Unveiling the potential fatality of refeeding syndrome in malnourished patients: A case series

Ramizah Mohd Shariff, MBBS[1], Kavinmithra Visuvanathen, MBBS[1], Mohammad Shukri bin Jahit, MMed Surg[1], Tee Sze Chee, MMed Surg[1], Khong Khei Chong, MPharm[2]

[1]Department of Surgery, National Cancer Institute, Putrajaya Malaysia, [2]Department of Pharmacy, National Cancer Institute, Putrajaya Malaysia

SUMMARY

Detecting refeeding syndrome is always challenging unless a thorough assessment is conducted. In some cases, despite all efforts for replenishment, the condition remains refractory. We present three cases of upper gastrointestinal cancer patients with severe malnutrition who were fed without prior electrolyte replenishments and succumbed to severe refeeding syndrome. The discussion emphasises the importance of precautionary measures in managing such cases. A high index of suspicion, especially given the background of severe malnutrition, is pertinent to detecting potential cases of refeeding syndrome. Initiation of hyperosmolar, hyperglycaemic parenteral or enteral feeds shall be withheld before any electrolyte replenishment or vitamin supplementation. Current guidelines emphasise screening followed by diligent resuscitation, replenishment, and supplementation.

INTRODUCTION

Refeeding syndrome is a potentially lethal condition that occurs among malnourished patients who are fed immediately after a period of prolonged starvation with high volumes of calories.[1] It is a spectrum of clinical manifestations as a result of fluid and electrolyte shifts from the intravascular space into the intracellular space. This fatal shift results from the metabolic requirement of a sudden increase in calories in the background of depleted body resources.[2] The biochemical hallmarks of refeeding syndrome are hypophosphatemia, hypomagnesaemia and hyopokalaemia.[3] Untreated, refeeding syndrome will cause a myriad of clinical consequences due to protracted depletion of thiamine, phosphate, magnesium, potassium and on the contrary fluid and sodium overload.[4] Replenishments of thiamine, phosphate, magnesium, potassium, vitamins and trace elements are crucial before any provision of feeding or calories.[5] Once stable feeding or calorie provision can be initiated or increases slowly. Available guidelines in the management of potential or overt refeeding syndrome incorporate risk stratifications, specific risk factors (e.g., cancer, chronic alcoholic, post bariatric surgery), nutritional assessment, baseline electrolyte checks and thorough monitoring during the treatment and provision of calories.[6] Three cases of severe refeeding syndrome are presented here to highlight precautionary steps and pertinent points in managing such fatal but commonly missed cases.

CASE PRESENTATION

As standard protocol, all upper gastrointestinal cancer patients referred to the National Cancer Institute Putrajaya Malaysia for definitive treatment were screened for malnutrition and the risk of refeeding syndrome before any nutritional and physical rehabilitation. Throughout 2022, there were 236 cases of upper gastrointestinal cancer, and among them, three cases were identified suffering from severe refeeding syndrome. Refer to Table I for their characteristics and risk stratifications.

Case 1

A female with stage III obstructed adenocarcinoma of the stomach was diagnosed after 12 weeks of post-prandial vomiting, inadequate oral intake and 16% weight loss. Cancer confirmation and staging by endoscopy, histopathological report and CT imaging was done. She had severe hypophosphatemia, hypomagnesaemia, and borderline low potassium. Total parenteral nutrition was initiated by the referring hospital without any electrolyte replenishment. We withheld the feeding, resuscitated her, and replenished the phosphate, magnesium and potassium. Intravenous vitamins and trace elements were given concomitantly. She succumbed to cardiac failure, which is one of the most common sequelae of severe refeeding syndrome.

Case 2

A case of non-familial gastric polyposis who suffered post-prandial vomiting and 20% weight loss over a period of 2 months. Immediate enteral tube feeding was initiated up until 86% of his total energy requirement without prior electrolyte assessment and replenishment. We withheld the feeding and resuscitated him with intravenous vitamins and trace elements. He responded well initially; thus the low-calorie provision was reinitiated at 13 kcal/kg/day. Concurrent electrolyte replenishment was continued with cautious monitoring. Further increments of calories did not progress well, evidently with the deterioration of his electrolytes. He succumbed to cardiac arrhythmias and cardiac arrest.

