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Refeeding Syndrome in a Woman with Colorectal Cancer: A Case Report

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Abstract **Case Report**

In digestive surgery, nutritional management of an undernourished patient is nowadays systematic and well codified, and must be part of the initial management measures. However, it is not always risk-free, as inadequately managed renutrition of a patient during a period of undernutrition, or during the post-operative period, can have deleterious clinic-biological manifestations, all too often ignored by practitioners, which we group together under the name of refeeding syndrome. Refeeding syndrome reflecting the transition from catabolic to anabolic metabolism usually occurs within five days of refeeding in patients who have undergone prolonged fasting or in a postoperative context including digestive cancer surgery. Patients may present with water-electrolyte disorders, in particular hypophosphatemia and/or hypokalemia and/or hypomagnesemia, thiamine deficiency, as well as neurological, pulmonary, cardiac, neuromuscular and hematological complications, which can lead to the patient's death. Here we present the case of a patient who underwent surgery in the General Surgery Department at Mohamed 6 University Hospital in Tangier for colorectal cancer. The patient subsequently developed an inappropriate refeeding syndrome accompanied by shock and altered consciousness in the postoperative period. Unfortunately, the patient passed away within a few hours following these complications. This is a cause of mortality that can occur without any surgical complications but remains underdiagnosed in daily practice. The management of this syndrome involves first of all the identification of patients at risk and the prevention of it by careful clinic-biological monitoring, including special hydro electrolyte monitoring, as well as the development of feeding reintroduction protocols tailored to each patient's needs.

Keywords: Refeeding syndrome, renutrition, hypophosphatemia, hypokalemia, hypomagnesemia.

INTRODUCTION

Nowadays in digestive surgery, particularly in colorectal surgery, the nutritional management of a malnourished patient is well codified and systematized, starting from the patient's admission. However, it is not always without risks. Indeed, an orally assisted, enteral, or parenteral feeding implemented to address a state of anorexia and varying degrees of undernourishment, or refeeding after a prolonged period of fasting, can lead to a range of electrolytic, biochemical, and hematological alterations. These alterations can result in multiple organ impairments (neurological, hematological, respiratory, renal, skeletal, and cardiac), which can be life-threatening. They are collectively known as the refeeding syndrome [1].

It was very quickly described during the liberation of besieged people over 2,500 years ago during the siege of Jerusalem, and then rediscovered during the Second World War among Japanese prisoners [2]. Refeeding syndrome has been explained in particular at the time of the appearance of parenteral nutrition, and is thought to be due to the transition of the body from a catabolic state, established during fasting, to a state of anabolism [3].

Currently, the refeeding syndrome is defined as a state of metabolic disturbance (both clinical and biological) that occurs due to the resumption of nutrition (oral, enteral, or parenteral) after a prolonged period of fasting or food restriction. It is not dependent on the mode of refeeding but rather on the severity of pre-existing malnutrition and the rapidity of refeeding [4].

Appropriate management of this syndrome requires identification of patients at risk, in order to ensure prevention, as well as implementation of a real strategy for appropriate refeeding.

CASE REPORT

We report the case of a patient admitted to our facility for the management of a tumor in the sigmoid colon diagnosed based on chronic abdominal pain with alternating bowel movements of diarrhea and constipation, as well as low to moderate rectal bleeding. The patient also exhibited general deterioration, including symptoms such as asthenia, anorexia, and an estimated weight loss of 15% of their original weight over a period of 4 months.

The patient had a BMI of 18kg/m² and underwent a sigmoid resection with colorectal anastomosis, ensuring an adequate safety margin.

