

## Case Study

# Refeeding Syndrome and the Cancer Patient

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**Patient:** 81 year old woman

**Diagnosis:** Metastatic left sided breast cancer in axillary tail grade 3, invasive lobular, oestrogen receptor and progesterone receptor positive

**Weight:** 49.8kg

**Body Mass Index:** 22.1kg/m<sup>2</sup>

### Introduction

Refeeding syndrome is a combination of metabolic and biochemical changes that are seen when nutritional support is commenced in those who have been in a starved or fasted state.<sup>1</sup> Oncology patients often present with numerous risk factors for developing this condition; malnutrition may be present due to disease related factors such as anorexia, nausea, vomiting, chemotherapy, mucositis, dysphagia and radiotherapy induced side effects which limit oral intake.<sup>2</sup>

When reintroducing nutrition in starved patients, there is a shift to carbohydrate metabolism from preferential fat metabolism which occurs during starvation. This results in a rapid increase in serum insulin, which in turn causes movement of extracellular potassium, phosphate and magnesium into the cells.<sup>1</sup> Due to the concentration gradient that occurs there can be depletion of intracellular levels of these electrolytes. Hypophosphataemia is the hallmark electrolyte abnormality seen in refeeding syndrome; however hypokalaemia and hypomagnesaemia are also common.<sup>2</sup> Furthermore, in malnourished patients commencing feeding there is increased demand for phosphate due to its role in glycolysis, thus depleting stores.<sup>2</sup> Refeeding syndrome can affect multi-organ systems (cardiovascular, gastrointestinal, musculoskeletal, respiratory, neurologic and haematologic), which can result in multi-system organ failure and death.<sup>3</sup>

Thiamine is required for glycolysis and since it is not stored in sufficient quantities, it must be supplemented in patients at risk of refeeding syndrome when feeding is initiated.<sup>3</sup> Thiamine deficiency in refeeding syndrome can result in high-output cardiac failure, metabolic acidosis and Wernicke's encephalopathy.<sup>2</sup>

Furthermore, hyperglycaemia can occur during refeeding as glucose is delivered to a starved patient. Hyperglycaemia can have an effect on neutrophil function, thus increasing risk of developing an infection.<sup>3</sup> Hypophosphataemia also increases the likelihood of developing infection due to decreased intracellular ATP, which may result in impaired neutrophil chemotaxis and phagocytosis.<sup>2</sup> Hyperglycaemia and increased insulin levels can also result in sodium retention, which in turns takes water into the cell resulting in oedema.<sup>3</sup> Insulin may have an effect on renal tubules, having an antidiuretic effect, resulting in increased extracellular fluid volume.<sup>4</sup> This may cause cardiac-decompensation and pulmonary oedema.<sup>2</sup>

## Summary of presenting case

This patient was diagnosed with a high grade, oestrogen-receptor positive and progesterone receptor positive form of breast cancer, which was treated with hormonal therapy. Initially she was treated with Letrozole then Exemetestane (aromatase inhibitors, which work by blocking the production of oestrogen in body tissues<sup>3</sup>). The patient was later treated with Tamoxifen, an anti-oestrogen drug, which works by preventing oestrogen attaching to the breast cancer cells.<sup>6</sup> These therapies are used because oestrogen and progesterone can promote growth of some breast cancer cells.<sup>5</sup> The patient had an invasive lobular cancer which develops in the cells that line the lobes of the breast; ten per cent of breast cancers are invasive lobular cancers.<sup>7</sup>

The medical team approached the dietitian in order to establish whether nasogastric (NG) tube feeding was appropriate for this patient; as she was nil by mouth due to dysphagia. The medical team queried if the patient had an obstruction, therefore, a medical opinion was required to determine if NG feeding would be safe and possible. Following a medical review, which ruled out an obstruction, it was decided that an NG tube was the best method of providing nutrition support along with medicine and fluid. It was highlighted at this stage that this patient had a limited nutritional intake for five months and was therefore likely to be in a state of starvation. She also had hypophosphataemia, hypomagnesaemia and hypokalaemia prior to feeding; she was therefore at severe risk of refeeding syndrome.

