Ventricular Dysfunction Secondary to Refeeding Syndrome in an Infant, A Case Report

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Abstract: *Introduction*: Refeeding syndrome is a complex of signs and symptoms that occur following the abrupt initiation of enteral or parenteral nutrition in malnourished patients, among other causes. Most data focuses on adolescents and adults, with limited neonatal information and other pediatric group ages. This case presents an infant who developed ventricular dysfunction due to refeeding syndrome following starvation.

Case Report: A 5-month-old female with a one-month history of generalized maculopapular rash and lower limb edema. Physical examination revealed severe malnutrition and significant electrolyte imbalances. The initial echocardiogram was unremarkable. Despite nutritional and dermatological management, the patient developed respiratory distress, generalized edema, and anuria, necessitating Pediatric Intensive Care Unit admission. Subsequent echocardiograms revealed dilated cardiomyopathy with systolic-diastolic dysfunction. After receiving inodilator therapy and diuretics, her condition temporarily improved but deteriorated again, requiring further intensive care. Imaging ruled out significant structural heart disease, and after a prolonged hospital stay, the patient was eventually stabilized and discharged with gradual nutritional and growth improvement.

Discussion: Cardiac complications following refeeding have been reported primarily in older patients with comorbidities, unlike our case, hence the rarity. Malnutrition-induced myocardial alterations and the stress of refeeding may have contributed to the observed ventricular dysfunction.

Conclusion: Any malnourished patient should be considered for the potential onset of refeeding syndrome. Risks and complications should not be underestimated despite the patient's age. A multidisciplinary approach is crucial for the proper management of this condition, although its presence does not seem to warrant special considerations for the care of cardiac complications.

Keywords: Refeeding syndrome, ventricular dysfunction, case report.

INTRODUCTION

Refeeding syndrome is a collection of signs and symptoms that occur after the abrupt initiation of enteral or parenteral nutrition in patients experiencing starvation [1,2]. It was initially observed during World War II when prisoners of war died inexplicably after being provided with a regular diet [3]. Since then, multiple definitions have emerged, and no clear consensus on terminology was established until the American Society for Parenteral and Enteral Nutrition proposed a definition [4]. According to this consensus, the refeeding syndrome is characterized by a decrease in serum phosphorus, potassium, and/or magnesium levels, categorized as mild (10%–20% decrease), moderate (20%–30% decrease), or severe (>30% decrease or organ dysfunction related to these imbalances and/or thiamine deficiency), occurring within five days of caloric reintroduction [4].

Refeeding syndrome has been primarily associated with significant malnutrition and anorexia. However, it has also been described in cases of renal failure, hemodialysis, Celiac and Crohn's disease, bariatric surgery and bowel resections, alcohol and substance use disorders, hyperemesis, or cancer, among others [1,2,4,5]. Risk factors, specifically in newborns, are extremely low-birth-weight babies, short gestational age, intrauterine growth restriction related to maternal comorbidities, a high resistance index in the umbilical artery, severe prematurity, and a Z-score greater than 2 [5,6].

Most available information has been extensively described in adolescents and adult patients [2,7], and recently, the neonatal population has been the subject of some publications regarding this age group [5,8]. However, the information remains limited, leaving a

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gray area between neonates and adolescents, where data primarily comes from case reports, with no randomized trials available or consensus to guide recommendations among the general pediatric population. We present a rare case of an infant suffering from starvation secondary to neglect who developed ventricular dysfunction as a result of refeeding syndrome.

CASE PRESENTATION

In this case study, a 5-month-old female patient with no relevant personal or family history presented with a one-month history of generalized erythematous maculopapular rash and 24-hour evolution of lower limb edema. The initial physical examination revealed erythematous, scaly papules converging into plaques across the body, edema in the extremities, pale mucous membranes, dry skin, and brittle hair. Anthropometric parameters included a weight of 4.4 kg (W/H -3.73 SD), a height of 57 cm (H/A -3.22 SD), and a weight-for-height z-score of 0.08 (-1.62 SD), leading to a diagnosis of Kwashiorkor-type malnutrition. The mother reported inadequate practices in preparing infant formula, resulting in low nutrient intake.

