Cardiology in the Young

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Successful use of long-acting octreotide for protracted gastrointestinal bleeding related to protein-losing enteropathy after the Fontan procedure: a case report

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Brief Report

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Abstract

Gastrointestinal bleeding complicated with protein-losing enteropathy after the Fontan procedure has been often reported in recent years, but there is no established therapy for it.

We report the case of an 18-year-old boy who suffered from abdominal pain, melena, and anaemia due to intractable haemorrhagic protein-losing enteropathy after the Fontan procedure. He was successfully treated with octreotide therapy.

Protein-losing enteropathy is a late postoperative complication of the Fontan procedure; it occurs in 5–15% of the patients.[1] The relationship between gastrointestinal bleeding and protein-losing enteropathy has not been adequately reported in literature.[2-5] Moreover, the aetiology and specific treatment for it have not been established. The number of post-Fontan patients has increased, leading to an expected increase in gastrointestinal bleeding with protein-losing enteropathy after the Fontan procedure. Gastrointestinal bleeding with protein-losing enteropathy significantly compromises the patient's quality of life, requiring frequent blood transfusions for progressive anaemia in addition to the usual treatment for protein-losing enteropathy. In previous reports,[2,5] the treatments for this condition were highly invasive: enteroscopic argon plasma coagulation, displacement of the Fontan conduit, and cardiac transplantation.

The mechanism of octreotide is an anti-bleeding effect through decreased splanchnic flow and inhibition of neoangiogenesis.[6] We report a case of successful treatment with octreotide of intractable protein-losing enteropathy with gastrointestinal bleeding after the Fontan procedure.

Case report

The patient was diagnosed with a criss-cross heart, hypoplastic right ventricle, ventricular septal defect, and an atrial septal defect complicated by Holt-Oram syndrome. After a modified Blalock–Taussig shunt and a bidirectional cavopulmonary shunt, he underwent a staged Fontan procedure at the age of 3 years. A single-chamber ventricular pacemaker was implanted for a complete atrioventricular block that had developed after the bidirectional cavopulmonary shunt. The extracardiac conduit was fenestrated, but spontaneously closed within 6 years after the Fontan procedure.

At 15 years of age, the patient developed protein-losing enteropathy, which was confirmed by Tc-99 m scintigraphy, and required repeated intravenous albumin and immunoglobulin G infusions. The administration of prednisolone (60 mg/day) and low-molecular-weight heparin failed to improve the patient's condition ; however, improvement occurred after a dual-chamber pacemaker replaced the single-chamber ventricular pacemaker.

The patient received oral medications including diuretic, angiotensin-converting enzyme inhibitor, β-blocker, and pulmonary vasodilator drugs. Anti-platelet treatment with dipyridamole (200 mg/day) rather than aspirin (due to the risk of NSAIDs-related bleeding in the upper gastrointestinal tract) was followed but not anticoagulation treatment.

The patient was admitted to our hospital with complaints of exacerbating abdominal pain and melena when 18 years old. On admission, his haemoglobin (8.2 g/dL) and albumin (2.7 g/dL) levels were low (Fig 1). Despite prednisolone doses (5 mg/day), protein-losing enteropathy recurred.

As a differential diagnosis of gastrointestinal bleeding, there were no abnormal coagulation or tumour markers, and faecal *Helicobacter pylori* antigens were negative. No sources of bleeding were noted on enhanced abdominal CT, Meckel scintigraphy, or mesenteric angiography. Coagulation investigations also did not help ascertain the cause of bleeding. However, gastrointestinal bleeding scintigraphy revealed a haemorrhage from the distal duodenum to the ileum.

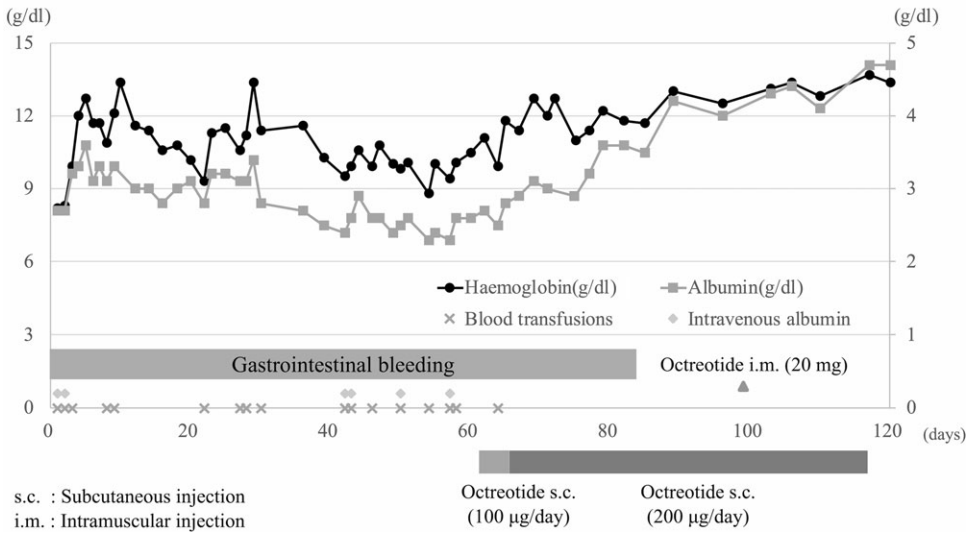

Figure 1. Clinical course during hospitalisation. The patient's clinical and laboratory parameters began to improve gradually after administering octreotide.