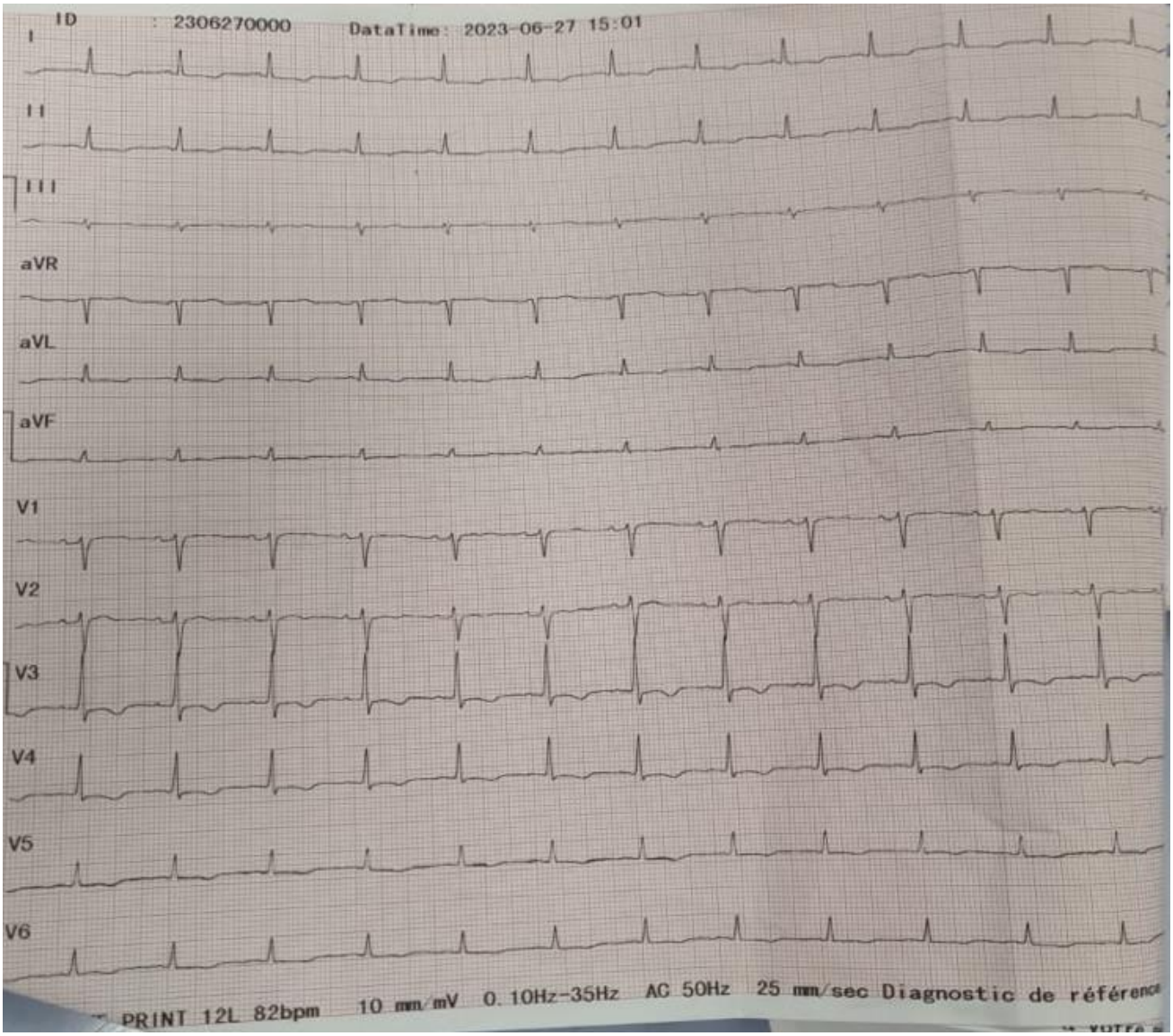
The patient was accidentally fed with oral nutritional supplementation on postoperative day 1. However, on day 3, she experienced severe abdominal pain accompanied by vomiting, confusion, and dyspnea.

The clinical examination revealed generalized abdominal tenderness, hypotension (blood pressure 8/5), and tachycardia at 120 beats per minute. The patient was admitted to the intensive care unit and underwent a comprehensive laboratory assessment (Table 1).

