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Recurrent Gastrointestinal Bleed Due to Small Bowel Vascular Malformation in a Patient with Turner Syndrome Diagnosed with Surgically Assisted Push Enteroscopy

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Study Design A
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Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Patient: Female, 14-year-old
Final Diagnosis: Small bowel vascular malformation
Symptoms: Anemia • gastrointestinal bleeding
Medication: —
Clinical Procedure: Colonoscopy • esophagogastroduodenoscopy • intraoperative enteroscopy • single balloon enteroscopy • video capsule endoscopy
Specialty: Gastroenterology and Hepatology • Pediatrics and Neonatology
Objective: Unusual clinical course
Background: Obscure gastrointestinal bleeding accounts for approximately 5% of all cases of gastrointestinal bleeding and the most frequent site is the small bowel. Turner syndrome (TS) is a genetic disorder of the second X chromosome in females. The association between gastrointestinal vascular malformations and Turner syndrome has been described in some case reports. Vascular malformation in Turner's syndrome can vary from asymptomatic to severe recurrent GI bleeds, but data on diagnosis and management of these patients are lacking.
Case Report: A 14-year-old girl with TS presented with recurrent symptomatic melena. The initial work-up included a negative upper endoscopy, negative bidirectional endoscopies, and a video capsule endoscopy (VCE) that demonstrated large amount of blood and small erythematous lesion in the small bowel without active bleeding, and a negative Meckel scan. CT angiography was remarkable for prominent left lower mesenteric blood vessels, and a single-balloon enteroscopy demonstrated prominent vasculature throughout the small bowel. A clip was placed at the site of a questionable bleed. The patient underwent a surgically assisted push enteroscopy due to recurrent bleeding; findings were consistent with diffuse vascular malformations. She was started on tranexamic acid and later transitioned to estrogen therapy without further reports of GI bleeding, anemia, or adverse effects from treatment 6 months after initial presentation.
Conclusions: Small bowel bleeding can be life-threatening, and evidence-based guidelines in children are needed. Turner syndrome is associated with gastrointestinal vascular malformations, and suspicion for this diagnosis should be high for these patients when presenting with gastrointestinal bleeding. Estrogen might be an effective therapy in TS adolescent patients in the setting of diffuse vascular malformations (DVM).
Keywords: Endoscopy • Estrogens • Intestine, Small • Single-Balloon Enteroscopy • Turner Syndrome • Vascular Malformations
Abbreviations: MRE – magnetic resonance enterography; CTE – computed tomography enterography; ASGE – American Society of Gastrointestinal Endoscopy; SBB – small bowel bleeding; IOE – intraoperative enteroscopy; CTA – computed tomography angiography; VCE – video capsule endoscopy; DVM – diffuse vascular malformations; IE – intraoperative endoscopy
Full-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/937259>

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Background

Turner syndrome phenotypically affects females and is a chromosomal disorder. The diagnosis requires complete or partial absence of the second X chromosome and one of the following clinical features: webbed neck, typical facial features, lymphedema, growth failure, ovarian failure, and cardiovascular, skeletal, digital, and renal abnormalities [1]. The association between gastrointestinal vascular malformations and Turner syndrome has been described in some case reports, but data regarding diagnosis and management of these patients are lacking [2-5]. OGIB accounts for approximately 5% of all cases of gastrointestinal bleeding [6]. Studies have suggested that 20-30% of OGIB are related to angiectasis [7]. Vascular malformation in Turner's syndrome can vary from asymptomatic to severe recurrent GI bleeds. In the case of a severe GI bleed, endoscopy and colonoscopy are used in the first step of evaluation, followed by either CTA, push enteroscopy, or CTE if obstruction is expected [7, 8]. Intraoperative enteroscopy (IOE) is usually reserved for patients with persistent or recurrent life-threatening gastrointestinal bleeding [8].