Laboratory tests revealed microcytic hypochromic anemia, hyponatremia, hypocalcemia, hypophosphatemia, and hypoalbuminemia, with decreased total proteins but no liver or renal function abnormalities. Vitamin D and B12 levels were normal. The initial echocardiogram showed adequate ventricular function, with no structural heart disease or signs of pulmonary hypertension.

Hospitalization was decided to initiate a nutritional recovery plan with mixed enteral nutrition, multivitamins, and dermatological management for impetiginized scabies with topical treatment and clindamycin. On the fifth day of hospitalization, the patient experienced clinical deterioration, with intolerance to enteral nutrition, generalized edema, anuria, abdominal distension with hepatomegaly, poor distal perfusion, respiratory distress, and elevated acute phase reactants, necessitating transfer to the Pediatric Intensive Care Unit. Ventilatory support and broad-spectrum antibiotic therapy were initiated. A follow-up echocardiogram showed signs of dilated cardiomyopathy, systolic-diastolic left ventricle dysfunction, and functional mitral regurgitation (Figure **1**).

Milrinone and intravenous furosemide were initiated, leading to a good clinical response, improved perfusion, and successful weaning from mechanical ventilation four days after arrival at the Pediatric Intensive Care Unit. A post-extubation echocardiogram showed a resolution of ventricular dysfunction. However, two days after extubation, the patient experienced another deterioration, showing signs of respiratory distress and crackles on lung auscultation, along with ventricular dysfunction, requiring reintubation, mechanical ventilation, and resumption of inodilator and diuretic infusion. Due to the patient's critical condition, total parenteral nutrition was started, initially with fluid restriction and caloric requirements at 40% of the total, and a multidisciplinary evaluation by pediatric cardiology and nephrology was requested. Cardiology recommended a cardiac MRI to assess cardiac function, volumes, and signs of cardiomyopathy. Additionally, an abdominal ultrasound performed due to nephrotic-range proteinuria raised suspicion of portal vein thrombosis, which was subsequently ruled out by angio-CT. However, a right renal infarction was identified, and clinical follow-up was deemed the only necessary course of action in this case.

The cardiac MRI could only be performed days later due to hemodynamic instability, showing normal biventricular systolic function and appropriate ventricular volumes in end-diastole and systole for the patient's age, without signs of hypertrophic, dilated, or non-compacted cardiomyopathy, and no late enhancement indicating macroscopic fibrosis or myocardial necrosis. Based on these findings, the inodilator was gradually discontinued, and heart failure management with oral medications was initiated.

With progressive clinical improvement, the patient was transferred back to the ward, where slow increases in enteral feeding through a nasogastric tube were resumed, followed by oral feeding with support from speech therapy until nutritional requirements were met. During the ward stay, the patient showed sustained weight gain and was discharged after 48 days of hospitalization. During outpatient follow-up six months later, she showed progressive weight gain with no new infectious episodes, hospitalizations due to any kind, or signs of heart failure.Unfortunately, follow-up with this patient was lost after her last visit to our institution.

DISCUSSION

Refeeding syndrome arises when feeding is reintroduced after prolonged malnutrition, causing

