


CASE REPORT

Malnutrition and chyle leakage: A life-threatening duo in heart transplantation post-Fontan procedure

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Abstract

Protein-losing enteropathy and chyle leakage may lead to severe malnutrition in heart transplantation for failing Fontan. Nutritional management may be challenging from defining nutrient needs to diagnosis of malnutrition enteropathy, and expertise is necessary. Body composition and hematological nutritional indices may help define malnutrition severity and guide nutritional strategy.

KEYWORDS

chyle leakage, failing Fontan, intestinal failure, malnutrition

1 | INTRODUCTION

Fontan procedure is a palliative procedure for what is otherwise fatal single-ventricle congenital defects.¹ Although the Fontan physiology may palliate the patient for decades, the pathway can decompensate in what is known as Fontan failure, for which the only definitive treatment is orthotopic heart transplantation (OHT).² The management of these patients is challenging, and the treatment strategy is not standardized.³ Nutritional status is commonly compromised due to the increased energy and protein requirements, protein-losing enteropathy or chyle leak, associated liver disease, nutrient deficiencies, and hospitalization needs. Effective nutritional

intervention is associated with survival and post-transplantation outcomes. Limited evidence is available on the use of measures of nutritional status, such as changes in lean body mass, and not routinely included in the recommendations.⁴

2 | CASE REPORT

We report a case of an 18-year-old boy who underwent OHT for failing Fontan, which was complicated by severe malnutrition.

Born in 2001 with neonatal diagnosis of univentricular heart (double-outlet right ventricle with absent left ventricle

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and mitral atresia), the boy underwent pulmonary artery banding at 1 month of age, bidirectional Glenn operation at 5 months, and an extracardiac fenestrated Fontan procedure at age 2.5 years. At 9 years of age, chest computed tomography scan revealed plastic bronchitis, probably due to moderately high pressures in the total cavopulmonary connection, compatible with failing Fontan.

At the age of 10 years, the patient was listed for cardiac transplantation. In 2015, protein-losing enteropathy was diagnosed (hypoalbuminemia, high alpha-1-antitrypsin clearance, low vitamin E, A, and D). Patient received dietary counseling at every visit, a personalized diet (low long-chain triglycerides (LCT), high medium-chain triglycerides

(MCT), and high protein) (Table 1), periodic intravenous (iv) albumin infusion, and liposoluble vitamin and antioxidant supplementation (zinc, selenium, and vitamin C) based on plasma levels.

The patient's condition worsened after developing Fontan-associated liver disease (FALD) with esophageal varices (F1 without red signs), splenomegaly, severe hepatic fibrosis (17.3 Kpa of stiffness), and compromised protein synthesis. In spite of high surgical and postsurgical risks, OHT was performed at the age of 17 years.

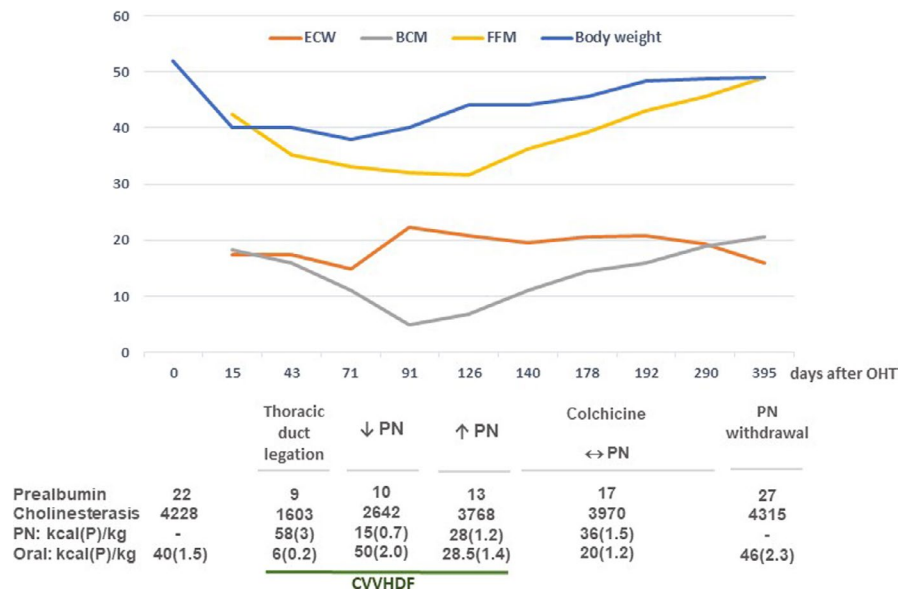
Post-OHT care was complicated by massive lymphatic leakage from mediastinal drainage (2000-3000 mL and up to 120 g of proteins/d) that persisted despite administration

