

Successful treatment of thalidomide for recurrent bleeding due to gastric angiodysplasia in hereditary hemorrhagic telangiectasia

X.-Y. WANG, Y. CHEN, Q. DU

Department of Gastroenterology, Second Affiliated Hospital of Zhejiang University College of Medicine, Hangzhou, Zhejiang Province, China

Abstract. – Hereditary hemorrhagic telangiectasia (HHT) is an autosomal dominant disorder, which is uncommon anomaly to recurrent gastrointestinal bleeding. Although there are several forms of therapy ranging from local therapy to operations or drug therapy, there is a lack of more effective treatment for the disease. In this report, we presented a Chinese patient with recurrent melena due to gastric angiodysplasia in HHT treated successfully with thalidomide.

Key Words:

Thalidomide, Gastric angiodysplasia, Hereditary hemorrhagic telangiectasia.

Introduction

Hereditary hemorrhagic telangiectasia (HHT), also known as Osler-Rendu-Weber syndrome, is an autosomal dominant genetic disease with epistaxis, telangiectasia and multi-organ vascular dysplasia. It is distinguished into three types which are due to mutations in the ENG (endoglin), ACVRL1 or MADH4 gene. The prevalence varies and may range from 1/3,500 to 1/5,000 in specific regions¹. Gastrointestinal bleeding is one of the most critical sometimes life-threatening symptoms in this disease. However, no effective therapy is available for that. Several case reports have been published on HHT patients who were treated with endoscopic argon plasma coagulation (APC) or bevacizumab only. We reported a case of a patient with HHT treated with thalidomide only after APC ineffectively.

Case Report

A 77 year-old Chinese man complaining of recurrent tarry stool for 9 months was admitted to our Gastrointestinal Department on 25 May, 2010. The patient had a prior history of epistaxis

for several years. In the past 9 months, he visited the local Health Clinic intermittently because of melena and fatigue, and has been receiving iron substitution for several months. Seven days ago he visited the clinic again due to syncope. The blood test result showed that his hemoglobin was 4 g/dl and fecal occult blood (OB) was positive.

Examination upon admission was unremarkable except pale, cardiac murmur and enlargement. Chest X-ray showed significantly increased heart shadow. Left hepatic artery and portal vein fistula was found on abdominal CT. The diagnosis of telangiectasia in the gastrointestinal tract was confirmed and angiodysplasia was limited to stomach only (Figure 1) by endoscopic investigations including of capsule endoscopy. Nasal endoscope showed the left nasal mucosa telangiectasia and local mucosal erosion. According to the 2000 Shovlin et al diagnostic criteria², the patient was diagnosed as HHT. Endoscopic intervention, more specifically endoscopic APC was performed (the argon gas flow at 2.0 liter per minute and power 60W). However the lesions were found bleeding easily during the procedure (Figure 2). Because of a lack of more effective treatment for the disease, we started a thalidomide therapy at a dose of 75 mg per day after informed consent. One week later no significant side effects were found, the dose of thalidomide was increased to 100 mg per day and the treatment had lasted for 4 months. The patient stool OB became negative and his epistaxis was controlled after he had received thalidomide for 2 months. The patient has been stable for the next 12 months during our follow-up.

Discussion

According to the 2000 Shovlin et al diagnostic criteria², a diagnosis can be made definitely

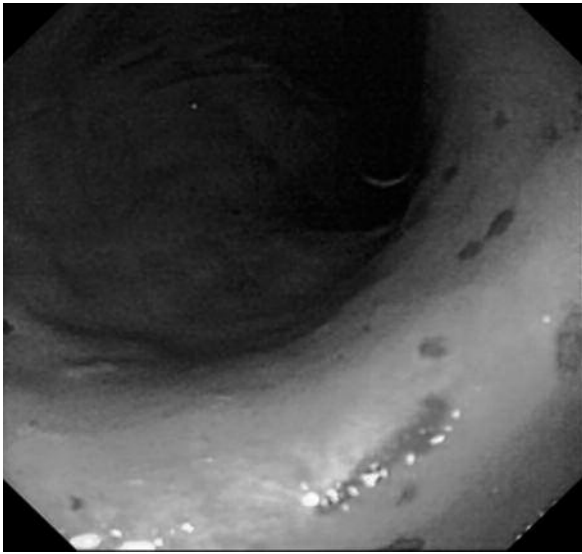


Figure 1. Upper gastrointestinal endoscopy view of telangiectasia.

if at least three criteria are present, suspected if two criteria are present. (1) spontaneous and repeated epistaxis (epistaxis at night to be highly considered), (2) multiple skin or mucous membranes of telangiectasia: include the lips, mouth, fingers and nose, etc.; (3) visceral arteriovenous malformations: can be expressed in the lung, brain, liver, kidney, gastrointestinal tract, kidney and bone and other parts; (4) family history.

