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CLINICAL CASE

Long-acting Release Octreotide for Pediatric Upper Gastrointestinal Bleeding

Octreótido de liberación prolongada para el tratamiento de hemorragia digestiva alta en Pediatría

I. Malla[a], S. López[a], L. Busquet[b], J. Lipsich[c], S. Sierre[d], G. Cervio[e], M. Cuarterolo[a]

[a]Unit of Hepatology, Department of Gastroenterology,. Hospital de Pediatría Prof. Dr. J.P. Garrahan, Buenos Aires, Argentina
[b]Unit of Gastrointestinal Endoscopy, Department of Gastroenterology, Hospital de Pediatría Prof. Dr. J.P. Garrahan, Buenos Aires, Argentina
[c]Department of Radiology, Hospital de Pediatría Prof. Dr. J.P. Garrahan, Buenos Aires, Argentina
[d]Department of Interventional Radiology, Hospital de Pediatría Prof. Dr. J.P. Garrahan, Buenos Aires, Argentina
[e]Department of Liver Transplant, Hospital de Pediatría Prof. Dr. J.P. Garrahan, Buenos Aires, Argentina

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What do we know about the subject matter of this study?

Digestive bleeding due to portal hypertension in Pediatrics is challenging for pediatric hepatologists, especially in cases with treatment difficulties. Long-acting release Octreotide administered intramuscularly emerges as a therapeutic option in such conditions.

What does this study contribute to what is already known?

Our study provides useful information regarding the successful treatment with OCT-LAR of a child with digestive bleeding due to portal hypertension with no other therapeutic options for the management of this complex and challenging pathology.

Abstract

Introduction: Upper gastrointestinal bleeding (UGIB) secondary to portal hypertension (PHT), without endoscopic or surgical treatment options due to an ectopic or unidentified bleeding site or the patient's anatomic characteristics, is challenging in pediatric hepatology. The usual treatment in these cases includes intravenous Octreotide. Recently, the availability of long-acting release Octreotide (OCT-LAR) for monthly intramuscular administration has become an interesting therapeutic alternative. **Objective:** To report the case of an infant with UGIB due to PHT who was successfully treated with OCT-LAR. **Clinical Case:** Eight-month-old patient with repeated episodes of UGIB due to extrahepatic portal vein malformation, requiring blood transfusions, and intravenous octreotide infusions. As neither endoscopic nor surgical treatment were feasible, we decided to start IM OCT-LAR monthly. After ten months of treatment, the patient did not present bleeding episodes. No medication-related events were observed. **Conclusion:** We consider that this report could help in the management of similar pediatric patients with UGIB due to PHT without conventional therapeutic possibilities.

Keywords:
Upper gastrointestinal bleeding;
portal hypertension;
long-acting release Octreotide

Correspondence:
Ivone Malla
ivonemalla@yahoo.com.ar

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Introduction

Treatment and prophylaxis of upper gastrointestinal bleeding (UGIB) secondary to portal hypertension (PHT) are controversial in pediatrics, mainly because of the lack of well-designed clinical trials with a high level of evidence in this population[1-6]. These difficulties increase if we consider the subgroup of patients without possibilities for endoscopic or surgical treatment due to ectopic or unidentified sites of bleeding, or because of their anatomic characteristics, making it a challenging treatment for pediatric hepatologists. Current treatment for UGIB due to PHT includes intravenous octreotide infusion for 5 days[2,3,7,8]. Long-acting release octreotide (OCT-LAR) is used both in adult and pediatric patients for treating acromegaly, neuroendocrine tumors, secretory diarrhea, pancreatitis, and chylothorax[8,9]. In recent years, an OCT-LAR presentation for monthly intramuscular administration has been used in adult and pediatric patients with UGIB due to PHT or vascular malformations. Several adverse effects were reported with octreotide, such as nausea, abdominal cramps, diarrhea, hypoglycemia, growth failure and development of gallstones[10-13]. There is a lack of evidence in pediatrics for treating patients with PHT and UGIB from ectopic or unidentified sites of bleeding.

The objective of this article is to report a case of an 8-month-old patient with extrahepatic portal vein malformation and recurrent UGIB episodes, who was successfully treated with OCT-LAR, in order to add information and likely useful therapeutic alternatives in a challenging scenario for Pediatric Hepatologists.

Clinical Case

8-month-old male patient with a history of maternal preeclampsia. He was born at 39 weeks of gestational age with a birth weight of 2600 gr. by vaginal delivery, with a double nuchal cord and meconium-stained amniotic fluid. He was admitted to the neonatal intensive care unit where he stayed for 11 days with respiratory distress syndrome and early-onset neonatal sepsis due to *Staphylococcus epidermidis*. He presented UGIB at 3 months of age. Repeated liver function tests and platelet counts were always within normal values. Physical examination showed pale skin and mucosa during the UGIB episodes, without hepato- or splenomegaly.

