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CASE REPORT | ENDOSCOPY

Successful Treatment of Hereditary Hemorrhagic Telangiectasia With Octreotide

Kimberly D. Houghton, MD[1], Beena Umar, MD[2], and Jason Schairer, MD[1]

[1]*Department of Gastroenterology, Henry Ford Hospital, Detroit, MI*
[2]*Pathology and Laboratory Medicine, Henry Ford Health System, Detroit, MI*

ABSTRACT

Hereditary hemorrhagic telangiectasia (HHT) is a disorder characterized by telangiectasias and arteriovenous malformations. We present a case report of a 74-year-old man diagnosed with HHT having a favorable response to a somatostatin analogue for treatment. This patient had been suffering from chronic anemia from recurrent gastrointestinal bleeding, requiring oral/intravenous iron replacement, frequent endoscopic ablations, and blood transfusions. Due to insufficient treatment, he was started on subcutaneous octreotide, with significant improvement as evidenced by a steady increase in the hemoglobin level, decreased endoscopic interventions, and decreased blood transfusions, making this the first case of HHT successfully treated with octreotide.

INTRODUCTION

Hereditary hemorrhagic telangiectasia (HHT), or Osler Weber Rendu syndrome, is an autosomal dominant disorder resulting from a multisystem vascular dysplasia, characterized by telangiectasias of the skin and mucosal lining of the gastrointestinal tract as well as arteriovenous malformations (AVMs) within the internal organs. Gastrointestinal bleeding affects 20% of patients with HHT in the fourth to the fifth decade in primarily proximal lesions, and telangiectasias are thought to result from vascular fragility and elevated vascular endothelial growth factor.[1] Endoscopic coagulative therapy is the standard of care for controlling bleeding from telangiectasias but is often challenging given multiple sites involved or poor access to the small bowel. Because alternative medical therapies such as anti-angiogenics, antifibrinolytics, and hormones have been used with inconsistent outcomes, the treatment of HHT is largely endoscopic and supportive in the form of frequent blood transfusions.[2]

In limited published case series, somatostatin analogues have been considered in patients with AVMs, which are similar but separate entities from telangiectasias. Whereas AVMs are aberrant connections between the veins and arteries outside the gastrointestinal system, telangiectasias occur in the mucocutaneous surfaces including the gastrointestinal tract, and angiodysplasias are isolated to the gastrointestinal tract and can include small capillaries. The presumed pathogenicity of angiodysplasias consists of chronic, low-grade, intermittent blood vessel obstruction in the aging population, leading to local hypoxia and induction of neovascular growth factors, which then propagate new abnormal vessel formation.[6] In one case series, 17 patients with bleeding AVMs received 100–500 μg of octreotide subcutaneously b.i.d.; more than 58% of these patients no longer required blood transfusions and 23% had decreased transfusion requirements after the treatment.[1] In a 2010 meta-analysis by Brown et al, the pooled clinical response rate of angiodysplasias to octreotide was 0.76 (95% confidence interval, 0.64–0.85).[3] In a meta-analysis by Jackson and Gerson looking at cessation of bleeding as the primary outcome, the pooled odds ratio was 14.52 (95% confidence interval, 5.9–36).[4] Therefore, although data are limited and a randomized controlled trial does not exist that evaluates the use of octreotide in HHT, octreotide may be useful in patients with chronic gastrointestinal bleeding from vascular abnormalities when endoscopic therapy is insufficient.

CASE REPORT

We present a case report of a 74-year-old man diagnosed with HHT at the age of 9 years who had a favorable response to a somatostatin analogue. This patient had been suffering from chronic anemia due to gastrointestinal bleeding which required numerous endoscopic

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Correspondence: Kimberly D. Houghton, MD, Department of Gastroenterology, Henry Ford Hospital, 2799 West Grand Blvd, Detroit, MI 48202 (kimberlydhoughton@gmail.com).

ablations of telangiectasias, oral and intravenous iron replacement, and frequent blood transfusions. Because excessive telangiectasia ablations and blood transfusions were insufficient in controlling the symptoms and significantly compromised the quality of life, subcutaneous octreotide (50 μg every 12 hours) was initiated in June 2017. A compassionate use exemption was awarded based on the lack of Food and Drug Administration-approved therapies for this indication combined with data that octreotide is an effective treatment for similar conditions. In September 2017, the patient was noted to have an excellent partial response without hospitalization, blood transfusion, endoscopic therapy, or emergency department visits since the initiation of octreotide. Given a slight dip in hemoglobin, his octreotide dosage was increased to 50 μg subcutaneous octreotide injection every 8 hours. In the 6 months preceding octreotide initiation, the patient was averaging 4.3 blood transfusions per month; after octreotide initiation, he averaged 1.0 transfusion each month, including requirements in the setting of plastic surgery during this time frame. In the 6 months before octreotide initiation, the patient underwent 3 endoscopic procedures for ablation of gastrointestinal telangiectasias. After octreotide initiation, he did not require any endoscopic interventions over the first 6 months and his hemoglobin remained above 8 g/dL. At approximately 13 months from the time of octreotide initiation, the patient required his first endoscopic intervention, with a total of 2 endoscopic interventions at the 17-month time point.

