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The Use of Thalidomide in Severe Refractory Anaemia Due to Gastric Antral Vascular Ectasia (GAVE) in Cirrhosis?

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ABSTRACT

Gastric antral vascular ectasia (GAVE) is a rare cause of upper gastrointestinal bleeding associated with cirrhosis. The first-line treatment is endoscopic therapy with argon plasma coagulation (APC). There is a high recurrence rate, but some evidence suggests that thalidomide could play an important role in controlling refractory anaemia due to GAVE. The authors present the case of a cirrhotic patient with a recent diagnosis of GAVE, who underwent multiple endoscopic treatments and blood transfusions because of haematemesis. The patient started thalidomide and 6 months later, there was no recurrence of haematemesis and haemoglobin levels were stable, with no reported adverse effects.

LEARNING POINTS

- The chronic bleeding associated with gastric antral vascular ectasia (GAVE) presenting with cirrhosis is more severe than that associated with portal hypertensive gastropathy.
- Argon plasma coagulation remains the first-line treatment, but GAVE has a high recurrence rate.
- Thalidomide could be an effective and safe option for recurrent bleeding due to GAVE in patients with cirrhosis.

KEYWORDS

GAVE, thalidomide, cirrhosis

INTRODUCTION

Gastric antral vascular ectasia (GAVE) is a rare cause of upper gastrointestinal bleeding, and accounts for approximately 4% of all non-variceal gastrointestinal bleeding [1]. The majority of patients present with iron-deficiency anaemia secondary to occult blood loss, and about 60–70% of patients are transfusion-dependent [2, 3]. GAVE is commonly associated with chronic illnesses, most frequently liver cirrhosis and connective tissue diseases [4]. The prevalence in the general population is unknown, but a prevalence of 12% was reported in patients with cirrhosis [5]. Endoscopic therapy is the mainstay of management for patients with GAVE [6]. In patients with active haemorrhage or anaemia, the available evidence favours endoscopic therapy with argon plasma coagulation (APC) [7, 8], with the disadvantage of a high recurrence rate of 30–60% [6]. A few medical therapies have been proposed to reduce the need for endoscopic intervention. Thalidomide has previously been shown to exert a potent antiangiogenic effect in experimental studies [9]. This is maybe due to the reduction in vascular endothelial growth factor (VEGF) levels in these patients.

European Journal of Case Reports in Internal Medicine

CASE DESCRIPTION

The authors present the case of an 84-year-old woman with recently diagnosed cryptogenic cirrhosis with portal hypertension and GAVE. She was referred to the emergency department in June 2019 because of severe anaemia (haemoglobin of 5.8 g/dl) that required red blood cell (RBC) transfusion and endoscopic treatment with APC. Between June 2019 and January 2020, the patient visited the emergency department seven times because of severe episodes of haematemesis. She was transfused with a total of 15 units of red blood cells to maintain haemoglobin levels above 8 g/dl and underwent five endoscopic treatments with APC in 6 months. During the last hospitalization, endoscopic treatment was considered no longer effective so it was decided to start therapy with 50 mg/day thalidomide for 2 weeks increasing to 100 mg/day. Haemoglobin levels, renal function and hepatic enzymes were closely monitored during this initial phase and remained stable. The patient was discharged with close follow-up and, 6 months after thalidomide initiation, there was no recurrence of haematemesis. Haemoglobin levels remained steady at 8.9 g/dl, with no adverse effects reported.

DISCUSSION

GAVE is a poorly understood pathology that was first reported by Rider et al. in 1953[10]. It is a rare cause of upper gastrointestinal bleeding (UGIB) and most commonly affects females (about 71%), who are an average age of 73 years at presentation. Patients with GAVE associated with cirrhosis have a worse Child-Pugh classification, and present with more severe chronic bleeding than those with portal hypertensive gastropathy [11]. GAVE, unlike portal hypertensive gastropathy, does not respond to beta-blockers or nitrates[10,12].

Endoscopic therapy with APC is the first-line treatment[7,8], but due to the high recurrence rate and the burden associated with a repeated invasive procedure, other strategies have been proposed. There is evidence to support the efficacy of medical therapy as an alternative to laser therapy in GAVE [8]. Multiple drugs, such as oestrogen-progesterone[13,14], octreotide[15,16], steroids[17,18], tranexamic acid[19], and even bevacizumab [7], have been tried to control GAVE-related bleeding. In 2006, the first patient with refractory anaemia secondary to GAVE was successfully treated with thalidomide [20]. Since then, thalidomide has sometimes been administered to cirrhotic patients with gastrointestinal bleeding related to vascular malformations. There are some case reports on the efficacy of thalidomide in this setting[21–23]. However, in the particular context of cirrhosis and GAVE, the efficacy of thalidomide still remains to be adequately studied. The side effects of thalidomide are generally not severe (fatigue, peripheral neuropathy and skin rash) and they resolve after drug withdrawal[24]. In very rare cases, thalidomide can induce hepatotoxicity [25], and therefore, liver enzymes should be closely monitored.

European Journal
of Case Reports in
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