Case 3

Stage III obstructed adenocarcinoma of the stomach was diagnosed after 6 weeks of post-prandial vomiting and 19.0% weight loss. Cancer confirmation and staging by endoscopy, histopathological report, and CT imaging. She was initiated

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Corresponding Author: Ramizah Mohd Shariff
Email: skyzlimit49@gmail.com

Table I: Characteristic of the severe refeeding syndrome cases encountered among the upper gastrointestinal cancer patients

Demographic and risk stratifications	Case 1	Case 2	Case 3
Gender	Female	Male	Female
Age	62	46	66
Cancer	Stage III gastric cancer	Non-familial gastric polyposis	Stage III gastric cancer
Symptoms	Malnourished and post-prandial vomiting	Malnourished and post-prandial vomiting	Malnourished and post-prandial vomiting
Weight and BMI	56 kg, 23.4	50 kg, 19	42 kg, 17
Unintentional weight loss	16% over 12 weeks	20% over 8 weeks	19% over 6 weeks
Little/no nutritional intake	Very high risk	Very high risk	Very high risk
Nutritional screening	SGA C	SGA C	SGA C
Electrolytes deficiency	Phosphate 0.56 Magnesium 0.60 Potassium 3.3	Phosphate 1.34 Magnesium 0.75 Potassium 3.7	Phosphate 0.94 Magnesium 0.49 Potassium 2.7
Calorie provision before electrolytes replenishment	TPN 30% of TEE	EN 86% of TEE	TPN 34% of TEE

BMI – Body mass index, SGA – Subjective global assessment, TPN – Total parenteral nutrition, EN- Enteral nutrition, TEE- Total energy expenditure

on total parenteral nutrition without proper electrolyte assessment and replenishment prior to referral to our centre. She had severe hypomagnesaemia and hypokalaemia. Feeding was withheld, and she was resuscitated with intravenous vitamins and trace elements. We were very cautious with fluid and sodium retention, as she has manifested evidence of peripheral oedema. She responded well; hence a modest calorie provision was reinitiated at 10 kcal/kg/day. However, her condition slowly deteriorated, and she finally succumbed to cardiac and respiratory failure.

DISCUSSION

During periods of prolonged fasting or severe malnutrition, the body adapts by utilising stored energy sources such as glycogen, fat, and protein. This adaptation results in decreased body weight, reduced basal metabolic rate, and altered metabolic pathways. When nutrition is abruptly reintroduced, there is a rapid shift in metabolism from catabolism to anabolism, which can overwhelm the body's compensatory mechanisms. Pourhassan et al. reported that the majority of hospitalised patients who are malnourished are at high risk of developing refeeding syndrome.[7] Current updated nutritional protocols strongly recommend nutritional screening as mandatory to enable the timely implementation of refeeding protocols.[8] Patients shall be stratified according to the potential risk of developing refeeding syndrome based on the nutritional screening, severity of starvation and weight loss. Provision of intravenous thiamine 100 to 200 mg should take precedence before any provision of calories, even in the simplest form of intravenous dextrose in maintenance fluid therapy.[9] Electrolyte depletion (phosphate, magnesium and potassium) shall be replenished accordingly as suggested by Freidli et al. Following electrolyte replenishment, supplementation of vitamins (lipid-soluble and water-soluble vitamins) and trace elements shall be given too.[10] There are various approaches to the provision of calories, but most guidelines recommend cautious increments depending on the severity of the potential risk of refeeding syndrome. Basically, the pathophysiological changes of refeeding syndrome are as follows:

1. Electrolyte and fluid imbalances: Rapid delivery of calories or refeeding leads to increased insulin secretion, which promotes cellular uptake of glucose, electrolytes, and water from the extracellular into the intracellular space.
2. Thiamine deficiency: Malnourished patients often have depleted thiamine (vitamin B1) stores. Thiamine is important for the metabolism of glucose; hence, with the abrupt provision of calories, there will be increased demands for thiamine.

