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The Use of Lanreotide Autogel® in the Treatment of Intestinal Obstruction in a Patient with Adenocarcinoma

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Key Words
Intestinal obstruction · Adenocarcinoma · Somatostatin analogue · Lanreotide Autogel®

Abstract
Intestinal obstruction is a common complication in patients with advanced abdominal or pelvic cancer. The synthetic somatostatin analogue octreotide can help relieve nausea, vomiting and pain in patients with inoperable obstruction. Here, we report a case of recurrent intestinal obstruction in a patient with adenocarcinoma. Although the obstruction was resolved after 3 days of treatment with octreotide, new episodes of obstruction occurred, resulting in a delay of the chemotherapy treatment. After 3 episodes of obstruction, we initiated treatment with a longer-acting somatostatin analogue, lanreotide Autogel® 120 mg, administered once every 4 weeks. The treatment with lanreotide Autogel is being continued, allowing for continuation of the chemotherapy without further episodes of intestinal subocclusion or obstruction. Until November 2013, the patient received eighteen 4-weekly injections of lanreotide Autogel and did not report side effects. This case report demonstrates the successful treatment of intestinal obstruction with lanreotide Autogel in a patient with adenocarcinoma.

Introduction

Intestinal obstruction is a common complication in patients with advanced abdominal or pelvic cancer and has a significant impact on their quality of life. In patients with inoperable malignant bowel obstruction, the synthetic somatostatin analogue octreotide relieves nausea, vomiting and pain, and decreases drainage from a nasogastric tube [1].

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Here, we report the use of the long-acting somatostatin analogue lanreotide Autogel® (Somatuline®; Ipsen NV) in the treatment of bowel obstruction in a patient with adenocarcinoma and peritoneal carcinomatosis.

Case Presentation

In January 2012, a 60-year-old woman presented with a 3-month history of increasing abdominal pain and a change in the stool pattern with a single episode of anal red blood loss in the past week. She had a medical history of hypercholesterolemia and had previously undergone appendectomy. An ultrasound of the abdomen showed several masses dispersed over the peritoneum, compatible with significant peritoneal metastasis. Diffuse ascites fluid was also noted and could not be tapped. Clinical examination and auscultation showed a slightly enlarged abdomen with good peristalsis of the intestine. No clangor was noted. Colonoscopy revealed a large ulcerating lesion at the level of the sigmoid colon, which was diagnosed as a moderately differentiated adenocarcinoma after biopsy.

No surgery was performed due to the presence of peritoneal carcinomatosis. Chemotherapy with 18 biweekly cycles (1 cycle every 2 weeks) of FOLFIRI and bevacizumab (Avastin®, Roche) was started. FOLFIRI was administered according to the following schedule: day 1, irinotecan 180 mg/m^2; days 1 and 2, leucovorin 100 mg/m^2, 5-fluorouracil bolus 400 mg/m^2 and 5-fluorouracil infusion 600 mg/m^2. Avastin was given at a dose of 5 mg/kg every 2 weeks. If the patient had responded to this treatment, the possibility of performing debulking surgery and hyperthermic intraperitoneal chemotherapy would have been considered. The abdominal pain disappeared after the first month of chemotherapy, while the ascites disappeared after 6 weeks. There was also a slight regression of the peritoneal masses.

During the 5th, 6th and 7th cycle of chemotherapy, the patient was hospitalized because of clinical signs of intestinal subocclusion (vomiting, absence of stools and flatus) that evolved into complete obstruction. A CT scan of the abdomen did not reveal the cause of the obstruction or deterioration of the oncological lesions. Based on this observation, a FOLFIRI-induced mucositis, motility disturbances due to peritoneal metastasis or a combination of these two factors were suspected. During hospitalization, fluids, alizapride (Litican®, 300 mg/day; Sanofi-Aventis) and methylprednisolone sodium succinate (Solu-Medrol®, 40 mg/day; Pfizer Inc.) were administered intravenously, paracetamol (1 g/dose) was administered intravenously 4 times a day and octreotide (Sandostatin®, 0.5 mg/dose; Novartis) was administered subcutaneously 3 times a day until the obstruction resolved. Oral consumption of food and fluids was withheld, and a nasogastric tube was placed. At each of the 3 hospitalization episodes, an enema was performed. After the first episode of obstruction, the dose of FOLFIRI was decreased to 75%, while the dose of Avastin was not decreased. All episodes of obstruction resolved after 3 days, and the chemotherapy was reintroduced after 1–2 weeks following resolution of the obstruction. After the third episode of obstruction, we initiated treatment with lanreotide Autogel 120 mg, injected deep subcutaneously once every 4 weeks. The 120-mg dose was chosen based on our experience that the 90-mg dose has a lower efficacy. The treatment with lanreotide Autogel continued during the remaining 11 cycles of chemotherapy, and no further episodes of intestinal subocclusion or obstruction occurred.