DISCUSSION

Whereas literature supports the use of somatostatin analogues in cases of nonhereditary angiodysplasia, this is the first case of telangiectasias in HHT successfully treated with octreotide. The potential mechanisms by which octreotide reduces bleeding are multifactorial, including inhibition of pepsin, gastrin, and acid secretion; improved platelet aggregation; decreased duodenal and splanchnic blood flow; increased vascular resistance; and inhibition of angiogenesis by decreasing vascular endothelin growth factor synthesis.[5] Side effects of octreotide are minimal, including diarrhea, weakness, early abdominal pain, dysgeusia, worsening blood sugar control in patients with diabetes, and pain at the injection sites. Rare side effects include cholelithiasis, nephrolithiasis, pancreatic enzyme deficiency, bradycardia, and negative inotrope effects.[6] Ultimately, treatment with octreotide has been well tolerated for the treatment of AVMs with no serious adverse side effects noted in multiple studies.[5] Given this low rate of side effects and similarity between AVMs and telangiectasias, octreotide is a reasonable drug to try as a primary or adjunctive therapy for bleeding gastrointestinal telangiectasias, especially when other treatments are inadequate. Ultimately, as shown in our case report, octreotide has decreased endoscopic intervention and blood transfusions, although it is unclear if this finding is sustainable over time, because the transfusion requirement in the 17 months after octreotide initiation averages 2.8 transfusions per month. That said, one cost-effectiveness study did reveal significant reduction in the length of admissions per year (22.79 vs 2.01 days; $P < .0001$) and in the number of blood transfusions administered (11.19 vs 2.55 per year; $P = .002$), and had an overall cost reduction of 61.5% over the first year of treatment of bleeding angiodysplasias, totaling over $16,000 per patient on average.[7]

Although fairly heterogeneous literature supports the use of octreotide in gastrointestinal angiodysplasias, there are limited data to support the specific use of octreotide in gastrointestinal telangiectasias, especially in genetically inherited disorders such as HHT where the bulk of bleeding telangiectasias may exist outside the easily accessible small bowel. Because up to 20% of people within the HHT population are affected by bleeding telangiectasias, additional adjunctive therapies beyond endoscopic treatment and blood transfusions must be available for more difficult-to-treat cases. Our case report reviews one such case with successful treatment with octreotide, and we propose that further research be explored with randomized control trials within this specific population to determine the long-term effectiveness.

DISCLOSURES

Author contributions: KD Houghton and B. Umar wrote the manuscript. J. Schairer revised the manuscript. KD Houghton provided the images and is the article guarantor.

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Informed consent was obtained for this case report.

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REFERENCES

1. Kritharis A, Al-Samkari H, Kuter DJ. Hereditary hemorrhagic telangiectasia: Diagnosis and management from the hematologist's perspective. *Haematologica.* 2018;103(9):1433–43.
2. Jackson SB, Villano NP, Benhammou JN, Lewis M, Pisegna JR, Padua D. Gastrointestinal manifestations of hereditary hemorrhagic telangiectasia (HHT): A systematic review of the literature. *Dig Dis Sci.* 2017; 62(10):2623–30.
3. Brown C, Subramanian V, Wilcox CM, Peter S. Somatostatin analogues in the treatment of recurrent bleeding from gastrointestinal vascular malformations: An overview and systematic review of prospective observational studies. *Dig Dis Sci.* 2010;55(8):2129–34.
4. Jackson CS, Gerson LB. Management of gastrointestinal angiodysplastic lesions (GIADs): A systematic review and meta-analysis. *Am J Gastroenterol.* 2014;109(4):474–83.
5. Becq A, Rahmi G, Perrod G, Cellier C. Hemorrhagic angiodysplasia of the digestive tract: Pathogenesis, diagnosis, and management. *Gastrointest Endosc.* 2017;86(5):792–806.
6. Szilagyi A, Ghali MP. Pharmacological therapy of vascular malformations of the gastrointestinal tract. *Can J Gastroenterol.* 2006;20(3): 171–8.
7. Klímová K, Padilla-Suárez C, Giménez-Manzorro Á, et al. Octreotide long-active release in the treatment of gastrointestinal bleeding due to vascular malformations: Cost-effectiveness study. *Rev Espanola Enfermedades Dig.* 2015;107:79–88.