Case Report

A 14-year-old girl with Turner syndrome, hypertension, and Hashimoto's thyroiditis presented to an outside facility with melena and anemia (initial hemoglobin 7.6 mg/dl and repeated 6.3 mg/dl) requiring 2 blood transfusions. She had a history of a similar episode (melena and anemia -Hgb 4 mg/dl) 3 years prior to this presentation but did not have significant gastrointestinal evaluation.

Work-up for the current presentation at the outside facility included: normal coagulation studies and negative upper endoscopy followed by negative bidirectional endoscopies. She had repeated upper endoscopy with VCE placement that demonstrated a small erythematous lesion without active bleeding and a large amount of blood obscuring visibility (**Figure 1**). A CTA demonstrated prominent mesenteric gastrointestinal wall blood vessels without active hemorrhage (**Figure 2**).

The patient was transferred to our facility for small bowel evaluation. Meckel scan was negative and a single-balloon enteroscopy showed prominent vasculature throughout the small bowel (**Figure 3**). A small, questionably bleeding focus was identified and clipped. The patient remained stable after enteroscopy and was discharged home on iron therapy.

She presented 4 days later to our facility with a third episode of melena and anemia requiring blood transfusion. Surgically assisted push enteroscopy was performed. External examination of the bowel revealed prominent, dilated, tortuous, diffuse



Figure 1. Video Capsule endoscopy. Small erythematous lesion without active bleeding (see arrow).



Figure 2. CTA (Computed tomography angiography) – Coronal view. Prominent mesenteric gastrointestinal wall blood vessels without active hemorrhage (see arrows).

intestinal surface blood vessels throughout the antimesenteric region of the small bowel (**Figures 4-6**).

Hemoglobin remained stable following the procedure and she was discharged on tranexamic acid without recurrence of bleeding. She was transitioned to estrogen (vivelle-Dot 0.0375 mg/24-h one patch onto skin twice a week) 2 months later. Estrogen levels prior to starting estrogen therapy were 1.3 pg/mL and testosterone level was 4.7 ng/dL. Repeated



Figure 3. CTA (Computed tomography angiography) – Axial view. Prominent mesenteric gastrointestinal wall blood vessels without active hemorrhage (arrows).

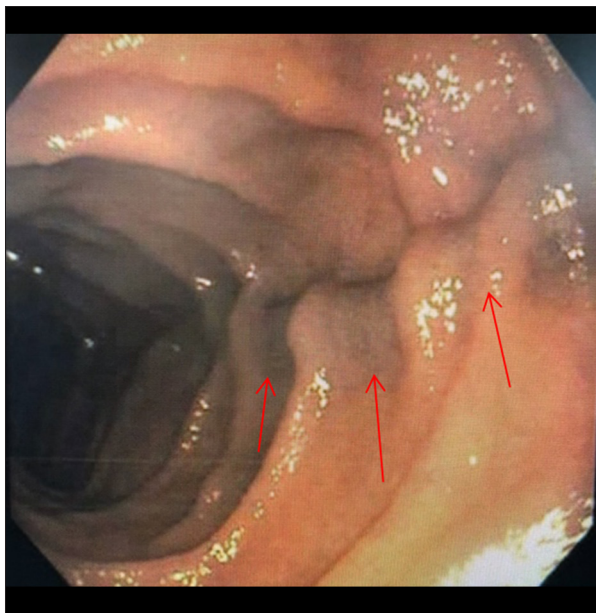


Figure 4. Single-Balloon Enteroscopy. Prominent vasculature, large blood vessel (arrows).

estrogen level in follow-up evaluation (1.5 years later) was 1.4 pg/mL, and she was noted to have breast development but no menarche. There were no documented adverse effects of estrogen therapy in this patient and she remained stable without further bleeding since identification of the vascular malformation.

