Case report

Gastrointestinal haemorrhage in protein-losing enteropathy associated with the Fontan circulation

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Case presentation

A 29-year-old patient was born with a double inlet left ventricle with transposition of the great arteries and pulmonary valvular stenosis. This was initially treated with a right modified Blalock–Taussig shunt, and 2 years later he underwent a Fontan operation. Aged 13 years he had an aortic valve replacement with reconstruction of his Fontan circulation, making it more haemodynamically streamlined. Due to clinical signs attributable to deteriorating cardiac function, his Fontan circulation was further surgically revised at the ages of 14 and again at 21 years.

Aged 14 years the patient developed a protein-losing enteropathy (PLE), which had been progressively worsening. His serum albumin gradually declined from 35 g/dl to troughs of 10 g/dl. He became peripherally oedematous and developed bilateral pleural effusions and ascites, which gradually worsened despite optimal treatment. He was malnourished and was commenced on total parenteral nutrition. However, this resulted in little improvement in the serum albumin concentration.

The diagnosis of PLE was confirmed with a technetium-labelled radioisotope scan (protein loss study), which revealed a diffuse generalized protein leak as well as more localized areas of protein leak from a loop in the small intestine with ‘hot spots’ in the duodenum. This is illustrated in Figure 1. In addition to this, his serum α1-anti-trypsin clearance was increased consistent with PLE. There are case reports regarding re-section of the bowel for treatment of localized PLE. Therefore, a video capsular endoscopy was performed to look for any potentially re-sectable precipitating lesions such as focal lymphangiectasia. This demonstrated oedematous villi with atrophic changes and is illustrated in Figure 2.

The patient developed a deep vein thrombosis that required heparinization and soon after this he suffered two episodes of haematemesis coupled with fresh per rectal bleeding. An endoscopy of his upper gastrointestinal tract demonstrated an oedematous duodenum that was very congested and macroscopically showed bleeding both spontaneously and on contact.

Discussion

The Fontan circulation is surgically created to palliate single ventricular physiology. It provides total venous bypass of the single ventricle, thereby establishing obligatory venous hypertension and variable limitation in cardiac output reserve.

PLE is a devastating disorder that has an almost invariable mortal outcome during late follow-up. We describe here an alternative mechanism whereby the disease advances and which may account for its late poor prognosis.
PLE has a number of potential underlying mechanisms. Raised venous pressures are intrinsic to the Fontan circulation and are associated with albumin loss in animal models through the disruption of heparan sulphate membranes. Depression in cardiac output, common in the Fontan circulation, may contribute through raising mesenteric resistance as blood flow is shunted away from the gut to conserve flow to working muscles, brain, kidneys and liver. Not infrequently a contemporary insult to the gastrointestinal tract by means of a viral infection is demonstrable. This may contribute to disruption of the basement membrane and also directly contributes to elevation in tumour necrosis factor and interferon-α concentrations, which play an important role in the pathophysiology of PLE. The Fontan circulation is also known to be associated with a high incidence of cardiac cirrhosis in up to 30% of the cases. Under such circumstances, hepatic resistance may be elevated and contributes to higher portal pressures and, therefore, mesenteric resistance, and hence may contribute to the development of PLE.

The pathophysiologic mechanisms underlying gastrointestinal blood loss in PLE are not completely understood, but may involve widening of gap junctions between gastric epithelial cells with resultant fluid and protein losses. It is known that

Figure 1. Nuclear medicine scan (technetium labelled) demonstrating diffuse loss of protein in the small but also in the large bowel.

Figure 2. Capsular endoscopy: oedematous villi with atrophic changes.
TNF-α impairs epithelial barrier function by altering structure and function of the tight junction, which could be of pathogenic relevance in PLE. The average diameter of an erythrocyte is reported to be between 7.2 μm and 7.4 μm. The median area of a gap junction under physiological conditions varies between 0.05 μm² and 0.41 μm². We postulate that the mechanism for gastrointestinal blood loss in PLE is due to disruption of basement membrane integrity to such a degree that blood loss is possibly because of erythrocyte translocation through pro-inflammatory cytokine-mediated widened gap junctions. However, further research is needed to verify this.

Conflict of interest: None declared.

References