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Hernia enlargement and pancreatitis in a patient with short bowel syndrome treated with teduglutide: a case report

Crecimiento de hernias y pancreatitis en una paciente con síndrome de intestino corto tratada con teduglutida: caso clínico

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ABSTRACT

Introduction: teduglutide (TED) is indicated for the treatment of patients with short-bowel syndrome (SBS) who are dependent on parenteral support.

Clinical case: we report the case of a 60-year-old woman with SBS treated with TED. She had previously undergone multiple surgical resections due to Crohn's disease. Her remnant bowel included only the duodenum and 50-60 centimeters of jejunum. The patient was dependent on intravenous fluids (2,320 mL/48 h) and had a high stoma output (3,000 mL/day). After four months of TED the jejunostomy output had decreased to 2,200 mL/day with a thicker consistency, and intravenous fluid therapy was reduced to 2,010 mL/48 h. TED was withdrawn due to acute pancreatitis and enlargement of two supraumbilical hernias with high strangulation risk.

Discussion: pancreatitis has been reported in clinical studies, and determination of amylase and lipase is recommended in all patients receiving TED. In contrast, there are no recommendations for the surveillance of hernia enlargement in patients on TED therapy, but we suggest the need for surveillance based on this case report.

Keywords: Teduglutide. Short bowel syndrome. Pancreatitis. Hernia enlargement. Case report

RESUMEN

Introducción: la teduglutida (TED) está indicada para el tratamiento de pacientes con síndrome de intestino corto (SBS) que precisen soporte parenteral.

Caso clínico: mujer de 60 años con SBS tratada con TED. Previamente se había sometido a múltiples resecciones quirúrgicas por su enfermedad de Crohn. Su intestino remanente incluía el duodeno y 50-60 centímetros de yeyuno. La paciente era dependiente de líquidos por vía intravenosa (2320 ml/48 h) y tenía una ostomía de

alto débito (3000 ml/día). Después de cuatro meses de TED, el débito de la yeyunostomía disminuyó a 2200 ml/día, con una consistencia más espesa, y la fluidoterapia intravenosa se redujo a 2010 ml/48 h. Se retiró la TED por pancreatitis aguda y agrandamiento de dos hernias supraumbilicales con alto riesgo de estrangulamiento.
Discusión: se han descrito casos de pancreatitis en estudios previos, por lo que se recomienda la determinación de la amilasa y la lipasa en los pacientes tratados con TED. Sin embargo, no hay recomendaciones específicas sobre la vigilancia del agrandamiento de hernias, pero sugerimos su idoneidad basada en este caso clínico.

Palabras clave: Teduglutida. Síndrome de intestino corto. Pancreatitis. Crecimiento de hernias. Caso clínico.

INTRODUCTION

Short bowel syndrome (SBS) is characterized by a significant decrease in effective intestinal surface due to anatomical or functional losses. The main causes of SBS are surgical resections, congenital defects, and diseases affecting the bowel. Crohn's disease is one of the underlying conditions that may require intestinal resection. Symptoms of SBS are variable, but normally characterized by diarrhea, fatty stools, abdominal pain, malnutrition, and dehydration (1). Patients suffering from SBS may require long-term IV supplementation (1).

Teduglutide (TED) is an analogue of glucagon-like peptide-2 (GLP-2), a hormone-based treatment that helps intestinal rehabilitation by reinforcing the structural and functional integrity of the remaining intestine in SBS (2). GLP-2 receptor activation stimulates mucosal growth, thereby leading to the expansion of epithelial surface area (3). This can enhance absorption of macronutrients and drugs (4).

TED is used in SBS patients requiring chronic parenteral support (PS). The pivotal trials of TED demonstrated that, in patients with intestinal

failure (IF) who required PS ≥ 3 times per week for at least 12 months, 63 % of those treated with TED had a relative reduction in their PS volume of > 20 % from baseline at weeks 20 and 24, compared with 30 % of patients receiving placebo ($p < 0.01$) (5,6). TED decreases dependence on parenteral support and, in some cases, independence from parenteral support can be achieved. This can markedly improve patient quality of life as well as decrease the risk of PS-related complications. However, as TED is a relatively new drug, the potential side effects are not well known yet. We report the case of a patient who presented with mild acute pancreatitis and enlargement of two supraumbilical hernias with peristomal location probably due to TED therapy.

CLINICAL CASE

A 60-year-old woman with Crohn's disease underwent multiple surgical resections (colectomy, duodenectomy, jejunostomy, proctectomy) between December 2008 and October 2014, which resulted in a remnant bowel including only the duodenum and 50-60 centimeters of jejunum distal to the ligament of Treitz. Her medical history included obesity, hypothyroidism, fibromyalgia, rheumatoid arthritis, scoliosis, hiatus hernia, and gallbladder removal. No previous history of pancreatitis was noted. Her regular medications included levothyroxine, ranitidine, sodium bicarbonate, fluoxetine, azathioprine, benzbromarone, magnesium, calcium, vitamins D2 and D3, sodium chloride, vitamin B12, omega-3 fatty acids, and taurine.