The recurring issues that we encountered in the reported cases were almost similar, as summarised below:

1. There was no nutritional screening; hence, the risk of refeeding was not highlighted.
2. Electrolyte assessment (magnesium and phosphate) was not a standard practice prior to the initiation of feeding.
3. Vitamin and trace element supplementation were not a standard practice in severely malnourished patients fed with either enteral or parenteral feeding.
4. In Case 2, calorie provision was given at 86%, which is considered too high and too fast for a severely malnourished patient.

As described by the NICE guideline, the ASPEN guideline, and Freidli et al.,[10] all malnourished patients shall have the following assessment and treatment:

The management of refeeding syndrome as outlined by NICE guideline, ASPEN guideline and Freidli et al.[10] focuses on gradual and cautious refeeding, close monitoring, and correction of electrolyte imbalances and other metabolic abnormalities. Key management strategies include:

1. Risk assessment includes significant weight loss, low body mass index, prolonged fasting or other risk factors such as cancer patients and post-bariatric surgery.
2. Gradual feeding: initiate feeding at a low caloric intake of 10 to 20 kcal/kg/day and gradually increase the energy intake over 3 to 4 days while closely monitoring electrolyte levels and other clinical responses.
3. Electrolyte supplementation: correct and replenish phosphate, magnesium and potassium.
4. Thiamine deficiency: administer thiamine (vitamin B1) to all at risk patients.

CONCLUSION

Malnutrition is highly prevalent among hospitalised patients. Any intended treatment plan may be hampered by the patient's poor general well-being or progress. Refeeding syndrome is one of the teething issues that often accompany severe malnutrition, as showcased here. Unless precautionary steps are taken in vigilant screening, we often miss the opportunity to salvage them and proceed with the intended treatment plan. Basic nutritional knowledge and protocols should be made mandatory for all clinicians handling frail and malnourished patients. Implementing these strategies in clinical practice can help mitigate the risks associated with refeeding syndrome and improve patient outcomes and chances of survival.

REFERENCES

1. Culkin A, White R. Refeeding syndrome. Med (United Kingdom). 2023; 51(7): 498-502.
2. Abdelfatah MM. Refeeding syndrome: a fatal adverse event of gastric peroral endoscopic pyloromyotomy. Gastrointest Endosc 2021; 94(2): 425-6.
3. Turner P. NHS Trust policies for correction of hypokalaemia and their suitability for use in refeeding syndrome related to eating disorders. Clin Nutr ESPEN 2023; 57: 851.
4. Bioletto F, Pellegrini M, Ponzo V, Cioffi I, De Francesco A, Ghigo E, et al. Impact of refeeding syndrome on short- and medium-term all-cause mortality: a systematic review and meta-analysis. Am J Med 2021; 134(8): 1009-18.e1.
5. de Vargas Cony K, de Magalhães Francesconi CF. An unexpectedly high incidence of refeeding syndrome in patients with total parenteral nutrition in a reference university hospital. Clin Nutr 2021; 40(6): 3702-7.
6. Buitendag J, Variawa S, Davids R, Ahmed N. Refeeding syndrome in surgical patients post initiation of artificial feeding, a prospective cohort study in a low-income country. Clin Nutr ESPEN 2021; 46: 210-15.
7. Pourhassan M, Cuvelier I, Gehrke I, et al. Risk factors of refeeding syndrome in malnourished older hospitalized patients. Clin Nutr 2018; 37(4): 1354-9.
8. Reber E, Gomes F, Vasiloglou MF, Schuetz P, Stanga Z. Nutritional risk screening and assessment. J Clin Med 2019; 8(7): 1065.
9. Pacei F, Tesone A, Laudi N, Laudi E, Cretti A, Pnini S, Varesco F, Colombo C. The relevance of thiamine evaluation in a practical setting. Nutrients 2020; 13; 12(9): 2810.
10. Reber E, Friedli N, Vasiloglou MF, Schuetz P, Stanga Z. Management of refeeding syndrome in medical inpatients. J Clin Med 2019; 8(12): 2202.