Because tumor response following the 18 cycles of chemotherapy was not sufficient, debulking surgery or hyperthermic intraperitoneal chemotherapy treatment were not recommended. After a 3-month break in the chemotherapy treatment requested by the

patient, a second-line chemotherapy course was initiated. Lanreotide Autogel administration was continued during this treatment break. The patient is currently undergoing second-line chemotherapy with FOLFOX4 at 75% of the usual dose, administered once every 2 weeks in 12 cycles according to the following schedule: day 1, oxaliplatin 85 mg/m^2 at 75%; days 1 and 2, 75% of leucovorin 100 mg/m^2, 5-fluorouracil bolus 400 mg/m^2 and 5-fluorouracil infusion 600 mg/m^2. The 4-weekly lanreotide Autogel injections have been continued without interruption to support the quality of life of the patient. No new episodes of obstruction occurred until November 2013, and the patient reported no side effects due to lanreotide Autogel.

Discussion

Intestinal obstruction is reported in up to 51% of the patients with ovarian cancer and up to 28% of those with gastrointestinal cancer [2] and has an important impact on their quality of life. Due to contraindications such as intra-abdominal carcinomatosis, poor nutritional status or a large volume of ascites, surgery is not an option in a substantial portion of these patients [3, 4]. A nasogastric tube can be placed to drain secretions; however, this often causes a great amount of distress in the patient as well as nasal or pharyngeal irritation, nasal cartilage erosion, occlusion of the tube or spontaneous expulsion [1].

Short-acting somatostatin analogues such as octreotide (Sandostatin) are antisecretory drugs used in the treatment of patients with inoperable bowel obstruction. Somatostatin was initially discovered as an inhibitor of growth hormone release [5], but was later found to play an inhibitory role in the regulation of several organ systems such as the central nervous system, the immune system, vessel walls, the pancreas and the gastrointestinal tract [6]. Somatostatin analogues are valuable in the treatment of patients with malignant bowel obstruction because of their inhibitory effect on gastrointestinal motility and secretions and their ability to increase the absorption of water and electrolytes from the intestinal lumen [1]. The efficacy of short-acting somatostatin analogues in the management of symptoms due to malignant bowel obstruction has been reported in numerous patients, with control of vomiting obtained in more than 60% of the patients (reviewed in [7]). Reversal of malignant bowel obstruction after treatment with short-acting somatostatin analogues has also been reported [8]. The synthetic somatostatin analogue lanreotide has shown efficacy in the symptomatic treatment of inoperable bowel obstruction in patients with peritoneal carcinomatosis when administered in the form of microparticles [9].

Here, we report a case of intestinal obstruction in a patient with adenocarcinoma, which resolved after treatment with octreotide. However, new episodes of obstruction occurred, which each time led to a delay in the administration of chemotherapy. After the third episode, we initiated treatment with lanreotide Autogel. Until November 2013, the patient received eighteen 4-weekly injections of lanreotide Autogel and did not experience any further episodes of obstruction, suggesting that lanreotide prevents recurrence of intestinal obstruction in patients with intestinal cancer. Another advantage is that while short-acting octreotide has to be administered 3 times a day, lanreotide Autogel is administered only once a month, improving a patient's quality of life. Treatment with lanreotide Autogel prevented recurring episodes of obstruction, allowing the patient to continue the chemotherapy course without further delays and to start the second course.

To our knowledge, this is the first report of a successful use of lanreotide Autogel in the management of malignant bowel obstruction. Our results indicate that lanreotide Autogel

could be used as an alternative to a long-acting formulation of octreotide, which has recently shown efficacy in the symptomatic treatment of inoperable malignant bowel obstruction due to peritoneal carcinomatosis [10]. A long-term treatment with lanreotide, as reported herein, is further supported by the results of a study in which 3 patients with malignant bowel obstruction due to ovarian cancer received a monthly-administered long-acting depot form of octreotide (Sandostatin LAR® Depot) for a period of over 9 months, with no significant toxicities reported [11]. The efficacy and safety of lanreotide in the palliative treatment of inoperable malignant intestinal obstruction are currently being investigated in a phase II clinical trial (www.clinicaltrials.gov: NCT01076803).

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Disclosure Statement

Dr. Lybaert is a consultant for Ipsen.

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