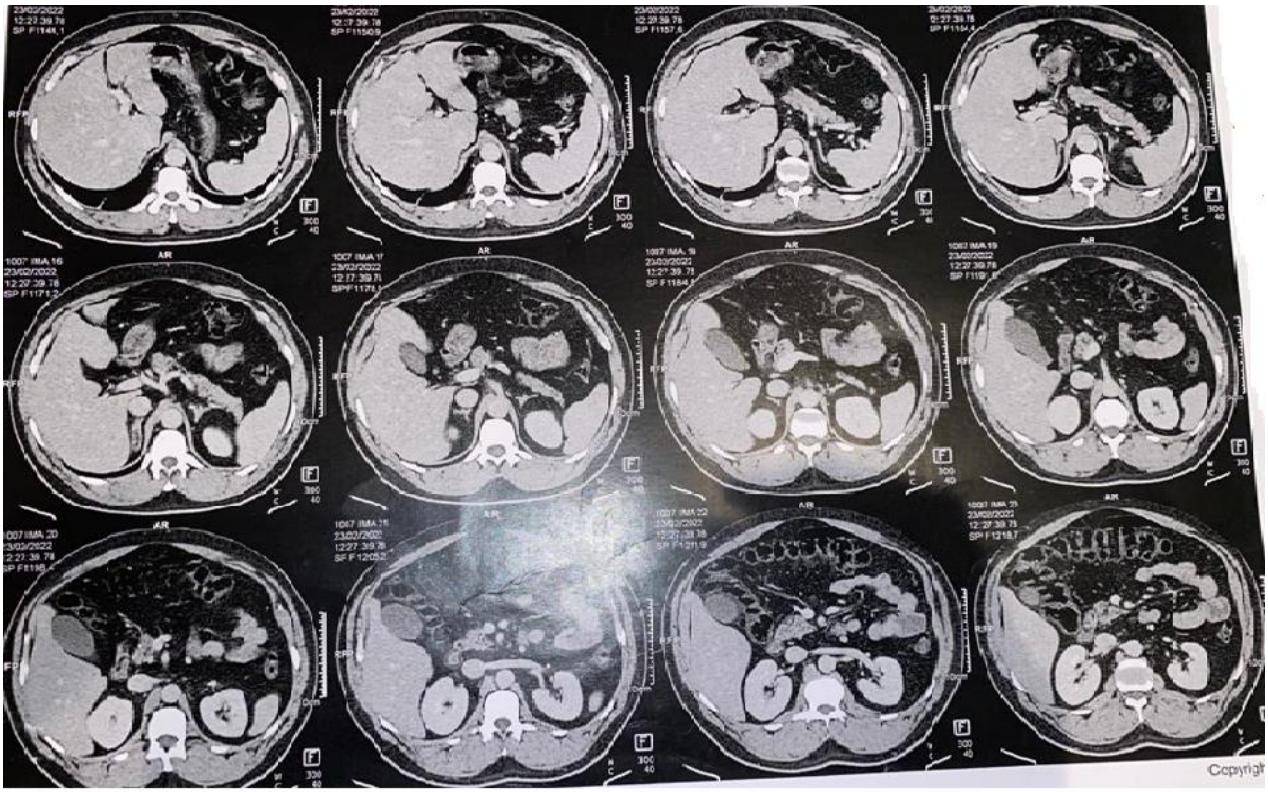
Table 1: Laboratory test results

hemoglobin	9,5 (13-16 g/dl)
leukocyte	10 (4000-10000/mm3
CRP	150 (0-6 mg/l)
urea	0,3 (0.18-0.4 g/L)
creatinine	8 (6-12 mg/L)

The ECG performed revealed signs of hypokalemia.



The abdominal CT scan did not reveal any postoperative complications, including postoperative peritonitis due to an anastomotic leak, which was initially considered as the primary hypothesis based on the clinical presentation.



Based on these results, further investigations were conducted, particularly a nutritional assessment, which revealed the following findings:

Table 2: Laboratory test results

kalemia	2,66 (3,5 - 5 mmol/L)
natraemia	136 (135- 145 mmol/L)
magnesimia	0,62 (0,7-1,1mmol /L)
phosphatemia	0,4 (0,8 -1,5mmol/L)

During her stay in the intensive care unit, on day 5, the patient's hemodynamic status deteriorated, and she developed a state of shock characterized by severe respiratory distress and altered consciousness. Afterward, she experienced a cardiac and respiratory arrest after 30 minutes. The diagnosis of refeeding syndrome was established based on the following criteria: the patient's cachectic state, BMI, early refeeding, and the laboratory findings, which revealed hypophosphatemia, hypomagnesemia, and hypokalemia.

DISCUSSION

Refeeding syndrome is considered a significant complication of nutritional rehabilitation as it significantly increases the complications and morbidity and mortality in malnourished patients. When the syndrome is severe or very severe, the mortality associated with it is reported to be 3.3 to 5.5 times higher than the usual mortality rate in intensive care units [5].

The prevalence of refeeding syndrome has long been associated with hypophosphatemia following refeeding. The publication by Miller adds the role of water and sodium retention in the development of peripheral edema [6]. Inappropriate refeeding syndrome is now the subject of numerous studies and has been observed in individuals undergoing hunger strikes [7], cases of anorexia nervosa [8], and chronic alcoholics [9].

This is known as refeeding hypophosphatemia syndrome.

Due to the lack of precise diagnostic criteria, the estimated prevalence of refeeding syndrome varies between 0.43% and 34% in different hospital populations [3].

A definition provided by the National Institute for Health and Care Excellence (NICE) describes the syndrome as a life-threatening condition characterized by extremely low electrolyte concentrations in the serum, biochemical disturbances, and fluid imbalances resulting from inappropriate or rapid refeeding [10]. These abnormalities can lead to organ dysfunction.

More recently, the refeeding syndrome has been defined according to the guidelines of the American Society for Parenteral and Enteral Nutrition (ASPEN). It is characterized by a decrease in plasma levels of phosphorus, potassium, and/or magnesium, with or without organ dysfunction resulting from a deficiency of one of these electrolytes or thiamine

(severe refeeding syndrome), occurring within 5 days following the resumption or substantial increase in nutritional intake [11].

