Refeeding syndrome after small bowel obstruction - a case report

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ABSTRACT

Background: Refeeding Syndrome (RS) is an under-recognized pathophysiological process that can result in arrhythmias, coma, and death if not identified and managed appropriately.

Case Presentation: This case report discusses RS in a 77-year-old female who presented with 6 days of total anorexia secondary to abdominal pain and vomiting. The patient was identified to have an ischaemic closed loop obstruction of the small bowel in a right femoral hernia with associated proximal small bowel obstruction. Following a small bowel resection, nutrition was reintroduced where on day 3 the patient developed hypophosphataemia, the hallmark of RS.

Conclusion: This case highlights the importance of considering RS in patients with a seemingly short duration of starvation due to acute intercurrent illness such as in this case a small bowel obstruction.

Keywords: Refeeding syndrome, hypophosphataemia, starvation, acute illness, small bowel obstruction, emergency medicine, intensive care.

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Background

Prolonged starvation and malnourishment can cause changes in metabolism that result in dangerous and sometimes fatal electrolyte derangement upon reintroducing nutrition. The pathophysiological processes of refeeding syndrome (RS) were first investigated during the World War II period as a result of starvation in conscientious objectors of war and Japanese prisoners of war [1,2]. Similar pathophysiological processes have been identified in modern society; more commonly in malnourished individuals secondary to an acute illness, people suffering from eating disorders, poor social circumstances limiting food intake, or in patients with alcoholism. Older patients with coexisting disease are particularly at risk of developing RS. Other high risk patient groups include poorly controlled diabetics, oncology patients, chronic alcoholics, and those with malabsorptive syndromes such as inflammatory bowel disease and chronic pancreatitis [3]. Underdiagnosis of RS is well documented; therefore, incidence in various published reports vary, ranging from 6% to 34% [4–6]. This case report is important to raise awareness as RS is relatively common and underreported and it can lead to arrhythmias, coma, and death if not managed appropriately.

Case Presentation

This case study is based on a 77-year-old retired Caucasian female who presented to the Emergency Department (ED) with a 6-day history of vomiting and abdominal pain. The past medical history included hypertension, vasovagal episodes, gastric oesophageal reflux disease, hypercholesterolaemia, and a prolapsed uterus. She had undergone a rectal polypectomy in previous years but no surgical history. Her medications were amlodipine, alendronic acid, bisoprolol, and atorvastatin. Alendronic acid was prescribed to prevent fragility fractures as osteoporosis was diagnosed following a bone density scan in 2017. She lived with her husband who she cared for and smoked four cigarettes a day. She did not consume alcohol and had a healthy body mass index (BMI) of 22.6. It was noted that the patient had felt unable to eat for 6 days preceding her visit to the ED. She had visited her general practitioner three times and the ED once, each time informed that she was suffering from gastroenteritis. The patient had no history of diarrhoea, she had not passed a stool in four days and she reported decreased urine output. The patient was complaining of epigastric pain, rated 9/10 when asked for a pain score and right lower quadrant pain which was worse on vomiting, which was later identified as feculent vomiting. The patient's initial venous blood gas (Table 1) demonstrates a number of abnormalities, the most concerning initially was the metabolic lactic acidosis and hyperkalaemia.

She was treated for the hyperkalaemia and an acute kidney injury (AKI) stage one. The AKI was likely caused

Table 1. Initial venous blood gas.

pH	7.27
pCO_2	3.91
pO_2	3.93
HCO_3^-	13.1
BE	–12.3
Na^+	127.9
K^+	6.20
Ca^{2+}	0.98
Cl^-	87
Glu	9.7
Lac	8.37

by decreased kidney perfusion secondary to renal artery vasoconstriction, due to the limited intake of food and fluid and frequent vomiting causing hypovolaemia [7]. Fluid resuscitation was commenced and a urinary catheter inserted for ongoing monitoring of urine output. Her electrocardiogram demonstrated tall peaked T waves suggestive of hyperkalaemia with tachycardia; there were no P wave changes, QRS complex prolongation, or sine wave patterns suggesting severe hyperkalaemia (Figure 1). The hyperkalaemia could have been caused by the decreased excretion of potassium by the kidneys due to the AKI, but also compounded by the cell destruction in the ischaemic bowel and concurrent metabolic acidosis [7]. On examination, she looked ill, dehydrated with a dry tongue, and could barely keep her eyes open. She had cold and cyanosed peripheries, a distended suprapubic region, scant bowel sounds, and an irreducible right femoral hernia was noted.

