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Author

Logan, Jennifer

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CLINICAL VIGNETTE

Prevention of Refeeding Syndrome in the Outpatient Setting

Jennifer Logan, M.D.

Introduction

Refeeding syndrome (RFS) is a constellation of potentially fatal metabolic derangements that may occur in the context of recommencement of caloric supplementation after a prolonged period of malnutrition. Although typically thought of as relating to anorexic patients, it was in fact first observed when liberated prisoners of World War II became severely ill after return to a normal diet; RFS may also occur in those with malabsorptive syndromes, malignancy, or even chronic weight loss in the context of obesity. Because of its broad spectrum of clinical presentations, the lack of well-defined diagnostic criteria, and the high risk of morbidity and mortality, it is important to understand this complicated illness. Presented here is the case of a 48-year-old woman at high risk of RFS and managed on an outpatient basis.

Case Report

A 48-year-old otherwise healthy female presented to a primary care clinic to establish care for her annual physical examination. She had no complaints and her history was notable only for a total abdominal hysterectomy with bilateral salpingo-oophorectomy for a benign ovarian cyst and early cervical cancer, for which she sees a gynecologist. Vital sign measurement revealed temperature 36.8°C, blood pressure 86/55 mm Hg, pulse 67, and oxygen saturation 98% on room air. Her height was five feet nine inches and weight was 95 pounds and 9.6 ounces, resulting in a body mass index of 14.11 kg/m² (67% of her ideal body weight). She was observed to be a cachectic woman in no apparent distress; exam was otherwise unremarkable. Upon further questioning regarding her weight, she stated that she generally had low body weight throughout her life, which she felt worsened when she was distracted with work. She denied intentional restricting or purging. A clinical nutrition referral was placed but delayed due to the holidays. Bone density scan and echocardiogram were ordered and laboratory evaluation performed; pertinent results included potassium 2.7 and bicarbonate 40, confirmed on repeat testing. Other labs were normal including CBC, CMP, FLP, TSH, vitamin D, ionized calcium, phosphorus, magnesium, amylase, lipase, and thiamine. EKG showed only normal sinus rhythm with nonspecific T-wave changes. The patient was prescribed potassium repletion and thiamine supplementation and was given strict instructions to not advance her diet until

electrolyte normalization given high risk for RFS and its potentially fatal complications. Hospitalization was considered but could not be arranged. Upon electrolyte repletion, her diet was advanced and she was seen at three day intervals for repeat lab testing, lengthening to one week intervals after the first two weeks, then monthly. Her echocardiogram was normal and her bone density scan revealed osteopenia, for which she started calcium and vitamin D supplementation. After one month, she had gained ten pounds and was attending psychological and nutritional counseling. She is doing well.

Discussion

The pathophysiology of RFS begins with the metabolic abnormalities of the chronically malnourished patient, in whom the body shifts to lipid metabolism once glycogen stores are depleted. This leads to a reduction of insulin secretion and a subsequent reduction of intracellular and extracellular phosphorus, potassium, magnesium, sodium, and water; thus, many such patients have baseline hypokalemia in addition to commonly-found anemia and leukocytopenia, as well as bradycardia and hypotension.¹ When carbohydrates are reintroduced with refeeding, the already-low extracellular electrolytes move intracellularly for anabolic processes, resulting in devastating deficiencies. Hypophosphatemia is perhaps the most significant metabolic derangement, given its role in ATP synthesis, as it can lead to ischemia of multiple organs including the muscles that support respiration. Hypomagnesemia and hypokalemia can lead to cardiac arrhythmias, the most common cause of death in RFS.² Furthermore, fluid overload secondary to sodium retention can place strain on a heart that may already be atrophied by chronic malnutrition. Acute thiamine deficiency is also a grave concern as it is consumed rapidly for glucose metabolism and thus may lead to precipitation of Wernicke-Korsakoff encephalopathy.

Because of this complex array of effects, there exist no standardized diagnostic criteria for RFS. The diagnosis is based on risk factors for RFS and the occurrence of symptoms after refeeding, which may range from diarrhea and vomiting to respiratory failure, arrhythmias, rhabdomyolysis, coma, and death.³ Despite the importance of slow reintroduction of calories, the severity of RFS appears to be more closely

correlated with degree of initial malnutrition as measured by body mass index.⁴ Other factors found to be associated with high risk of RFS include pre-refeeding electrolyte abnormalities, little or no nutritional intake for over 10 days, or weight loss of >15% in the last three to six months.⁵

Treatment focuses on what is essentially permissive underfeeding with close monitoring and repletion of electrolytes: specifically, phosphorus, magnesium, calcium, sodium, and potassium.³ Reducing the reintroduction of carbohydrates will result in a smaller insulin surge and thus a more gradual shift in electrolytes. The rate of nutritional advancement is controversial but should typically not exceed 5-10 kcal/kg/d, or 200-300 kcal every 3-4 days.² This can generally be achieved with oral nutrition, although total parenteral nutrition may be reserved for extremely high-risk patients. Patients should be monitored for signs of fluid overload, respiratory distress, or cardiac compromise; even a mildly elevated heart rate can be an ominous sign of RFS in a normally bradycardic anorexic patient.⁶ Patients should be placed on thiamine supplementation to prevent Wernicke-Korsakoff syndrome. The risk of RFS is highest in the first two weeks; after this, clinical and laboratory reassessment may be performed with reduced frequency.

Conclusion

Because of her severely low body weight in the context of marked baseline hypokalemia, bradycardia, and hypotension, the aforementioned patient was at high risk of RFS—particularly the cardiac complications that are the most frequent cause of death. In this instance inpatient monitoring may have been the safest course but often cannot be arranged; thus, the outpatient physician must proceed with aggressive electrolyte repletion, cautious dietary advancement, and extremely close clinical follow-up particularly in the first two weeks. Further studies are needed to establish consensus guidelines regarding the diagnosis and management of RFS.

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