Although not clearly identified at the time, several cases of refeeding syndrome have been described in literature throughout history. For example, in the first century AD, the historian Flavius Josephus reported that Hebrew prisoners who had escaped from Roman prisons ate excessively and died as a result. The historian noted that those who indulged in the food were the ones who primarily died, while those who managed to control their appetite escaped death [12]. In 1892, Émile Zola wrote in "La Débâcle": "On that Saturday, the scarcity ceased. Night fell, and they were still eating, and they continued to eat until the next morning. Many died from it." This statement describes the delivery of a large quantity of food to French prisoners held by the Prussians after the defeat of the Franco-Prussian War in 1870.

It was mainly the atrocities of the Second World War that allowed for a more precise description of refeeding syndrome. For instance, after the lifting of the siege of Leningrad by German troops, many Russians, both civilians and military personnel, died from heart failure or anasarca due to inappropriate refeeding [13, 14]. Other studies described various symptoms (coma, convulsive seizures, paralysis) following refeeding that led to the death of Japanese prisoners [15] or, after liberation, of inmates in Nazi concentration camps [16].

In the aftermath of World War II, a famous study known as the "Minnesota Experiment" examined the effects of calorie restriction on healthy volunteer soldiers over six months [17]. Authentic cases of heart failure were observed despite monitored and gradual refeeding. However, it was with the development of parenteral nutrition in the 1970s that refeeding syndrome was properly identified and described [18]. The role of hypophosphatemia in inappropriate refeeding syndrome was first suggested by Weinsier and Krumdieck in 1981, based on a case series involving two patients: a 28-year-old malnourished woman with anorexia nervosa and a 66-year-old malnourished woman with malabsorption following complex abdominal surgery, both of whom died rapidly due to rapid hypercaloric parenteral refeeding [19].

The case of our patient aligns with what has been reported in the literature, and the signs in favor of inappropriate refeeding syndrome were the early refeeding following a low-residue diet and prolonged fasting imposed on the patient in the context of preparation for abdominal surgery. The patient had a BMI of 18 kg/m², hypophosphatemia, hypokalemia, rhythm disturbances on the ECG, and the absence of signs indicative of postoperative peritonitis due to an anastomotic leak on the CT scan.

One of the challenges of refeeding syndrome is the early detection before its consequences appear. The National Institute of Health and Clinical Excellence (NICE) has established risk factors for the development of refeeding syndrome (Table 3) [20]. The presence of a single major criterion or two minor criteria, taking into account the duration of fasting, nutritional status, rate of weight loss, underlying pathology, and/or medication use that may disrupt electrolyte imbalances, is sufficient to identify the patient at risk and thus prevent the occurrence of refeeding syndrome [20].

Table 3: NICE guidelines for identification of patients at high risk for refeeding syndrome

Patient has 1 or more of the following:
• BMI less than 16 kg/m^2
• unintentional weight loss greater than 15% within the last 3 to 6 months
• little or no nutritional intake for more than 10 days
• low levels of potassium, phosphate or magnesium before feeding.
Or patient has 2 or more of the following:
• BMI less than 18.5 kg/m^2
• unintentional weight loss greater than 10% within the last 3 to 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.

Very recently, the American Society of Parenteral and Enteral Nutrition (ASPEN) has issued new recommendations regarding the clinical definition and risk stratification criteria for refeeding syndrome [11]. Various pathological processes can increase the risk of developing refeeding syndrome (Table 4) [21]. The new ASPEN criteria also consider electrolyte measurements before refeeding [11].

Patients with anorexia
Patients with chronic alcoholism
Oncology patients
Postoperative patients
Elderly patients (comorbidities, decreased physiological reserves)
Patients with uncontrolled diabetes mellitus (electrolyte depletion, diuresis)
Patients with chronic malnutrition:
Marasmus
Prolonged fasting or low energy diet
Morbid obesity with profound weight loss
High stress unfed for > 7 d
Malabsorptive syndromes (inflammatory bowel disease, cystic fibrosis, short bowel syndrome)

Table 4: Various pathological processes can increase the risk of developing refeeding syndrome

Our patient had several risk factors, including a weight loss estimated at 15% over 4 months, an BMI<18.5 kg/m², and colorectal cancer, which was the diagnosis for which she was admitted to our facility. These factors contributed to her increased risk for refeeding syndrome.

CONCLUSION

Refeeding syndrome is often underestimated despite its potentially fatal complications during nutritional rehabilitation. This frequent underestimation is due to its heterogeneous clinical and laboratory presentation, which is incompatible with a clear and fundamental definition.

Screening patients at risk and identifying malnutrition through various clinical and laboratory examinations are essential for preventing the occurrence or effectively managing refeeding syndrome. Early detection allows for appropriate interventions and nutritional support to mitigate the risks associated with refeeding.

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