TABLE 1 Nutritional support strategy

Clinical phase/issues	Nutritional intervention	Rationale
Failing Fontan, PLE	<ul style="list-style-type: none"> Diet: Low fat (max 25% kcal), MCT (40%-50% kcal from lipids), high-protein diet (2.5 g/kg/d) Liposoluble vitamin supplementation Oligoelement and antioxidant supplementation if necessary Albumin iv infusion (periodically) 	<ul style="list-style-type: none"> Compensate protein losses, contain lymphatic leakage Fat malabsorption Oxidative stress If albuminemia <3 g/dL
Post-OHT	<ul style="list-style-type: none"> PN initially exclusive + minimal enteral feeding (SNG) Mixed PN + oral diet Oral alimentation completely covers nutritional needs Progressive decrease in phase angle, FFM, BCM, and PhA and increase in ECW; stable body weight Reduction of oral intake restoration of PN (50%-70% of total energy needs) 	<ul style="list-style-type: none"> NE and oral diet started and increased as tolerated. PN proportionally decreased. BIA weekly malnutrition-related malabsorption contain osmotic diarrhea due to nonabsorbed foods intestinal failure
Definition of nutritional needs	<ul style="list-style-type: none"> Energy: BMR (Harris-Benedict formula) x 1.5 Protein: 2-3 g/kg/d (thoracic drainage up to 3000 mL, 120 g protein/24 h); Lipids: 1.5 g/kg/d by fish oil containing lipid emulsions mostly parenterally 	<ul style="list-style-type: none"> Redefinition of energy needs by indirect calorimetry to afford catabolism and protein losses; avoid hyperazotemia to help reaching caloric goal and contain leakage
Chyle leakage management	<ul style="list-style-type: none"> Exclusive PN, nil by mouth Fat-free diet + PN (slightly reduce amino acid provision) Thoracic duct ligation (40 d after OHT); no more mediastinal leakage Reduced PN and increased oral alimentation; energy intake: 70% orally and 30% PN Severe malnutrition (BMI z-score: -4.17) persisted; body weight stable energy intake: 50% orally and 50% PN Extreme reduction of FFM, BCM, PhA oral intake reduced to 30% kcal, PN increased to 70% kcal Colchicine (0.125 mg/kg/d) from 5 mo post-OHT, low-fat MCT diet + PN 	<ul style="list-style-type: none"> if leakage volume >3 L/d Unsuccessful diet and pharmacological therapy (octreotide) Good compliance Intestinal malabsorption Malnutrition Anti-inflammatory effect to control chyle ascites
Monitoring efficacy of nutritional intervention	<ul style="list-style-type: none"> Body composition (BIA): phase angle, FFM, BCM, and ECW—weekly Body weight: constantly monitored but highly influenced by ECW Indices of protein synthesis: prealbumin and cholinesterase—weekly 	
Follow-up	<ul style="list-style-type: none"> PN in hospital and at home for 7 mo. Withdrawal after complete recovery of nutritional status, muscle mass, body composition, and valid oral alimentation. Dietary counseling at every visit 	<ul style="list-style-type: none"> PN reduced progressively 4 mo after discharge; withdrawal after 7 mo. Progressive increase in oral intake

Abbreviations: BCM, body cell mass; BIA, bioelectrical impedance analysis; BMR, basal metabolic rate; ECW, extracellular water; FFM, fat-free mass; MCT, medium-chain triglyceride; OHT, orthotopic heart transplantation; PN, parenteral nutrition.

