake including food, liquids, and medications. From HD 1 to HD 7, the patient had no oral intake noted by nursing staff. On HD 5, he had a weight recorded of 57.3 kg (BMI 17.6 kg/m^2), which was a decrease of 1.7 kg from his initial weight at the OSH. He appeared cachectic as noted by staff and, therefore, was sent to the hospital's urgent care clinic and was given 1000 mL of normal saline IV and also received a 1-time dose of haloperidol 5 mg IM. No other medications were administered on HD 6 or HD 7. On HD 8, it was noted that the patient was more talkative and appeared less paranoid. He also began taking haloperidol 5 mg by mouth and began eating and drinking. He allowed nursing staff to complete a blood draw, which was remarkable for aspartate aminotransferase (AST) 84 U/L, alanine aminotransferase (ALT) 55 U/L and calcium 10.6 mg/dL. By HD 11, nursing staff noted that he was eating at least 50% to 75% of all 3 meals daily. On HD 18, haloperidol was titrated to 10 mg by mouth at bedtime, and on HD 19, an initial loading dose of haloperidol decanoate 100 mg IM was given. Oral haloperidol 10 mg at bedtime was continued after the haloperidol decanoate injection for overlap. Additionally, on HD 19, the patient complained of generalized body swelling, and it was noted that the patient had 2+ pitting edema in his lower extremities. Labs obtained that day were significant for albumin 3.1 g/dL, AST 94 U/L, ALT 104 U/L, and Mg 1.5 mg/dL. Due to hypomagnesemia, he was started on magnesium oxide 400 mg daily. Labs were drawn again on HD 22, and they were remarkable for AST 112 U/L, ALT 180 U/L, NT-proBNP 711 pg/mL, and nonspecific ST changes on EKG. A phosphate level was also obtained, and it resulted as within normal limits at 3.5 mg/dL. His weight was recorded at 73.5 kg, and this was a 16.2 kg weight gain from his recorded weight on HD 5. After discussion, the oral overlap of haloperidol was discontinued on HD 22 due to concerns that it could potentially be contributing to increases in liver function tests. Transaminases peaked on HD 24 with a recorded AST of 115 U/L and ALT of 201 U/L. On HD 29, given continued improvements in symptomatology and lab values and resolution of edema, the patient was administered a second loading dose of haloperidol decanoate 100 mg IM and discharged with a diagnosis of schizophrenia. The patient was instructed to continue haloperidol decanoate injections monthly in the outpatient setting. See the Table for a summary of the patient's weights and laboratory values.

Discussion

This case reflects a potential atypical presentation of RFS. According to the NICE 2006 guidelines, our patient met criteria for being at high risk for RFS due to a BMI <18.5 kg/m^2 and little or no oral intake for more than 5 days.[12] Whereas RFS traditionally presents with hypophosphatemia, this patient's

TABLE: Patient labs and weights over the course of the hospital stay

Timeline	Weight kg	BMI kg/m^2	Na mmol/L	CK U/L	Mg mg/dL	CO^2 mmol/L	SCr mg/dL	AST U/L	ALT U/L	UDS	BAL mg/dL	Ca mg/dL	Alb g/dL	Ph mg/dL	NT-proBNP pg/mL
OSH	59.1	18.2	149 (H)	657 (H)	1.6 (L)	12.7 (L)	1.4 (H)	33	16	Neg	< 10	–		–	–
HD 2	60.7	18.7	–	–	–	–	–	–	–	–	–	–	–	–	–
HD 5	57.3	17.6	–	–	–	–	–	–	–	–	–	–	–	–	–
HD 8	–	–	–	–	–	–	–	84 (H)	55	–	–	10.6 (H)	–	–	–
HD 19	–	–	–	–	1.5 (L)	–	–	94 (H)	104 (H)	–	–	–	3.1 (L)	–	–
HD 22	73.5	22.6	–	103	1.7	–	–	112 (H)	180 (H)	–	–	–	–	3.5	711 (H)
HD 24	–	–	–	–	–	–	–	115 (H)	201 (H)	–	–	–	–	–	–
HD 29	–	–	–	–	–	–	–	41	131 (H)	–	–	–	–	–	163 (H)

