Therapeutic failure with thalidomide in patients with recurrent intestinal bleeding due to angiodysplasias

Fracaso terapéutico a talidomida en paciente con sangrado intestinal recurrente debido a angiodisplasias

Abstract

Angiodysplasias are one of the reasons of gastrointestinal bleeding, whose origin is usually due to vascular malformations. There are different types of therapies for angiodysplasia such as endoscopic, angiographic and pharmacological techniques. Among the last ones, there is little variety of effective drugs to treat the disease.

We describe the therapeutic failure with thalidomide in a male with recurrent gastrointestinal bleeding due to angiodysplasias. A thorough diagnostic work-up, including gastroscopy, enteroscopy, angiography and capsule endoscopy were performed. Despite treatment with high-dose somatostatin analogues and oral iron, the patient continued bleeding. The patient was administered then thalidomide for three months with no clinical response. Thalidomide had to be withdrawn owing to adverse effects.

PALABRAS CLAVE
Angiodisplasias; Thalidomide; Sangrado gastrointestinal

KEY WORDS
Angiodysplasia; Thalidomide; Digestive bleeding
There are numerous types of vascular malformations affecting the gastrointestinal tract. Usually, they are due to abnormal formations in the structure of the vascular wall. Some of them can be benign such as hemangioma, while others may be malignant, as angiosarcomas.

The mechanism of appearance is not well defined. The emergence of new vessels as a result of tissue hypoxia, angiogenesis, is the most accepted theory. Angiogenesis is caused by an imbalance between proangiogenic and antiangiogenic factors following hypoxia. In vitro studies have shown an increased expression of vascular endothelial growth factor (VEGF) in tissues undergoing hypoxia; all this explains the appearance of the intestinal mucosa lesions and the bleeding.1

Available treatment options include: endoscopic (such as argon plasma coagulation or electrocoagulation), angiographic and surgical techniques. All of them are associated with an increased risk of complications and may be ineffective. As an alternative, drug therapy includes the hormone therapy with estrogen and progesterone, somatostatin analogues and thalidomide.2

Thalidomide inhibits angiogenesis by suppressing VEGF expression. It is used in multiple myeloma, erythema nodosum secondary to leprosy, Behçet’s disease, among others.

Case description

75 years-old man diagnosed of hypertension and dyslipidemia, colon adenocarcinoma with colostomy in 1995 and subsequent radiotherapy with multiple submisions in Gastroenterology Department because of gastrointestinal bleeding with obscure origin during 2012-2013.

He was first admitted in Hospital in January 2013 where he underwent a colonoscopy and gastroscopy in which acute erosive lesions and endoscopic capsule without significant findings were observed. Successful eradication treatment against Helicobacter pylori was also performed. A few days after discharge, he was readmitted because of melena, a new gastroscopy, enteroscopy, angiography and capsule endoscopy were performed. Active bleeding in proximal jejunum but without apprehended injury was observed.

The patient was discharged with an hemoglobin value of 10.9 g/dl, and treatment with 50 mcg Octreotide every 12 hours and orally Iron once daily.

In May 2013, the patient was admitted to bring about a new enteroscopy where angioectasias are objectified in jejunum and were treated with coagulation, with good initial response.

One month later, the patient was readmitted again for gastrointestinal bleeding receiving transfusion of 7 packed red blood cells. Octreotide dose was increased to 100 mcg every 12 hours, and he started treatment with thalidomide 100 mg daily. The hemoglobin level at discharge was 11 g/dl.

Some days later, the patient was readmitted in the Gastroenterology Department with melena and anemia syndrome. The hemoglobin value has fallen to 8.8 g/dl. A new enteroscopy was made and fresh blood in the middle-proximal jejunum and a possible ulcerated lesion with a clot of 1.5 cm are seen.

Almost most time of the admission, the patient had hematochezic melena and required transfusion of more than 24 packed red blood cells. The patient also referred paresthesias in lower extremities. After Surgery Department consultation, resection of jejunal areas affected of angiodysplasias is decided.

In August 2013, the patient was readmitted because of severe anemia (hemoglobin 4 g/dl).

As bleeding persists, adverse events related to treatment with thalidomide (paresthesias) and the hemoglobin value does not recover, thalidomide treatment was decided to be stopped. Finally, the patient underwent surgery (segmental small bowel resection with manual LL jejunum-jejunal anastomosis). The treatment with Octreotide 100 mcg every 12 hours orally and Iron every 24 hours was kept.

Nowadays, he is being followed by the Home Care Unit receiving blood transfusions according to his necessities.

In view of the results of previously published cases of angiodysplasia treated with thalidomide, whose success is attributed to its antiangiogenic mechanism, this patient was decided to start the treatment. The use of thalidomide in patients with recurrent bleeding due to angiodysplasia is sporadic. Efficacy results are from isolated cases or case series. Thalidomide has been useful to stop bleeding in a short time, reduction/elimination of transfusions and hospitalizations. Beneficial doses have varied from 50-400 mg/day being achieved with 100 mg/day. The beneficial effect is not only achieved when the drug is administered, it may persist for months or years after its interruption, although bleeding may recur and force to reintroduce it. Side effects that have motivated to stop the treatment are mainly fatigue, peripheral neuropathy, constipation and skin rash.4.5.6.7.8.9

This case shows that, unlike what happens in previously cases described in the literature, the use of thalidomide as a treatment of angiodysplasia has not always favorable results. The use of thalidomide is not supported by randomized control trials but could be an alternative to reduce the number of hospitalizations, the necessity of transfusions, as well as the delay of surgery and its associated complications.

Conflict of interest

There is not conflict of interest.
Bibliography


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