FIGURE 1 Observed body composition parameters: fat-free mass—FFM (kg); body cell mass—BCM (kg); extracellular water—ECW (% of total body water); nutritional hematological indices: prealbumin (mg/dL) and cholinesterase—CHE (IU/L), energy, and protein intake provided by parenteral nutrition (PN) and oral alimentation. ↔, stable PN; ↑, increase; ↓, decrease; CVVHDF, continuous venovenous hemodiafiltration; OHT, orthotopic heart transplantation; TPN, total parenteral nutrition



of octreotide and daily iv plasma and albumin supplementation. Low-LCT or fat-free, high-protein diet and fasting were unsuccessful. Thoracic duct ligation was performed 40 days after OHT, achieving cessation of thoracic leakage and progression of the chylous ascites. Intraperitoneal leakage was also observed. Significant reduction was obtained with administration of colchicine 5 months after OHT, at minimum dosage (0.125 mg/d) in order to avoid leukopenia.

The patient was furthermore diagnosed with diuretic resistant renal failure 3 weeks after OHT and subsequently underwent continuous venovenous hemofiltration (CVVHDF) for 4 months.

Ongoing plastic bronchitis led to respiratory failure, thus making bronchoscopy necessary during the first 3 weeks after OHT, along with discontinuous NIV support and dornase alfa nebulization (subsequently maintained for 4 months post-OHT).

In addition to the complex clinical history, severe protein-calorie malnutrition was observed post-transplant due to massive losses, with an unintentional weight reduction of 10 kg (19.2% of body weight; BMI z-score $-1.17 \rightarrow -4.46$). Initially, PN was used to provide energy and protein needs integrating nil by mouth or an extremely low or fat-free diet. Caloric needs were fixed at 2240 kcal (basal metabolic rate—BMR $\times 1.5$) and lipid intake max 1.5 g/kg/d by fish oil containing lipid emulsion.⁴ Given the severe catabolism, amino acid load was increased to 3 g/kg/d parenterally in order to compensate protein losses, generating hyperazotemia despite CVVHDF, that regressed reducing amino acid intake to maximum 1.5-2 g/kg/d parenterally (3 g/kg/d overall PN + diet).

Given the increasing intake provided by oral alimentation and oral nutritional supplements, PN was progressively reduced up to 30% of caloric needs. As shown in Figure 1,

body weight remained stable during this period hiding the progressive decrease in fat-free and body cell mass while extracellular water increased up to 82.3% of total body water (normal values $<40\%$). This was probably due to malnutrition-induced enteropathy and malabsorption, a peculiar form of intestinal failure caused by severe malnutrition (Figure 2).⁵ Therefore, we resumed PN providing 60%-70% of total energy needs and reduced oral intake in order to contrast malabsorption and osmotic diarrhea due to unabsorbed residual foods. We tried administering PN mostly during CVVHDF-free hours to gather maximum effect. As shown in Figure 1, we obtained a steady increase in FFM and BCM and a progressive reduction in ECW. The psychological impact of this strategy was just as challenging and had to be addressed to assure patient compliance. Once peritoneal leakage was reduced with colchicine therapy, we arranged the patient's discharge, continuing parenteral nutrition at home in order to give time to recover intestinal function and nutritional status. In this phase, the increase in FFM and BCM coincided with the increasing body weight. Monitored prealbumin and cholinesterase, indices of protein synthesis, documented the efficacy of renutrition process (Figure 1). The proportion of PN and oral alimentation was functional to sustain an increasing trend of all the aforementioned parameters.

Home parenteral nutrition was successfully carried out from 6th to 13th month after OHT improving quality of life, functional status, and weight gain, with no PN-related complications. Physical activity helped regaining muscle mass.