The patient had total anorexia for 6 days due to vomiting and in total seven days due to the surgery. Post-surgery she started parenteral nutrition and after doing so, developed clinically significant hypophosphataemia. RS is defined by severe shifts in electrolytes and fluids after refeeding in patients who have been starved or who are severely malnourished [8]. Fluid balance abnormalities can occur, alterations in glucose metabolism,

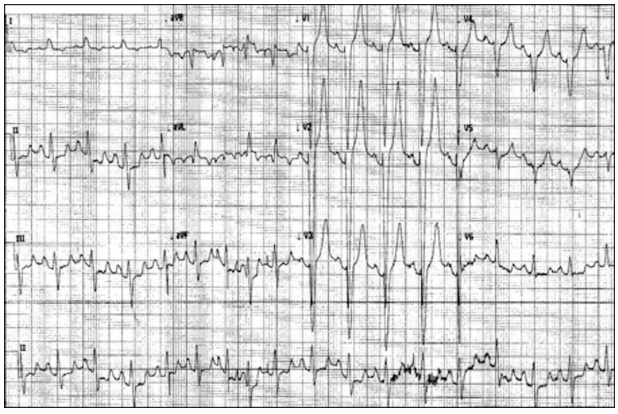

Figure 1. *Electrocardiogram at presentation.*

hypophosphataemia, hypomagnesaemia, hypokalaemia, and low thiamine levels [8]. During the initial stages of starvation, the body compensates by using glycogen stores from the liver for energy and skeletal muscle catabolism which provides amino acids for gluconeogenesis [9]. Additionally, a number of glucose counterregulatory hormones are released to maintain homeostasis and prevent hypoglycemia [10]. Insulin secretion from the beta cells of the pancreas are reduced thus the inhibition of glucose secretion is reduced [10]. The initial counterregulatory hormones secreted are glucagon from the alpha cells of the pancreas and adrenaline secretion from the adrenal glands resulting in glucose release from the liver [10]. In times of chronic hypoglycemia, growth hormone and cortisol may be released which increase blood glucose by glucose sparing [10]. The prolonged stress on the body in this patient may have increased the cortisol secretion resulting in use of fat and protein as a fuel source resulting in weight loss and hyperglycemia. This is evident as the blood glucose on presentation was slightly elevated at 9.7 mmol/l and the patient noted that she had lost weight over the preceding 6 days. After approximately 4 days, energy is derived from the beta oxidation of free fatty acids which increases ketone production and results in cessation of protein catabolism within skeletal muscles [9]. This ketosis combined with the lactate production is likely the cause of the raised anion gap metabolic acidosis of 34 where normal is less than 20 [11].

$(Na^+ + K^+) – (Cl^- + HCO3^-)$ = anion gap

(127.9 + 6.20) – (87 + 13.1) = 34 mEq/L

In turn, less insulin is secreted from the pancreas which depletes many intracellular electrolytes, but specifically phosphate. The serum phosphate may appear normal if tested at this point [3]. When refeeding occurs either parenterally or enterally, insulin is secreted due to increased carbohydrate consumption, rather than gaining energy from fat and protein catabolism. Insulin promotes the shift of potassium back into the cells through action on sodium potassium pumps, along with magnesium, phosphate, glucose, and finally water by osmosis [3]. This results in low serum levels of these electrolytes and significant fluid shifts.

Normal serum phosphate concentration is between 0.80 and 1.50 mmol/L, so a phosphate less than 0.80 mmol/L is considered hypophosphataemia; however, levels less than 0.50 mmol/L are when clinical features of RS may manifest [12]. Phosphate is an important intracellular anion by forming the phospholipid bilayer, enzymatic and second messenger activation, energy storage in the form of adenosine triphosphate (ATP), and assists oxygen release from oxyhaemoglobin to the tissues by regulating levels of 2,3-diphosphoglycerate (2,3-DPG) in erythrocytes [13]. Hypophosphataemia can result in significant abnormalities of the neurological, cardiovascular, respiratory, and haematological systems [9]. More specifically,

the decrease in 2,3-DPG results in greater affinity of haemoglobin for oxygen and less oxygen being available for release to the tissues [14].

Potassium is an intracellular cation that moves back into the cell on refeeding due to the action of insulin, thus resulting in hypokalaemia. This in turn causes instability of the electrochemical membrane potential resulting in increased duration of the action potential and refractory period which often manifests as cardiac arrhythmias potentially leading to cardiac arrest.

