

**Title:**

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**Using octreotide for refractory ascites after liver transplantation**

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**ABSTRACT**

Refractory ascites is a condition associated with a reduced survival and a poorer quality of life. Portal hyperflow after liver transplantation is one of the main causes. We report the case of a female patient with refractory ascites after liver transplantation who was treated with splenic embolization. Ascites persisted despite embolization due to splenic revascularization by short gastric vessels and repeat embolization was technically unfeasible. Based on pathophysiology data, she was treated with octreotide, a somatostatin octapeptide analog, which resulted in splanchnic vasoconstriction and a reduction of the portal flow and venous pressure. After four months of treatment with octreotide, the patient had a good clinical status without ascites.

**Key words:** Octreotide. Refractory ascites. Splenic embolization.

**INTRODUCTION**

Refractory ascites, defined as persistent ascites that cannot be controlled with medical treatment, are associated with reduced survival and a poorer quality of life (1). Portal hyperflow may cause refractory ascites after liver transplantation. Furthermore, procedures such as splenic artery ligation or embolization, splenectomy, porto-systemic shunt (2) or transjugular intrahepatic portosystemic shunt (TIPS) are usually required to regulate the portal flow.

We report the case of a female patient with refractory ascites secondary to portal hyperflow following a liver transplantation, under treatment with octreotide.

### **CASE REPORT**

The case was a 67-year-old female who had received a liver transplant from a brain-dead donor due to cirrhosis secondary to non-alcoholic steatohepatitis (NASH). Two months after transplantation the patient developed tense ascites and pancytopenia, which required regular evacuation paracentesis procedures. Doppler ultrasound showed patent vessels and an 18-cm splenomegaly. Other causes of ascites were excluded, including cardiac, renal and infectious ascites. Furthermore, a transjugular liver biopsy was performed and venous pressures were measured, which revealed a 13-mmHg gradient. Liver biopsy findings were nonspecific with lobular lymphohistiocytic infiltrates. Therefore, the final diagnosis was portal hyperflow and a splenic artery embolization procedure was performed. The procedure was uneventful and the ascites diminished gradually. However, the ascites recurred three months after embolization. Doppler ultrasound showed revascularization from gastric collateral vessels, with occlusion of the origin of the splenic artery. A repeat embolization was considered, which could not be performed as it was technically impossible (Fig. 1). Therefore, the idea of surgical splenectomy was entertained but was not implemented due to clinical deterioration (pancytopenia and renal impairment). Due to this, and based on the pathophysiology of somatostatin, a decision was made to initiate treatment with subcutaneous octreotide at 100 mcg every eight hours. This regimen was previously assessed by the Pharmacy Department and Ethics Committee of the hospital, who eventually approved the use of this medication in the compassionate setting. After one month, the patients'

weight was stable, there was improved renal function and there were no ascites, which allowed the discontinuation of diuretics. Four months after treatment onset with octreotide, the patient has a good clinical condition and remains free from ascites (Fig. 2).

## **DISCUSSION**

Octreotide is a synthetic, octapeptide analog of somatostatin with a greater potency and longer standing inhibitory effects compared with somatostatin (3). It is used to treat pancreatic fistulae or chylous ascites after extended para-aortic lymphadenectomies. Its use is well established in patients with acromegaly or carcinoid tumors. An increase in the mean blood pressure has been primarily reported among its associated side effects, likely due to its direct vasoactive activity (4).

The use of somatostatin as hepatic flow modulator in patients with refractory ascites has not been reported thus far in the literature. Somatostatin reduces portal venous pressure via five types of receptors, both inside and outside the liver. It induces splanchnic vasoconstriction, thus reducing portal flow and venous pressure.

Troisi et al. (4) reported the use of this drug as a flow modulator during transplantation in liver recipients with severe portal hypertension. The use of somatostatin in this setting reduces the hepatic gradient, while having no impact on hepatic artery flow. However, this study was performed in cirrhotic livers and little is known about the action of the drug in healthy organs. Somatostatin induces sinusoidal vasodilation by stimulating vagal activity in patients with chronic liver disease; this effect is lost after implantation of a new liver graft (4). In our case, the drug was used in a female liver transplant patient with a normal liver function but with refractory ascites. Its effects are similar to those of complete splenic embolization or splenic artery ligation. As splanchnic vasoconstriction develops, the venous return through the portal system decreases, as does hyperflow. On the other hand, portal hyperflow results in a reduced hepatic arterial flow via a “buffer” or “washout” response mechanism in the hepatic artery. This is an intrinsic self-regulatory system that uses the release of adenosine, a powerful arterial vasodilator,

to reduce arterial flow (5). This may result in increased hepatic artery resistive index, biliary damage and elevated transaminases. Therefore, when portal hyperflow is avoided, the arterial flow returns to normal and prevents the potential consequences in a recently transplanted liver.