3 | DISCUSSION

Several studies have outlined higher risks and worse outcomes for congenital heart disease (CHD) patients after OHT.⁶

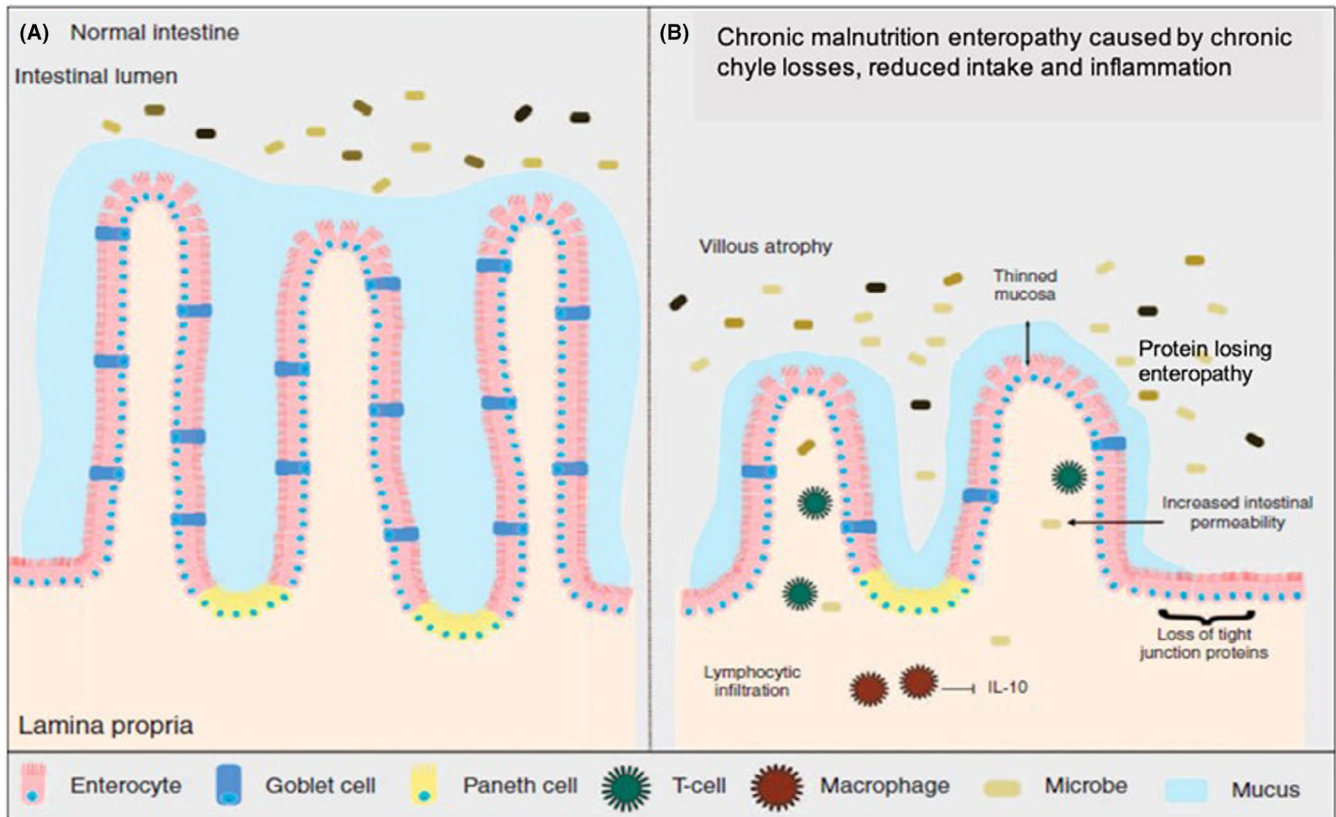


FIGURE 2 Intestinal alterations in malnutrition enteropathy. As compared to normal intestinal structure and function (A), the malnourished intestine (B) exhibits reduced absorption (villous atrophy and mucosal thinning), altered gut barrier function, and inflammation (lymphocytic infiltration, increased CD3 + T-cell activity, and repression of IL-10 expression by macrophages). All of these are aggravated by protein-losing enteropathy. Modified with permission from Attia et al⁵

