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Case Report

Management of Refeeding Syndrome in the Intensive Care Unit: A Case Report

Aslı MELEK SAVAŞ[1]*, Elif Beyza BASKAN[1]

1. Atatürk Sanatoryum Training and Research Hospital, Department of Anaesthesiology and Reanimation, Subdivision of Intensive Care Medicine, Ankara, Türkiye
**Corresponding author*

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ORCID:
AMS: 0000-0003-4187-4735
EBB: 0000-0002-3053-2003

Corresponding author:
Aslı Melek Savaş,
Atatürk Sanatoryum Training and Research Hospital, Ankara, Türkiye
aslimelek121@gmail.com

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Abstract

Introduction: Refeeding syndrome is a serious clinical condition that occurs when nutrition is reintroduced after a period of prolonged malnutrition. It can lead to edema and heart failure due to sodium and water retention, as well as hypokalemia, hypophosphatemia, hypomagnesemia, thiamine deficiency, and even fatal outcomes.

Case Presentation: A 58-year-old male patient was admitted to the ICU with soft tissue infection in the left foot and septic shock. Due to hypoglycemia, a dextrose infusion was initiated. On the second day, the patient developed hypophosphatemia, hypokalemia, and hypomagnesemia. Given his low body mass index (BMI) and history of prolonged malnutrition, refeeding syndrome was diagnosed. Phosphate, potassium, magnesium, and thiamine replacement were administered. Since the patient refused enteral feeding, low-dose parenteral nutrition was initiated. Due to a decrease in platelet count, a peripheral blood smear was performed, and a hematology consultation was requested. Hematology specialists suggested that the thrombocytopenia might be related to the patient's clinical condition.

Conclusion: Since malnutrition is highly prevalent in ICU patients, refeeding syndrome remains a significant risk factor. Early recognition and appropriate management of the syndrome are crucial in preventing serious complications.

Keywords

Refeeding syndrome, hypophosphatemia, phosphate replacement, thrombocytopenia, electrolyte imbalance

Introduction

Refeeding syndrome is a serious complication that occurs when nutrition is reintroduced after a period of prolonged malnourishment, potentially leading to severe metabolic and electrolyte imbalances and, in some cases, even death. Its clinical features include oedema and heart failure due to sodium and water retention, along with hypokalaemia, hypophosphatemia, hypomagnesemia, and thiamine depletion, which can result in Wernicke's encephalopathy and lactic acidosis [1].

Prolonged starvation leads to the depletion of the body's energy reserves and intracellular electrolyte stores. A sudden increase in blood glucose levels triggers a rise in insulin secretion, leading to the intracellular shift of glucose, potassium, and phosphate. Increased glycolysis leads to the utilization of phosphate and thiamine. These mechanisms result in a decrease in serum potassium, phosphate, and thiamine levels. Additionally, serum magnesium levels drop, the exact cause of which is not fully understood but may be related to intracellular shifts, increased metabolic demands, and possible gastrointestinal losses [2].

Suspicion, recognition of risk factors, and careful adjustment of the initial feeding dose are key to preventing serious complications [3].

The aim of this case report is to review the important points in the management of refeeding syndrome in intensive care, to draw attention to the limitations in the management of hypophosphatemia considering the formulations available in our country and to discuss whether there is a relationship between refeeding syndrome and thrombocytopenia.

Case Presentation

A 58-year-old patient with sepsis was admitted to our intensive care unit. On admission his pulse rate was 54/min, blood pressure was 74/54 mmHg and oxygen saturation was 98%.

On admission, he presented with a severe soft tissue infection in his left foot with a white blood cell count of 10.9 10^3/uL, C-reactive protein (CRP) of 102 mg/L and procalcitonin (PCT) of 0.19 uq/L. He was in septic shock. His medical history included squamous cell carcinoma removal from his left foot ten years prior. Empirical sulbactam-ampicillin therapy was initiated promptly by the infectious diseases department.

Following an initial fluid bolus of 30 mL/kg with a balanced electrolyte solution, a norepinephrine infusion was started due to a mean arterial pressure below 65 mmHg and elevated lactate levels on arterial blood gas analysis.

He was cachectic, with a body weight of 45 kg, height 165 cm and a body mass index (BMI) of 16.52. His son reported that he had been eating very little for at least a month, had experienced weight loss, and had refused to seek medical care for his foot until his overall condition worsened. At admission, his Glasgow Coma Scale score was 15. He continued to refuse food in the intensive care unit and declined nasogastric tube placement for enteral feeding. Due to a blood glucose level of 78 mg/dL, 20% dextrose solution was initiated at a rate of 10 ml/h. His initial phosphate level was 3.4 mg/dL. A total of 120 kcal (2.66kcal/kg) was administered on the first day over a period of 12 hours in the intensive care unit.

On the second day of admission, his phosphate, potassium, and magnesium levels were detected to be low, with phosphate at 1.3 mg/dL, potassium at 2.9 mEq/L, and magnesium at 1.5 mg/dL. We gave intravenous potassium and magnesium replacement. Since phosphate replacement was not available in the hospital pharmacy, a magistral oral phosphate replacement solution was prescribed from an external pharmacy. The formulation contained 15 mmol of phosphate per 10 mL.

Due to hypoglycaemia, intravenous dextrose therapy was continued. Given the patient's prolonged malnourishment, low BMI, and high risk of refeeding syndrome, we aimed to start at a conservative dose of 5 kcal/kg. A total of 192 kcal (4.26 kcal/kg) was administered to the patient on the second day. We initiated thiamine replacement at a dose of 50 mg twice daily.