The patient became dependent on intravenous fluids (saline with vitamins, electrolytes, minerals, and trace elements) and had a high stoma output (3,000 mL/day) despite support with slowing agent therapies. TED was started in February 2019, with a starting dose of 3.9 mg/day (0.05 mg/kg). Eighteen weeks after starting TED, the jejunostomy output had decreased from 3,300 to 2,254 mL/day (32 % reduction) and had a thicker consistency, so intravenous fluids were

reduced from 2,320 to 2,010 mL/48 h (13 % reduction). The clinical follow-up data are detailed in table I.

Twenty-four hours after starting treatment the patient developed a fever attributed to an intestinal virus. After a month of TED therapy, the patient experienced an episode of radiculopathy, not attributable to TED. To treat this, pregabalin was initiated. After two months of TED therapy, two peristomal supraumbilical hernias enlarged, thus increasing the risk of hernia strangulation. They were managed conservatively; had they grown larger, a further bowel resection would have been needed. During the fourth month the patient experienced an episode of sudden abdominal pain, intolerance of oral intake, and increased acute phase reactants and pancreatic lipase, and she was diagnosed with mild acute pancreatitis. TED was considered a possible cause of pancreatitis, and therefore the drug was discontinued. Lipase levels increased suddenly from normal levels (< 100 U/L) to 17,335 U/L when diagnosed, and returned to normal levels after two weeks. After analgesic treatment and 24 h of digestive rest, a progressive oral diet was restarted and well tolerated.

Treatment with TED was permanently withdrawn, the stoma output increased significantly again and, consequently, the same initial parenteral support of 2,320 mL/48 h was reintroduced. The risk-benefit of TED treatment for this patient is currently being reassessed due to difficulties in preserving her central venous access and the high risk of hernia strangulation and pancreatitis.

DISCUSSION

In this case report we describe the first experience of a patient with SBS receiving TED in our hospital. In the randomized, placebo-controlled trials of TED, responders were those subjects demonstrating a reduction ≥ 20 % in parenteral volumes from baseline at weeks 20 and 24 (5,6). In our case, TED had to be withdrawn before week 20, so our results cannot be compared to

those of those clinical trials. Nonetheless, the patient was considered a responder by the clinicians, as she had a 32 % reduction in stoma output and a 13 % reduction in the parenteral volumes administered after 18 weeks of treatment.

Although only a small number of patients have received TED so far, this drug appears to be safe (3). The most commonly reported adverse reactions are abdominal pain (30 %) and injection site reactions (22 %) (7). In our case, the patient presented two complications attributable to TED. First, an enlargement of two peristomal supraumbilical hernias was detected. The mechanism of action of TED could explain these enlargements, as this drug induces mucosal growth. Other complications due to the stimulation of mucosal growth have already been reported, such as the development of duodenal polyps (8,9). Second, a huge increase in lipase was detected after four months of treatment, and the patient was diagnosed with mild acute pancreatitis. This side effect had already been described in clinical trials but with a low frequency (6). Other authors have already described increases in amylase and/or lipase in subjects receiving TED treatment (10). In 2017, Kochar et al. conducted a retrospective study including 13 patients with Crohn's disease undergoing TED treatment. Among the adverse events observed, one patient developed pancreatitis and another patient had an asymptomatic lipase and amylase elevation. Likewise, Lee et al. reported the case of a 70-year-old female with Crohn's disease in whom an increase in amylase and lipase was detected during TED treatment. In our case, the increase in lipase levels, along with the abdominal pain reported by the patient, led to the diagnosis of acute pancreatitis. A biliary origin was considered unlikely due to her history of gallbladder removal. Although pancreatitis could have been caused by drugs concomitantly taken by the patient (ranitidine, azathioprine, pregabalin or fluoxetine) or the coexistence of all of them, the time sequence suggests the onset of acute pancreatitis could be attributable to TED. Because of the high risk of hernia strangulation

and her short bowel remnant, TED rechallenge has been considered inaproppriate.

In conclusion, our patient experienced benefits from TED treatment, but also some complications attributable to this drug that led to its withdrawal. Our experience suggests that patients undergoing TED warrant close monitoring in order to detect possible complications over time.

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Table I. Clinical follow-up data

	Baseline	Month 1	Month 2	Month 3	Month 4	Month 5
Weight (kg)	78.1	78.7	79.1	78.9	78.6	78.7
BMI (kg/m^2)	31.3	31.5	31.7	31.6	31.5	31.5
Oral volume intake (mL/day)	3300	2829	2807	2835	2771	3010
PS volume (mL/48 h)	2320	2320	2320	2110	2010	2010
Feces output (mL/day)	3300	2961	2822	2700	2376	2254
Urine output (mL/day)	1525	1571	1438	1349	1269	1549
Urea (mg/dL)	40	31	38	25	40	34
Creatinine (mg/dL)	0.76	0.79	0.80	0.84	0.81	0.76

PS: parenteral support.