## Dietetic intervention

### Day 1

Due to the risks associated with commencing feeding, medics were asked to prescribe thiamine and Dalavit drops (multivitamin). As thiamine is required to metabolise carbohydrate, it is given 30 minutes prior to feeding. The National Institute for Health and Clinical Excellence (NICE) recommend that thiamine, vitamin B co-strong and a multivitamin are prescribed for the first 10 days of nutrition support.<sup>8</sup> However, nursing staff found that they were unable to remove the contents of the multivitamin capsule with a syringe for NG administration, and that vitamin B

co-strong could not be crushed, therefore Dalavit drops were recommended instead.

Due to deranged blood results (Table One) and prolonged fasting, it was recommended that feeding be commenced at 5kcal/kg body weight/day (as per NICE guidance for extreme cases), and electrolytes were replaced as required alongside nutrition support. The patient was commenced on a 1kcal/ml fibre feed (Jevity, 10ml/hour for 20hours). Daily bloods were requested.

### Day 2

Over the weekend the rate of the feed was increased to 20ml/hour for 20 hours. The patient complained of diarrhoea. No changes were made to the feeding plan due to low potassium levels. Medics were advised to replace electrolytes as required.

### Day 3

Diarrhoea persisted; changed to a 1kcal/ml, non-fibre feed (Osmolite) to determine if diarrhoea was related to the fibre content of the feed. The patient had become oedematous; therefore nursing staff were advised to monitor fluid balance. No changes were made to the rate or volume of feed delivered, in order to monitor tolerance.

### Day 4

Blood results were unavailable at time of review, therefore, no changes were made to the feeding regimen. Nursing staff were advised to monitor temperature and blood sugar levels to assess if the patient was showing any further evidence of refeeding syndrome. The importance of monitoring strict fluid balance was reiterated.

### Day 5

The patients stool sample was confirmed Clostridium-Difficile positive. As she was tolerating her NG feed, staff were advised to increase Osmolite to 30ml/hour then 40ml/hour for 20 hours over the weekend, if her blood results were within acceptable range and she continued to tolerate the feed.

### Day 6

NG feed tolerated well. However, the patient was complaining of achy legs which she reported to have been present for around one week. This may have been a symptom of hypomagnesaemia<sup>1,3</sup> or a side effect of Tamoxifen.<sup>6</sup> No further diarrhoea was reported. NG feed increased (Osmolite, 50ml/hour for 16hours).

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Table One: Blood Results

Normal range (mmol/l)	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8
Magnesium 0.70-1.00	0.65↓	0.63↓	Haemolysed	0.66↓	0.67↓	0.68↓	0.72	0.71
Potassium 3.5-5.5	2.5↓	2.7↓	Haemolysed	3.6	3.4↓	3.9	4.2	4.3
Phosphate 0.80-1.40	0.47↓	n/a	Haemolysed	0.52↓	1.07	0.68↓	0.71↓	0.93

**Day 7**

The patient continued to tolerate NG feed well; no nausea or vomiting and no further diarrhoea. The feed had not been increased the previous night, therefore advised to commence Osmolite, 50ml/hour for 16hours.

**Day 8**

No new bloods were available; therefore no changes were made to the feeding regimen. Staff were advised to check bloods, with the aim to increase the rate of feed the following day.

**Day 9**

The patient continued to tolerate the NG feed, however, her arm had become more oedematous. It was noted that her albumin levels were low. It was recommended again that nursing staff monitor strict fluid balance; advised to meet fluid requirement of 1200-1400ml/day due to issues of fluid retention in refeeding syndrome. NG feed was increased (Osmolite, 60ml/hour for 16hours).

**Day 10**

Nursing staff were unable to obtain an aspirate from the NG tube at the weekend, therefore unable to deliver the NG feed. Suggested re-starting feed at 50ml/hour for 16 hours as per previous regimen, once position of NG tube confirmed.