Alb = albumin; ALT = alanine aminotransferase; AST = aspartate aminotransferase; BAL = blood alcohol level; BMI = body mass index; Ca = calcium; CK = creatine kinase; CO^2 = carbon dioxide; H = high lab value; HD = hospital day; L = low lab value; Mg = magnesium; Na = sodium; OSH = outside hospital; Ph = phosphate; SCr = serum creatinine; UDS = urine drug screen.

phosphate concentration was not checked until 14 days post refeeding and was normal at that time. However, the patient did experience hypomagnesemia, which resolved with oral supplementation. Based on 2020 ASPEN recommendations, this would not fall into the criteria for RFS as there was not a 10% to 20% decrease in value from his baseline Mg. However, the time between baseline Mg and the level on HD 19 makes it difficult to trend for any significant changes over the period of reintroduction of food.[10] Furthermore, our patient experienced elevated AST/ALT and NT-proBNP levels with edema, all of which can be clinical indicators of RFS. Elevations in liver enzymes may be seen in RFS in the first weeks after refeeding and typically remain <500 U/L.[5,6,11] This effect is more common in patients being refed enterally and typically resolve with a reduction in rate of feeding.[6,11] Given the elevated NT-proBNP and 2+ pitting edema, it is likely that our patient was also experiencing cardiac stress, which has been related to end-organ involvement in RFS.[10] In this case, our patient's symptoms resolved without significant intervention. Whereas limited data make this case hard to fully interpret, additional steps could have been taken to lower the patient's overall risk for developing RFS. Prevention and management of RFS rely on identifying at-risk individuals, obtaining baseline monitoring including magnesium and phosphate, and carefully initiating nutritional support. Per ASPEN 2020 guidance, recommendations for avoidance and treatment of RFS in at-risk adults include a slow reintroduction of calories at 10 to 20 kcal/kg for the first 24 hours and then advancing by 33% of goal every 1 to 2 days, frequent monitoring of electrolyte concentrations at least every 12 to 24 hours for the first 3 days in high-risk patients, and supplementation of thiamine.[10]

It is important to consider differential causes regarding this patient's presentation. There is a possibility of drug-induced abnormalities. Liver dysfunction is a possible adverse effect of antipsychotics as a class, but the exact underlying mechanisms remain unclear.[15,16] Applying the Naranjo scale, this case is classified as a possible adverse drug reaction with a score of 2.[17] Other case reports suggest a link between elevated transaminases and haloperidol; however, elevations were typically seen after several weeks at higher dosages or confounded by the presence of antipsychotic polypharmacy.[15,16,18,19] Given this and the presence of other, more compelling, factors addressed earlier, a medication-induced etiology is less likely.

There are various limitations within this case that speak to the importance of identifying high-risk patients. It is difficult to draw any definitive conclusions to the cause of this patient's symptoms due to its retrospective nature and the absence of laboratory monitoring at baseline and from the initiation of oral intake until the onset of edema. Moreover, it is unclear how the patient's weight was obtained, and it was likely not standardized. Standardization of weight monitoring, such as using standard scales, proper techniques, and calibration procedures, in patients at risk

for RFS is paramount to understanding the clinical picture. Additional monitoring and workup would have provided further insight into this patient's case. This underlines the importance of awareness, proper identification, and treatment of RFS within an inpatient psychiatric population.

Conclusion

This case emphasizes the complexity of diagnosing and managing RFS. Although our patient met criteria for being high risk for RFS per NICE guidelines, the atypical presentation and limited laboratory/weight monitoring hindered definitive diagnosis. The absence of significant hypophosphatemia and the presence of elevated liver enzymes, cardiac stress markers, and generalized edema highlight the variable clinical manifestations of RFS. This case demonstrates the importance of awareness, early identification, and implementation of preventative strategies in at-risk psychiatric populations.

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