Due to a CRP level of 102 mg/L and the presence of foul-smelling drainage in the wound on his foot, ciprofloxacin and metronidazole were added to the antibiotic treatment. Additionally, we requested a psychiatric consultation due to his refusal to eat and started quetiapine 25 mg once daily based on the psychiatric recommendation.

On the third day, the patient's oral phosphate replacement became available, and a replacement regimen of 3×15 mmol was planned to achieve a total daily dose of 1 mmol/kg. However, as the patient refused part of the replacement and the placement of a nasogastric tube, only 2×15 mmol could be administered.

On the 4th day, he developed diarrhea. To rule out an infection, we sent a stool sample for microscopic investigation, culture, and Clostridium difficile antigen testing. We suspected that this could also be related to oral phosphate supplementation however, phosphate replacement could not be switched to intravenous due to the unavailability of an intravenous formulation. With a CRP level of 124 mg/L and a PCT level of 0.28 µg/L, ciprofloxacin was discontinued in the patient who still required norepinephrine infusion, and therapy was switched to piperacillin-tazobactam. We initiated total parenteral nutrition (TPN) therapy because the patient refused enteral feeding, starting with a target of 5 kcal/kg.

By the fifth day of treatment, his phosphate level had risen to 2.2 mg/dL, potassium level to 2.6 mEq/L, and magnesium level to 1.7 mg/dL. Consequently, we increased his TPN dose to 10kcal/kg while maintaining oral phosphate supplementation and intravenous potassium replacement. On the 7th day, as the patient accepted oral intake, the oral diet was introduced while maintaining TPN support, with a total daily calorie intake targeted at 15–20 kcal/kg.

On the 8th day, empirical piperacillin-tazobactam was replaced with empirical meropenem due to the development of thrombocytopenia, with platelet levels decreasing from 498,000/µL to 86,000/µL. On the 10th day of hospitalization, daptomycin was added following the detection of osteomyelitis on MRI imaging.
Informed consent was obtained from the patient for the case to be presented and published.

Discussion

According to the nutrition guidelines of the National Institute for Clinical Excellence (NICE), individuals at high risk of developing refeeding syndrome can be identified based on specific criteria. A patient is

considered high risk if they meet one or more of the following conditions: a BMI below 16 kg/m^2, unintentional weight loss of more than 15% in the past 3–6 months, little or no nutritional intake for over 10 days, or low levels of potassium, phosphate, or magnesium before feeding. Alternatively, a patient is also classified as high risk if they meet two or more of the following criteria: a BMI below 18.5 kg/m^2, unintentional weight loss exceeding 10% in the past 3–6 months, minimal or no nutritional intake for over 5 days, or a history of alcohol abuse or medication use, including insulin, chemotherapy, antacids, or diuretics [4]. In patients at risk of refeeding syndrome, caloric replacement should be initiated at a low dose and gradually increased over 5–10 days. Daily electrolyte monitoring is recommended during the first 72 hours after starting nutrition [5].

Our patient had a BMI of 16.52, along with a history of malnutrition and weight loss; therefore, he was at risk of refeeding syndrome. Despite the administration of a low-calorie intake, the rapid development of hypophosphatemia, hypokalaemia, and hypomagnesemia confirmed this condition.

Hypophosphatemia can be classified as mild (2–2.5 mg/dL), moderate (1–1.9 mg/dL), and severe (<1 mg/dL) based on serum phosphate levels. Oral phosphate replacement can be administered in mild and moderate hypophosphatemia [6]. Intravenous replacement is recommended for symptomatic hypophosphatemia and severe hypophosphatemia. Intravenous phosphate replacement may lead to complications such as hyperphosphatemia, hypomagnesemia, hypocalcaemia, and hypotension. Therefore, it is crucial to administer it with the appropriate indication and at the correct dose [7].

In our case, after refeeding, the patient's phosphate level dropped to 1.3 mg/dL, and oral phosphate supplementation was initiated for the treatment of moderate hypophosphatemia. Even after the patient developed diarrhea, we were unable to switch to the intravenous route due to the current unavailability of the intravenous formulation in Türkiye.

Severe hypophosphatemia can lead to hematologic effects such as thrombocytopenia, impaired clotting processes, reduced leukocyte phagocytosis, and increased haemoglobin affinity for oxygen due to the depletion of erythrocyte 2,3-diphosphoglycerate (2,3-DPG) [8].

There are limited studies in the literature discussing the relationship between thrombocytopenia and hypophosphatemia. In a study conducted on dogs by Yawata et al., hypophosphatemia was found to be associated with thrombocytopenia [9]. In 2015, a case of severe hypophosphatemia-associated thrombocytopenia was reported in a 16-year-old patient with diabetic ketoacidosis [10].

In our case, a peripheral blood smear was performed, and a haematology consultation was requested due to a drop in platelet levels. However, since the patient was experiencing both refeeding syndrome and septic shock simultaneously, the exact cause of thrombocytopenia could not be definitively determined.

Conclusion

Refeeding syndrome is a clinical condition that can lead to fatal outcomes if not diagnosed and treated early. The high prevalence of prolonged starvation in intensive care units is a significant risk factor for the development of refeeding syndrome.

Author contribution statement

All authors (AMS, EBB) participated in the planning, writing, editing, and review of this manuscript.

Declaration of patient consent

Informed consent was obtained from the patient for the case to be presented and published.

Conflicts of interest

None Declared.

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