Similarly, magnesium is an intracellular cation and is important for the synthesis of DNA, RNA, electrical potential of nerve and muscle fibers, and many enzymatic reactions involving ATP [10]. Therefore, hypomagnesaemia may result in effects on the membrane potential and lead to cardiac and neuromuscular dysfunction [3].

The consumption of glucose after prolonged starvation will result in insulin secretion and suppression of gluconeogenesis. If excess glucose is consumed during the introduction of foods, this may result in hyperglycemia and osmotic diuresis precipitating dehydration, fluid shifts, and metabolic ketoacidosis [3].

Thiamine is a necessary component of the pyruvate dehydrogenase complex, which is an important enzyme utilized to convert pyruvate into acetyl coenzyme A for entry into the citric acid cycle to produce ATP [9]. Deficiencies in thiamine could lead to a significant decrease in energy production and instead produce excess lactate which may lead to lactic acidosis. Thiamine deficiency is common in malnourished patients who use alcohol, however, should also be considered in those with poor nutritional intake and bowel obstruction, as in this case, which may result in Wernicke's encephalopathy secondary to thiamine deficiency.

The patient underwent blood tests for full blood count, urea and electrolytes, blood cultures, group and save, a venous blood gas, electrocardiogram, and a computed tomography (CT) of the abdomen and pelvis. The CT scan demonstrated a small closed loop obstruction of the small bowel in the right femoral hernia that appeared ischaemic with associated proximal small bowel obstruction (Figures 2 and 3). With this information, the diagnosis of small bowel obstruction was made, and the patient was referred to general surgeons for discussion of further management. Severe sepsis secondary to a bowel perforation was also considered as a differential diagnosis given the abnormal observations.

The patient was taken to theatre where she had a laparotomy with 13 cm of ischaemic small bowel resected, primary anastomosis, and a right femoral hernia repair. The patient started parenteral nutrition for bowel rest post operatively. The patient subsequently developed hypophosphataemia which is the manifestation of RS in this patient. Table 2 illustrates the decline in serum phosphate after refeeding commenced and the exogenous phosphate required alongside the parenteral nutrition to normalize the phosphate.

Initially, on refeeding, patients who have been starved may retain sodium and subsequent extracellular water secondary to carbohydrate ingestion, this results in oedema and specifically pulmonary oedema which may precipitate cardiac failure [9]. Therefore, care must be given in the initial stages to limit sodium and water to reduce these deleterious consequences.

If a patient has not eaten for more than 5 days, then nutrition should be reintroduced at 50% of requirements for the first 2 days, if clinically and biochemically no RS signs present then RS can be ruled out and normal feeding resumed [15]. When a patient is at high risk of RS (Table 3), they should be managed by healthcare professionals such as dieticians and nutritionists using a controlled reintroduction of nutrition at a maximum of 10 kcal/kg/day

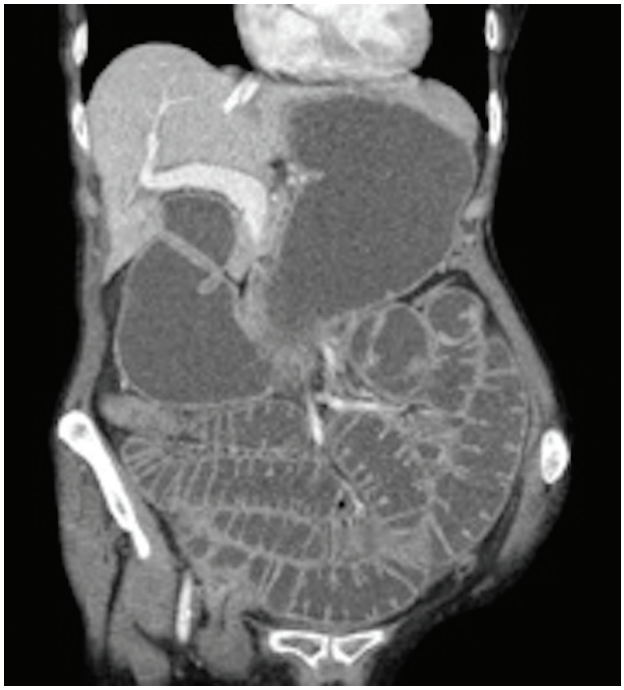

Figure 2. *Coronal plane of abdominal CT demonstrating right femoral hernia and dilated bowel loops.*