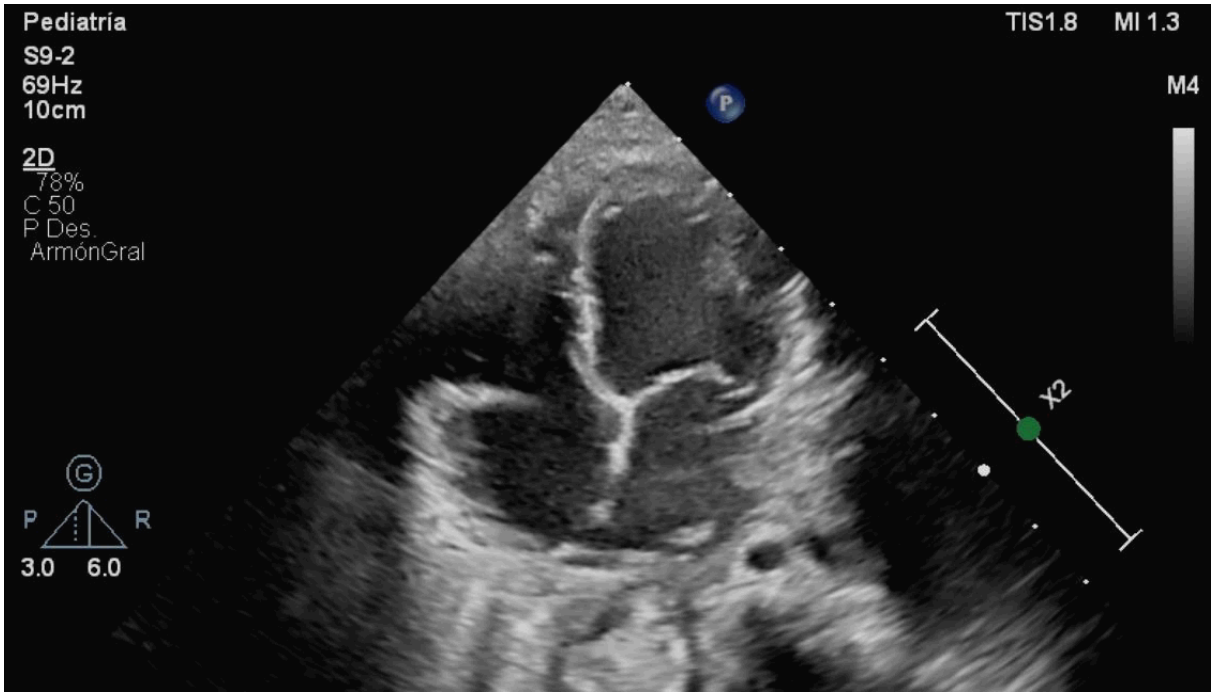

Figure 1: An echocardiogram in a four-chamber view shows left cavity dilation with rightward displacement of the interventricular septum, which suggests dilated cardiomyopathy.

shifts in electrolyte levels and metabolic function [9]. Starvation depletes intracellular phosphorus, potassium, magnesium, and vitamins, which diminishes the physiological capacity to tolerate stress [9]. Sodium shifts may occur, contributing to capillary leaks and fluid overload [4]. Thereby, the most common presentation in children includes hypophosphatemia, hypokalemia, and hypomagnesemia, with these findings posing direct risks to the patient [8]. Upon refeeding, insulin secretion increases due to glucose influx, driving potassium and phosphorus intracellularly, exacerbating the decline of these in serum levels [2,7]. Low potassium interferes with nerve and muscle function, increasing the risk of arrhythmias and paralysis [4]. Low magnesium worsens potassium loss and disrupts enzyme function, further affecting cellular activities [4]. Low phosphorus reduces ATP production, leading to respiratory distress and low oxygen levels [4]. Therefore, the severity of refeeding syndrome is largely dependent on the degree of malnutrition and electrolyte depletion before refeeding [2,9].

The introduction of adequate nutrition generates significant metabolic stress on the myocardium, where the heart, already affected by the state of starvation, may be unable to manage the additional fluid retention associated with the refeeding syndrome [10]. Most case reports describing heart failure following the reintroduction of feeding typically involve patients with underlying comorbidities and are generally observed in older individuals, in contrast to what was noted in our patient [7]. Additionally, the demand for thiamine significantly increases during the transition from starvation to refeeding, as it serves as a cofactor in glucose-dependent metabolic pathways [11,12]. This further impacts cardiac myocytes, contributing to the development of cardiac complications [11,12]. Studies of myocardial fibers in patients with varying degrees of starvation have shown altered myocyte arrangement, a reduced number of contractile cells that are atrophied, replacement of muscle fibers with collagen, and infiltration by fat and inflammatory cells, all of which impair myocardial contractility, reduce cardiac output, and diminish the heart's capacity to respond to stressors (sepsis, hypervolemia, hypoxemia, anemia, etc.) [9,13-15].