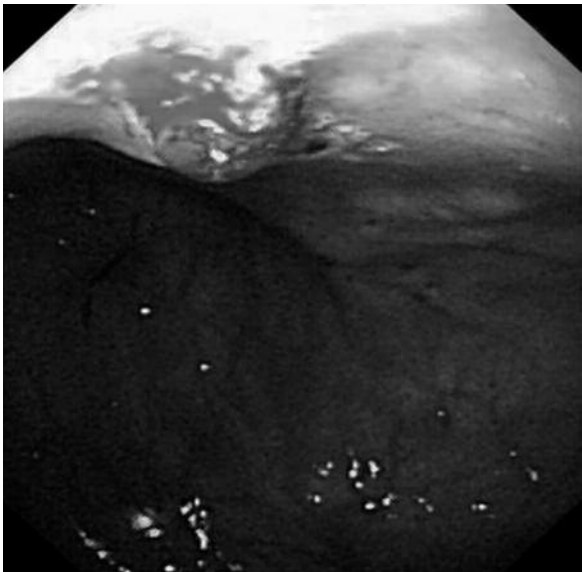


Figure 2. Upper gastrointestinal endoscopy showing telangiectasia bleeding during APC.

Therapy for epistaxis or gastrointestinal bleeding is supportive primarily, consisting of iron supplementation and blood transfusion. HHT can be treated with APC³, laser therapy⁴, embolization⁵, estrogen⁶, or operation⁷. Because APC (Argon Plasma Coagulation) is safer, easier and cheaper than other options, it was performed on our patient. However, the gastric lesions tend to bleed during the progress. So, the APC was not an effective method in the case due to an old age, increased vascular fragility or/and the mutated gene. Although there are cases reported on successful treatment of HHT using estrogen, it was not adopted in this case because of the patient's denial.

Several case reports have been published on HHT patients who were treated with bevacizumab alone. Another report mentioned that bevacizumab can be used when the effect of thalidomide is not good enough. Bevacizumab also has a nonnegligible toxicity and it may induce cardiac failure, hemorrhage, arterial thromboembolic events, hypertensive crisis or nephritic syndrome⁸. Considering the potential side effect and cost, bevacizumab is not used in our patient.

We chosen a medicine with less side effects, easy accessibility, low in price and high acceptance after endoscopic APC is no longer a choice. After thalidomide therapy the frequency of melena was decreased apparently without apparent effects, and the stool OB turned to negative after 2 months. Our case presented thalidomide was effective in controlling gastric bleeding and epistaxis. This implied that thalidomide could be a novel treatment of bleeding gastric angiodysplasia of HHT in the monitoring its side effects conditions. However, this agent should be used with great caution in these cases because of complications such as peripheral neuropathy, sedation⁹ and the thromboembolism¹⁰.

Funding Interest

This study was funded in full by Medical Scientific Research Foundation of Zhejiang Province (2008A087).

References

- 1) SABBA C, PASCULLI G, CIRULLI A, GALLITELLI M, VIRGILIO G, RESTA F, GUASTAMACCHIA E, PALASCIANO G. Hereditary hemorrhagic telangiectasias (Rendu-Osler-Weber disease). *Minerva Cardioangiol* 2002; 50: 221-238.

- 2) SHOVLIN CL, GUTTMACHER AE, BUSCARINI E, FAUGHNAN ME, HYLAND RH, WESTERMANN CJ, KJELSDEN AD, PLAUCHU H. Diagnostic criteria for hereditary hemorrhagic telangiectasia (Rendu-Osler-Weber syndrome). *Am J Med Gene* 2000; 91: 66-67.
- 3) GOTO T, DOHMEN T, YONEYAMA K, MONMA A, OHSHIMA S, SHIBUYA T, KATAOKA E, SEGAWA D, SATO W, TAKEUCHI S, ANEZAKI Y, ISHII H, YAMADA I, KOMATSU M, WATANABE S. Osler-Weber-Rendu disease with esophageal varices and hepatic nodular change. *Intern Med* 2007; 46: 849-854.
- 4) SARGEANT IR, LOIZOU LA, RAMPTON D, TULLOCH M, BOWN SG. Laser ablation of upper gastrointestinal vascular ectasias: long term results. *Gut* 1993; 34: 470-475.
- 5) INOUE P, MARCON N, PUGASH RA, HYLAND RH, FAUGHNAN ME. Embolization of a duodenal arteriovenous malformation in hereditary hemorrhagic telangiectasia: case report and review of the literature. *Can J Gastroenterol* 2003; 17: 661-665.
- 6) TAKESHI H, HIDEMASA K, TAKESHI T, KANEKO K, KUBOTA S, MIWA Y, MORI M. Hereditary hemorrhagic telangiectasia showing severe anemia which was successfully treated with estrogen. *Intern Med* 1995; 34: 589-592.
- 7) BESSON A, SAEGESSER F. Recurrent massive hemorrhage of the distal part of the digestive tract due to hemorrhagic hereditary telangiectasia. *Schweiz Med Wochenschr* 1977; 107: 1057-1064.
- 8) AMANZADA A, TOPPLER GJ, CAMERON S, SCHWÖRER H, RAMADORI G. A case report of a patient with hereditary hemorrhagic telangiectasia treated successively with thalidomide and bevacizumab. *Case Rep Oncol* 2010; 3: 463-470.
- 9) ANDERSEN TP, FOGH K. Thalidomide in 42 patients with prurigo nodularis hyde. *Dermatology* 2011; 223: 107-112.
- 10) PENALOZA A, VEKEMANS MC, LAMBERT C, HERMANS C. Deep vein thrombosis induced by thalidomide to control epistaxis secondary to hereditary haemorrhagic telangiectasia. *Blood Coagul Fibrinolysis* 2011; 22: 616-618.