To conclude, treatment with octreotide may be useful in cases of refractory ascites secondary to portal hyperflow.

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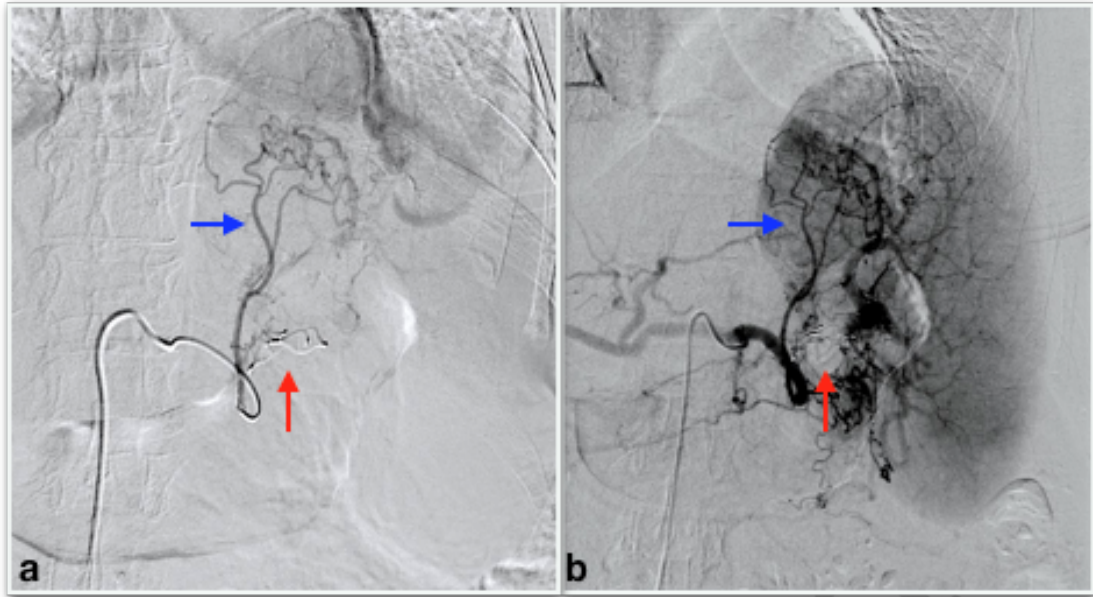


Fig. 1. A and B. Splenic revascularization by short gastric vessels (blue arrows). Positioning of an Amplatzer® embolization plug (red arrows) in the distal splenic artery.

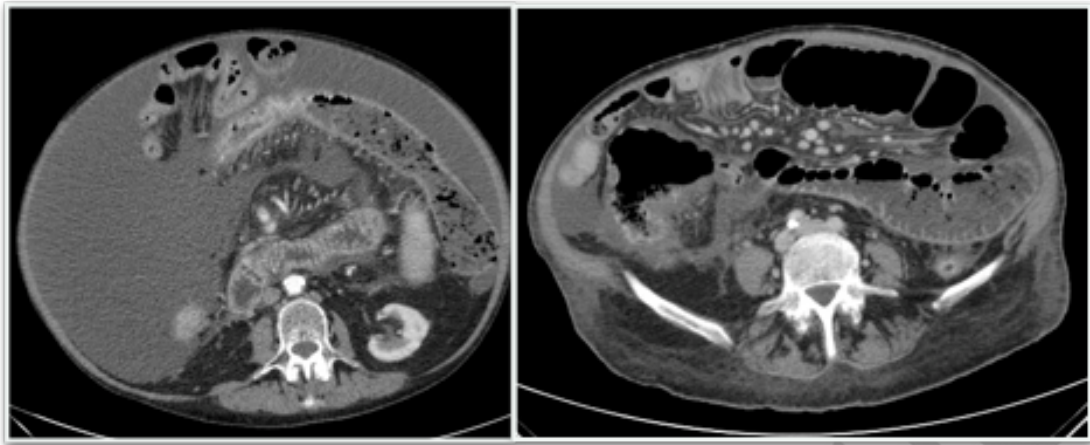


Fig. 2. A. Ascites prior to octreotide administration (after splenic embolization). B. Minimal ascites after treatment with octreotide.