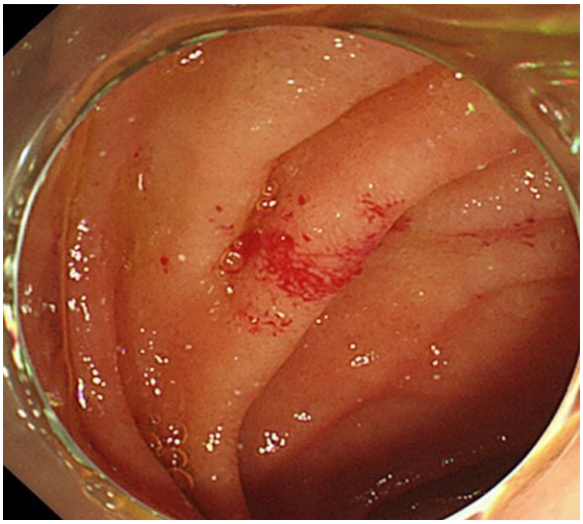

Figure 2. The endoscopic image reveals vascular ectasia and bleeding, both spontaneously and on contact, in the duodenum.

Furthermore, upper gastrointestinal endoscopic imaging showed vascular ectasia and bleeding, both spontaneously and on contact, in the duodenum (Fig 2). Haemorrhagic protein-losing enteropathy was diagnosed based on findings of hypoalbuminemia, upper gastrointestinal endoscopy, and gastrointestinal bleeding scintigraphy. A duodenal biopsy showed inflammation, with increased numbers of lymphocytes and plasma cells, but lymphangiectasia was absent.

Catheter examination did not show pressure difference between central venous pressure (15 mmHg) and pulmonary artery wedge pressure (12 mmHg) to require fenestration. Further, as no dyssynchrony was noted on echocardiography, cardiac resynchronisation therapy was not indicated.

As hospitalisation was prolonged by frequent transfusions of blood and blood products for anaemia and hypoproteinaemia, we commenced subcutaneous octreotide injection twice daily (100 μg/day); the dosage was increased 4 days later to 200 μg/day based on a previous report on its effectiveness in treating intractable protein-losing enteropathy.[7] This is the commonly used dose for carcinoid tumours and VIPomas. The patient's clinical and laboratory parameters showed improvement; abdominal symptoms improved 2 days after injections began, the faecal occult blood test was negative 3 weeks later, and haemoglobin and albumin levels stabilised without blood products (Fig 1). Octreotide was subsequently approved for off-label use in the hospital, and we switched from a subcutaneous injection to sustained-release intramuscular injection (Sandostatin LAR, 20 mg/time, once a month); the commonly used dose for carcinoid tumours, VIPomas, and acromegaly.

The patient was given octreotide once a month and discharged 8 weeks later. For a year, he was free of protein-losing enteropathy without any repeated transfusions and returned to school. No adverse events were observed.

Discussion

The Fontan circulation helps establish total venous bypass of the single ventricle, thereby causing obligatory venous hypertension and variable limitations of the cardiac output reserve.[3] Elevated venous pressure, increased ventricular end-diastolic pressure, elevated mesenteric vascular resistance, infection, and immunologic mechanisms have been associated with protein-losing enteropathy in patients after the Fontan procedure.[2] A few reports are available on gastrointestinal bleeding complicated with protein-losing enteropathy after the Fontan procedure,[2-5] but the underlying pathophysiological mechanisms are yet to be established.

Octreotide is a long-acting somatostatin analogue that suppresses gastrointestinal motility and pituitary, pancreatic and intestinal hormone secretion. The mechanisms by which octreotide might exert an anti-bleeding effect include decreased splanchnic flow and inhibition of neoangiogenesis.[6]

Alternatively, while subcutaneous octreotide administration requires multiple daily injections, octreotide long-acting release, an intramuscular injection, slowly releases octreotide and is injected every 4 weeks, reaching a steady-state after three injections.[8] This dosage technique may improve medication compliance and therapeutic effectiveness. Additionally, the side effects of octreotide long-acting release are tolerable with minimal impairment.[9,10]

There is no standard therapy for gastrointestinal bleeding complicated by protein-losing enteropathy after the Fontan procedure. Treatments detailed in previous reports are highly invasive: enteroscopic argon plasma coagulation, displacement of the Fontan

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conduit, and cardiac transplantation.[2,5] Though in a previously reported case, subcutaneous somatostatin, corticosteroids, and heparin had been effective,[4] it could not be determined which of those treatments was the most helpful.

From endoscopic and pathological findings, it is clear haemorrhagic protein-losing enteropathy can be caused by inflammatory cell infiltration, and mucosal haemorrhage from capillary beds, which can cause persistent anaemia. Since octreotide has the effect of decreased splanchnic flow and inhibition of neoangiogenesis,[6] it may have improved the capillary ectasia that can be considered as a source of bleeding observed by endoscopy.

Octreotide may be useful for resolving gastrointestinal bleeding after the Fontan procedure. It is a treatment worth considering in the case of intractable haemorrhagic protein-losing enteropathy. However, further studies are needed to establish a standardised treatment method.

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Conflicts of interest. None.

Ethical standards. The authors assert that all procedures contributing to this work comply with the Helsinki Declaration of 1975, as revised in 2008, and has been approved by the Ethics Committee for Human Research at Jikei University, and informed consent was obtained from the patient for publication of this case report.

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