By day 11 the patients' condition had deteriorated and her diarrhoea had returned. This lady was placed on the Liverpool Care Pathway. Due to her poor condition all active treatment was stopped and it was decided that this should include her NG feed.

**Discussion**

On initiating feeding this patient had deranged blood results. NICE<sup>5</sup> recommend that low levels of potassium, phosphate and magnesium should not delay feeding, but with a cautious, calorie-controlled approach, electrolytes may be replaced at the same time as feeding is commenced. In severe cases feeding should be started at only 5kcal/kg body weight/day.<sup>8</sup>

Feeding was increased gradually over a number of days dependant on clinical signs of refeeding, patient tolerance to feeding and biochemical parameters. There are differing opinions on the rate at which feeding should be increased, ranging from increasing by 5kcal/day<sup>1</sup> to 15-20kcal/day from days 4-10.<sup>3</sup> This decision is therefore based on clinical judgement from close monitoring. Due to this lady's severe risk of refeeding syndrome, it was deemed more appropriate to increase the feeding rate at no more than 5kcal/kg/day. Further research into how quickly feed can safely be increased and over what time frame would be beneficial.

This patient became oedematous shortly after feeding was initiated. This is a recognised issue in refeeding syndrome. Accordingly, fluid restriction may be necessary to avoid such complications. It has been recommended that total fluid intake should equal a maximum of 30ml/kg body weight/day.<sup>4</sup> This can be a challenge for the clinician as the patient may require intravenous

infusions of electrolytes, such as magnesium, to correct abnormalities, and due to the slow starting rate of feed IV fluids were prescribed. This issue should be discussed with medical staff and a pharmacist to determine if electrolytes can be delivered safely in a smaller volume of fluid.

Hypomagnesaemia can result as a consequence of hypokalaemia.<sup>9</sup> It is therefore important if both magnesium and potassium levels are low, that magnesium is replaced prior to potassium, otherwise hypokalaemia is likely to persist.<sup>9</sup> Management of this patient was further complicated with the diagnosis of Clostridium-Difficile diarrhoea, causing further losses of electrolytes.

Nursing staff were advised to monitor this lady's blood glucose levels due to the risk of hyperglycaemia in patients with refeeding syndrome. This may be a complication of nutrition support, even in those patients without diabetes mellitus, if given large amounts of glucose following starvation.<sup>8</sup> It should be routine practice to monitor blood glucose levels in patients at risk of refeeding syndrome, in order to prevent the complications of uncontrolled hyperglycaemia, which can include hyper-osmolar non-ketotic coma and death.<sup>4</sup> It was also advised that staff monitor body temperature as part of their observations, as hypothermia is common in those who are malnourished.<sup>4</sup>

**Recommendations**

Optimal management of refeeding syndrome requires a multidisciplinary approach. Input for this particular patient was required from the dietitian, doctors, pharmacist and nursing staff. Each has a unique role in managing this complex condition. For this reason, training and updates on refeeding syndrome should be provided for all staff identifying and managing the condition.

In a recent study it was reported that only 44 per cent of doctors and 70 per cent of dietitians (sample size 146) were following the NICE guidelines on refeeding syndrome.<sup>10</sup> This, in part, may be due to the guidelines being based on expert opinion rather than clinical evidence, and different departments may have their own guidelines. Further research on this topic and clinical evidence are required to guide future recommendations on the management of this condition.<sup>10</sup>

The use of prophylactic phosphate replacement in patients at risk of refeeding syndrome has been discussed.<sup>2</sup> Although not possible for the patient discussed in this case who already had severe hypophosphataemia, this could be a consideration for future practice.

**Conclusion**

This case study highlights the complexity of refeeding syndrome and its management. It is apparent that further research in this area is required to build upon clinical guidelines. A multidisciplinary approach must be adopted to ensure overall patient care is optimal.

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