The key expression of the post-OHT clinical course is persistence or worsening of generalized lymphatic insufficiency, as observed in our case. Loss of this protein, fat, fat-soluble vitamins, lymphocytes, immunoglobulins, and electrolyte-rich fluid may result in nutritional deficiencies and prolonged hospitalization that could potentially be fatal if not adequately treated.⁷

Although there is evidence to suggest that nutrition should have a role in the management of patients with chyle leakage, it is not known which dietary methods are most effective.⁷ The progressive reduction of fat-free and body cellular mass (respectively, 19.5 and 4.8 kg/m) revealed by bioelectrical impedance analysis (BIA) helped our decision-making process. As stated in the literature,⁷ long-term conservative therapy may be highly detrimental to the health of the patient. Therefore, monitoring the nutritional status is crucial, and short-term nutritional indices, such as prealbumin or cholinesterase, might also be useful to investigate.

Due to lack of scientific consensus on the optimal parenteral nutrition support in patients with chyle leakage, it is challenging to define the most suiting treatment strategy.

Compensating protein losses with high-protein intake may lead to excessive deamination capacity of the urea cycle and result in hyperazotemia. In our case, reducing the nitrogen

load to a maximum dose of 3 g/kg of free fat body mass improved protein levels without modification of the dialysis parameters.

Body weight is not a useful index in severely malnourished patients with expanded extracellular water (ECW) compartment. Our patient's ECW had reached 82.3% of the total body water (measured with BIA), thus lessening the efficacy of the hemodialysis. Albumin levels were not suitable to monitor nutritional status as it was periodically infused, while prealbumin and cholinesterase are not influenced by therapies and are useful protein synthesis indices.

Reduction of chyle leakage, ascitic effusion, and ECW was obtained by the administering colchicine. Action mechanisms of this molecule are not clearly understood, but it is known that it exerts a sustained anti-inflammatory effect. An effective therapy for familial Mediterranean fever (FMF) is also successfully used to treat idiopathic recurrent acute pericarditis (IRAP) and recurrent pericarditis and as primary prevention for postpericardiotomy syndrome.^{8,9}

As stated by the guidelines on nutritional support in critically ill patients, oral or enteral intake is the preferred nutritional route, having a lot of advantages compared to PN unless calorie and protein targets are difficult to achieve. Malnutrition enteropathy, characterized by villous atrophy,

upregulated intestinal inflammation, loss of goblet cells, and increased permeability (similar to chronic intestinal inflammatory diseases), is described in severely malnourished children,⁵ and it hampers the efficacy of conventional nutritional strategy. Long-term and successful home parenteral nutrition support was needed in our patient to treat the transient intestinal failure, as shown in Figure 1, with iv supplementation of vitamins and micronutrients.

4 | CONCLUSION

Chronic malnutrition, chyle leakage, and protein-losing enteropathy persist after failing Fontan OHT, aggravating pre-existent malnutrition, and shortages. Body composition and hematological nutritional indices, more than anthropometry, may help define malnutrition severity and treatment. Malnutrition enteropathy determines transient intestinal failure and inflammation. Therefore, parenteral nutrition is required to balance insufficient intestinal absorption and increased energy needs.

CONFLICT OF INTEREST

The authors have nothing to disclose.

AUTHORS' CONTRIBUTION

A.L: conceived the study, and drafted and revised the manuscript. EA, LD, MTC, AR, SI, LP, and F.R: critically revised and approved the manuscript.

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How to cite this article: Lezo A, Aidala E, Deorsola L, et al. Malnutrition and chyle leakage: A life-threatening duo in heart transplantation post-Fontan procedure. *Clin Case Rep*. 2020;8:2055–2059. <https://doi.org/10.1002/ccr3.3060>