Based on the above, the ventricular dysfunction observed in the infant was likely secondary to the multiple insults during her course, such as fluid overload, hormonal changes during refeeding, and the infectious episodes she experienced, compounded by a diminished physiological reserve. While it is impossible to determine the exact duration of malnutrition, it is considered that the cause was the mother's chronic poor technique in preparing infant formula, suggesting that it had been ongoing for several months. Additionally, it is probable that the

physiological cardiac reserve was low due to chronic malnutrition and was not capable of handling large blood volumes.

For the general population, it is emphasized to start nutritional support within 48 hours of admission, with a preference for enteral nutrition over parenteral, administering hypocaloric feeding during the first week in the intensive care unit, and providing sufficient micronutrient supplementation [16]. Afterward, nutritional support should continue to increase gradually [11]. Electrolytes such as phosphate, magnesium, and potassium should be monitored and corrected promptly to prevent life-threatening complications. Thiamine must be administered before refeeding to avoid congestive heart failure due to impaired ATP production in cardiac cells, and continuous ECG monitoring is essential to detect early cardiac abnormalities, ensuring timely intervention [8,11,16]. This approach minimizes the risk of complications and ensures safer recovery [11].

Patients may require individualized management strategies based on the clinical presentation of their complications. For instance, vasopressor support may be indicated in cases of hypovolemia, mechanical ventilation in cases of respiratory failure, and diuretics in cases of fluid overload, among other interventions [6]. In the present case, a complication-focused approach was sufficient for treatment. It was applied as if the patient did not have this condition, suggesting that the management does not differ even in the presence of refeeding syndrome. However, the impact of complications in mortality in this population remains unknown.

We believe that with a progressive increase in nutritional intake and early control of cardiovascular complications, this patient achieved an adequate recovery with complete restoration of ventricular function, thanks to multidisciplinary management. We suggest that the presence of refeeding syndrome should not warrant a management approach different from that which would be applied to a patient with cardiac complications who does not suffer from this condition.We hope that the presentation of this case will raise awareness among healthcare personnel about the early recognition of patients at risk of developing refeeding syndrome and the possibility that complications, although typically described in older populations, may arise even in the early stages of life.

Due to the retrospective nature of this study and the loss of follow-up with this patient, the availability of information that could be fundamental for the preventive aspect of the described disease course is limited. Prospective studies in pediatrics are necessary to strengthen the quality of evidence and reach consensus on the critical management of these patients.

CONCLUSION

This case underscores the importance of considering the potential onset of refeeding syndrome in any malnourished patient. It highlights the need not to underestimate the risks and complications it may pose, regardless of the patient's age. Cardiac complications have been documented in adult populations, but data on the pediatric population remains limited. A multidisciplinary approach is crucial for the proper management of this condition, although its presence does not seem to warrant special considerations for the care of cardiac complications.Further descriptive and analytical studies on this condition are needed in the pediatric group to enhance evidence quality and establish a consensus on the critical management of refeeding syndrome.

APPROVAL FOR PUBLICATION

The present study was reviewed and approved by the institutional ethics committee. Informed consents were signed and acquired from the patients' representative guardians.

AVAILABILITY OF DATA AND MATERIALS

All material is available to be delivered to the journal if required or requested with prior authorization from our ethics committee.

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CONFLICTS OF INTERESTS

The authors have no relevant financial or non-financial interests to disclose. No AI or large language model was used during the writing, processing, or editing of the present manuscript.

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Not applicable.

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