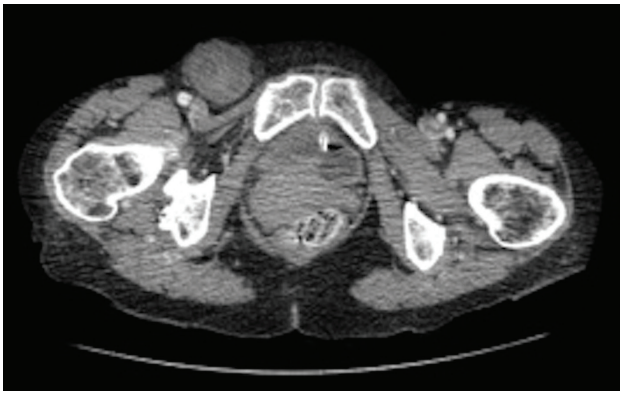

Figure 3. *Transverse plane of abdominal CT demonstrating right femoral hernia.*

Table 2. Serum phosphate levels, parenteral nutrition and exogenous phosphate administration.

Timeline post operatively	Serum phosphate (PO_4^{2-}) normal range 0.80–1.50 mmol/l	Parenteral nutrition (PN) rate (ml/hour)	Phosphate administration
Day 1	1.53	30	
Day 2	1.04	30	
Day 3	0.46	30	7.5 ml/hour IV
Day 4	0.89	40	
Day 5	0.78	50	Phosphate PO
Day 6	0.71	63	
Day 7	0.62	75	
Day 8	0.81	75 (ensure/fortisip/soft food)	

Table 3. Criteria for determining people at high risk of refeeding syndrome [19].

Patient has one or more of the following:
• BMI less than 16 kg/m^2
• Unintentional weight loss greater than 15% within the last 3–6 months
• Little or no nutritional intake for more than 10 days
• Low levels of potassium, phosphate or magnesium prior to feeding
Or patient has two or more of the following:
• BMI less than 18.5 kg/m^2
• Unintentional weight loss greater than 10% within the last 3–6 months
• Little or no nutritional intake for more than 5 days
• A history of alcohol abuse or drugs including insulin, chemotherapy, antacids or diuretics

with the aim to provide full nutritional intake between day 4 and 7 [15].

The patient's fluid status should be monitored alongside oral or intravenous thiamine/vitamin B and a balanced multivitamin supplement before and during refeeding [15]. Finally, the levels of phosphate, potassium, and magnesium should be supplemented as necessary alongside reintroduction of nutrition by using oral or intravenous supplements unless the levels are high before refeeding starts [15]. Finally, the potassium, phosphate, magnesium, calcium, urea, and creatinine should be monitored daily for 1 week then at least three times the following week [3].

The patient had lost 16 kg during her illness and was 42 kg on discharge, meaning she was underweight with a BMI of 16.4. The focus for this patient in the near future is on weight gain and nutritional repletion. Given her low BMI and significant weight loss over the preceding weeks, this patient is still an at-risk patient of RS [15].

Discussion

This case has highlighted significant electrolyte and fluid shifts that occur in the body after a period of starvation due to acute illness. The myriad of symptoms and effects of having low serum electrolytes are vast and the vitamin deficiency can have profound effect on the patient. If not considered, RS may not be detected and lead to low serum electrolytes and vitamins, fluid shifts, arrhythmias, and death if not treated. The patient was managed well with regard to correction of her hypophosphataemia and reintroduction of nutrition;however, care could have been improved with regard to the vitamin supplementation.

Conclusion

The main learning point from this case report is to consider RS in patients that have been poorly nourished or starved when they attend the ED or intensive care unit. Morbidity and mortality can be prevented by increasing awareness and suspicion of RS in these settings.

List of Abbreviations

AKI	Acute kidney injury
ATP	Adenosine triphosphate
BMI	Body mass index
CT	Computed Tomography
2,3-DPG	2,3-Diphosphoglycerate
ED	Emergency Department
RS	Refeeding Syndrome

Consent for publication

Written informed consent for this case to be published was gained from the patient.

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Summary of the case

Patients gender and age	1	77 Female
Final diagnosis	2	Refeeding Syndrome secondary to small bowel obstruction
Symptoms	3	Abdominal pain, nausea, vomiting
Medications (generic names only)	4	Amlodipine, alendronic acid, bisoprolol and atorvastatin
Clinical Procedure	5	Laparotomy with 13 centimetres of ischaemic small bowel resected, primary anastomosis and a right femoral hernia repair
Specialty	6	Emergency Medicine, General Surgery, Intensive Care