The patient was referred to our center with a history of multiple episodes of UGIB from a duodenal varix. In each episode, he presented with melena and anemia. Previously, he had received endoscopic cyanoacrylate injections without response (figure 1), a treatment that we do not perform in our center. He required repeated blood transfusions and intravenous octreotide infusions. An extrahepatic portal vein malformation was observed in the ultrasound and CT scan. A mesenteric portovenography was performed, showing the same features (figure 2). The mechanism of UGIB was presumed to be PHT due to the portal vein malformation, although pressure measurement was not possible. Anatomic characteristics and size of the patient (at 14 months, the weight was 8900 gr,

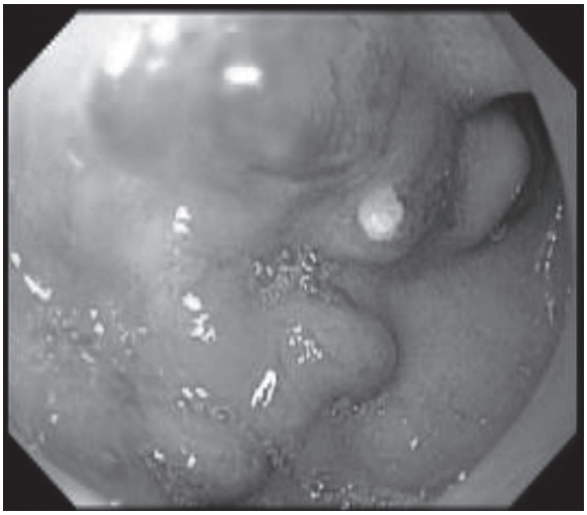

Figure 1. Upper digestive endoscopy. On the posterior wall of duodenal bulb there is a large ectopic varix protruding and occupying part of the lumen, with fibrin at its surface and positive red signs.

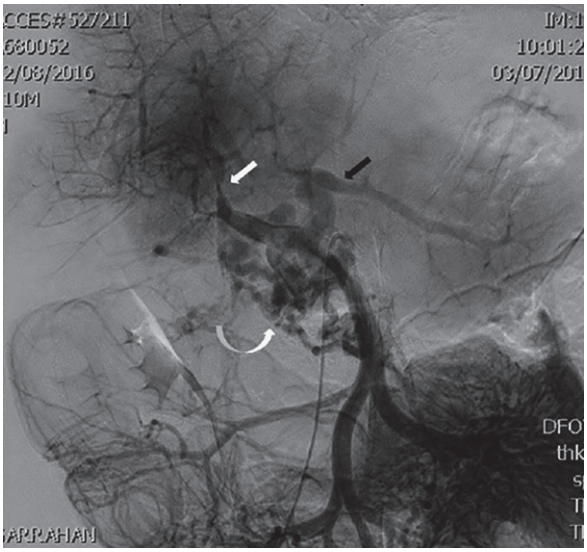

Figure 2. Mesenteric portovenography. Patent portal vein trunk without identification of its division. In right portal branch origin topography, there is a segmentary stenosis (straight white arrow). Left portal branch emerging from a collateral vein instead of the main trunk (black arrow). A network of collateral veins in hepatic hilum (curved white arrow).

Z-score: -1.5; the height 73.3 cm, Z-score: -3) made surgical alternatives, such as a meso-Rex or other shunts, not feasible. The patient was hospitalized once a month for six months because of UGIBs. At that moment, we decided to start the monthly administration of intramuscular OCT-LAR at a dose of 0.39 mg/kg, in order to avoid hospitalizations, transfusions, infections, and associated risks.

After 10 months of intramuscular OCT-LAR treatment, he did not have any further UGIB episodes. During this period, the patient did not present nausea, diarrhea, abdominal cramps, hypoglycemia or growth failure.

Discussion

UGIB due to PHT in children is a special challenge in the group of patients with ectopic or unidentified sites of bleeding, or anatomic characteristics that do not allow endoscopic or surgical treatments. The lack of guidelines or universal management recommendations is related to the absence of well-designed trials in the pediatric population. Current treatment of UGIB episodes in these patients includes intravenous octreotide infusion for 5 days. Octreotide is a somatostatin analog that inhibits the release of glucagon, insulin and growth hormone. It also reduces splanchnic blood flow[2,3,7,8].

The use of OCT-LAR presentations, initially designed for daily subcutaneous use[14] and more recently for monthly intramuscular administration[15], was reported in cirrhotic adult patients as adjuvants in variceal treatment due to their action in decreasing portal pressure and improving splanchnic hyperemia. In recent years, monthly intramuscular OCT-LAR has been indicated in adult patients and in a small series of pediatric patients with UGIB due to PHT or vascular malformations[10-13]. In adult patients, prevention and treatment of UGIB due to PHT include endoscopy, transjugular intrahepatic portosystemic shunts or pharmacological therapy with somatostatin analogs for acute bleeding episodes or beta-blockers as prophylaxis management. The administration of OCT-LAR which improves prognosis in cirrhotic patients is an attractive treatment option for long-term therapy in this scenario[12].

In the pediatric population, considerable technical and anatomic limitations add difficulties in cases of UGIB for conventional endoscopic and surgical treatments. In this age group, the lack of studies prompts to imitate adult experiences as well as pediatric case reports. The experience reported by O'Meara et al in 2015 provides evidence indicating that OCT-LAR could be effective for treating severe UGIB in children without conventional therapeutic options[13].

Conclusions

Our patient, with extrahepatic portal vein malformation and multiple UGIB episodes from a duodenal varix, represents a therapeutic challenge due to the ectopic site of bleeding and anatomic characteristics that prevent endoscopic or surgical management. Based on the report of nine pediatric patients by O'Meara et al[13], to our knowledge representing the largest number of pediatric patients treated with intramuscular OCT-LAR, we decided to use this drug at a dose of 0.39 mg/kg monthly. After 10 months of treatment, our patient did not present any further bleeding episodes or adverse effects previously reported with the use of octreotide.

We believe that this report may be helpful in the management of complex UGIB due to PHT in pediatric patients.

Ethical Responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the correspondence author.

Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

Financial Disclosure

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