A Case of Protein Losing Enteropathy after Fontan Operation

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Abstract

Protein Losing Enteropathy (PLE) is a condition in which an excessive amount of proteins are lost through the gastrointestinal tract leading to hypoproteinemia and manifesting as edema, ascites, and diarrhea. While in most cases PLE is a treatable disorder with good outcomes, the morbidity and mortality of the disorder is significantly elevated in patients with a history of Fontan surgery–an operation used to palliate patients born with a single ventricle by rerouting venous blood return directly to pulmonary circulation. After failure of first-line therapeutics of diuretics and steroids, this case study explores the successful treatment of a 5-year-old patient with PLE after fontan operation through lymphatic imaging and intervention.

Introduction

Protein Losing Enteropathy (PLE)

Causes
- erosive or ulcerative disorders (IBD), non-ulcerative disorders (celiac disease), disorders that increase interstitial pressure (congenital heart disease, lymphatic obstruction)

Increased mucosal GI tract permeability ➡ leakage of serum proteins in GI tract
Increased lymphatic pressure ➡ leakage of protein-rich lymph fluid in GI tract

Hypoproteinemia

(decreased serum protein reduces oncotic pressure of blood, causing fluid from intravascular compartment to be pushed into interstitial tissue)

Symptoms
- edema, ascites, abdominal pain, diarrhea, pleural effusion, pericardial effusion

Diagnosis
- HX, PE, elevated alpha-1 antitrypsin levels in fecal samples, decreased albumin

Treatment
- diuretics, oral controlled-release budesonide, liver lymphangiography embolization, cardiac catheterization/ Fontan revision, cardiac transplantation

Case Report

A 5-year-old boy presents to the hospital with his mother complaining of worsening generalized edema, significant in the face and abdomen, for the past week.

- **History**:
  - Birth- severely hypoplastic right ventricle, double-inlet left ventricle, mitral atresia, levo-transposition of the great arteries with a small bulboventricular foramen, and coarctation of the aorta
  - Age 3- staged palliation culminating in Fontan procedure
  - Age 4- diagnosed with PLE with albumin of 1.8 g/dL after presenting with periorbital edema, started on budesonide 3 mg and lasix 20 mg BID with symptomatic improvement
  - Age 5- attempt at weaning budesonide due to side effects of weight gain and unwanted hair growth resulting in presentation to hospital with significant generalized edema, worse in face and abdomen x 1 week

- **Physical Exam:**
  - Firm, distended abdomen with positive fluid wave test suggestive of mild to moderate ascites.
  - 2+ pitting edema in upper and lower extremities bilaterally throughout along with significant periorbital edema

- **Diagnostic Testing:**
  - Elevated alpha 1-antitrypsin feces levels at 205 mg/dL (reference range <55 mg/dL)
  - Decreased albumin level at 2.5 g/dL (reference range 3.8-5.4 g/dL)
  - Decreased total protein levels at 3.7 g/dL (reference range 5.9-7.9 g/dL)

Interventions/ Timeline

Hospitalized with acute exacerbation of PLE
Given albumin and restarted on budesonide 3 mg daily with improvement

Clearing for lymphatic intervention
- Echocardiogram normal (unobstructed proximal fontan pathway, normal LV function, no effusion)
- Cardiac cath normal (CVP, PA, LV filling pressures WNL)

Hepatic lymphangiogram and endoscopy
No lymphatic leaks in the GI tract identified

MRI lymphangiogram
Lymphatic leak into retroperitoneum identified and embolized

Right heart cath and venogram
Chronic occlusion of left innominate vein identified and obliterated with subsequent balloon angioplasty and stent implantation

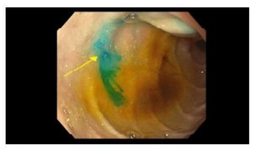
Discharged
-Albumin 2.7 g/dL alpha-1 antitrypsin 405 mg/dL improved symptoms but still requiring albumin and lasix treatments x1-2 weeks
-Revaluation 3 months later

Repeat cath and venogram
Stenosis of stented left innominate vein with near occlusive thrombus treated with aspiration thrombectomy and stent-in-stent implantation

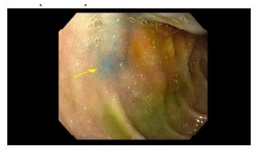
Subsequent venogram
Widely patent stent

MRI hepatic lymphangiogram
Leakage of hepatoduodenal lymphatics into duodenum confirmed with methylene blue injection and embolized with glue. **Figure 1.**

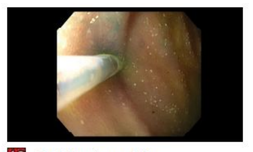
Discharged and 1 month f/u
Albumin 4.4 g/dL total protein 6.2 g/dL no edema or abdominal pain



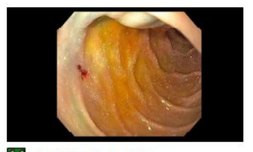
10 2nd Portion of the Duodenum
methylene blue dye - site of extravasation (arrow)



12 2nd Portion of the Duodenum
methylene blue dye - site of extravasation (arrow)



13 2nd Portion of the Duodenum
injection of site wtih glue



14 2nd Portion of the Duodenum
post injection

Figure 1. After the lymphatic system was injected with methylene blue dye, upper GI endoscopy was advanced to the duodenum where dye leakage was visualized and subsequently embolized with glue.

Discussion

"PLE is an uncommon but life-threatening complication of the Fontan operation that occurs in 4-13% of the patients and associated with a very high mortality and a 5-year survival rate of 46-50%".[2]

- The pathophysiology linking these patients to PLE is poorly understood.
  - Some believe it to be due to elevated systemic venous pressures causing dilated lymphatic vessels to leak lymph into the gastrointestinal tract.
  - Others believe decreased cardiac output leading to mesenteric vascular resistance has more of a correlation to the development of PLE than increased pressures alone. This has been supported by several studies showing resolution of PLE after undergoing creation of fenestrations in the cavopulmonary connection, which in turn increases the patient's cardiac output.
  - All studies however fail to come to concrete, statistically relevant, and evidence-based conclusions on this.

- The treatment of PLE in these patients is similarly ambiguous.
  - Children's Hospital of Philadelphia's approach includes diuretics, anticoagulation for risk of thromboembolism, aldosterone inhibition therapy and pulmonary vasodilators to lower pressures, and budesonide.
  - Chronic and severe patients lymphangiography embolization and cardiac catheterization or Fontan revision to lower pressures
  - Cardiac transplantation is definitive.

Conclusion

In the case of this patient, his PLE was initially symptomatically treated with chronic budesonide and diuretics before more definitive treatment through lymphatic intervention. Lymphangiogram with glue embolization stopped the leakage of lymph into the duodenum, and stenting of the occluded left innominate vein increased cardiac output while decreasing pressure. The main successes in treating this patient was in identifying the underlying causes of his PLE, improving his symptoms and laboratory values effectively. However it is important to note more research is needed in this field due to the poor outcomes and the unknown pathophysiology and disease processes linking PLE and patients who have undergone the Fontan procedure.

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