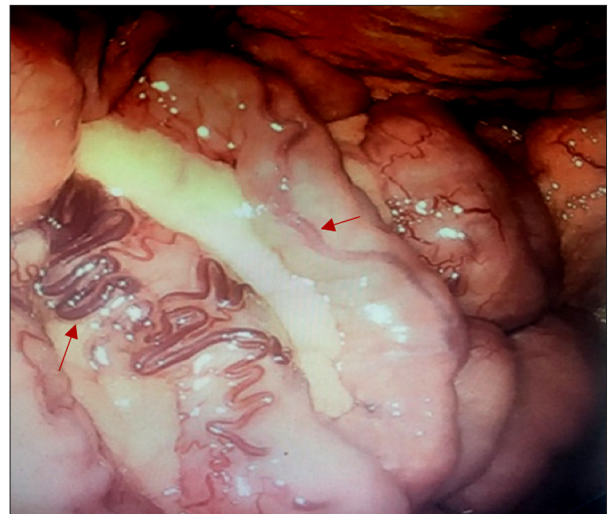


Figure 5. Surgically assisted push enteroscopy. External examination of the bowel with prominent, dilated, tortuous, diffuse intestinal surface blood vessels throughout the antimesenteric region of the small bowel (arrows).

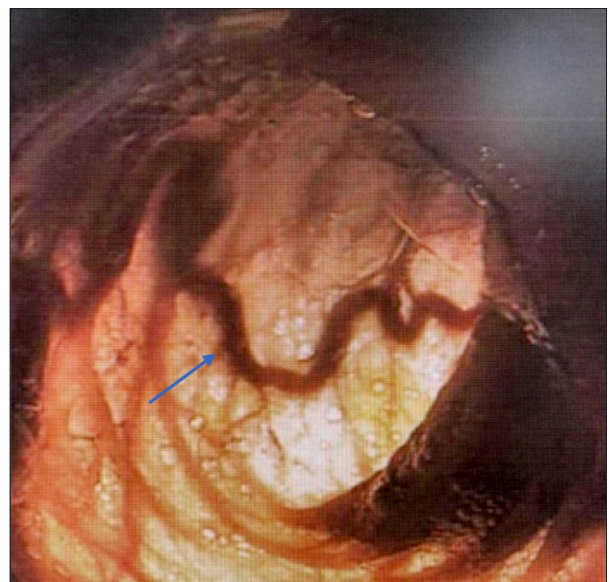


Figure 6. Surgically Assisted Push Enteroscopy. Endoscopic transillumination demonstrated prominent, dilated, tortuous, diffuse intestinal blood vessels in the small bowel (arrow).

Discussion

Obscure gastrointestinal bleeding is defined as overt or occult bleeding of unknown origin that persists or recurs after an initial negative bidirectional endoscopic evaluation including ileocolonoscopy and esophagogastroduodenoscopy [7]. Around 75% of episodes of OGIB are attributed to small bowel bleeding [6]. The most common etiologies for small bowel bleeding

in patients younger than 40 years include small intestinal tumors (such as lymphomas, carcinoid tumors, and adenocarcinoma, and polyps from hereditary polyposis syndrome), Meckel's diverticulum, Dieulafoy's lesion, and Crohn's disease [8].

Guidelines for small bowel bleeding were published by the American Society of Gastrointestinal Endoscopy (ASGE) in 2017. The algorithm of management recommends initially to repeat bidirectional endoscopies, followed by VCE or (CTE)/(MRE) in cases where obstruction is suspected [8]. CTA is recommended for brisk GI bleeding and RBC scintigraphy is helpful for slower bleeding [8]. Although there are no guidelines for small bowel bleeding in children, Meckel scan should be considered in the initial evaluations of children with obscure gastrointestinal bleeding, given the high incidence of Meckel diverticulum in the pediatric age group [9].

Push enteroscopy is utilized for both diagnostic and therapeutic interventions. Single-balloon enteroscopy improves diagnostic yields, followed by double-balloon with up to 90% yield [8]. In pediatrics, balloon-assisted enteroscopy has been deemed safe and effective for diagnosis and treatment of OGIB, but its use may be limited by technical aspects (patient age/size) or availability of specialized pediatric centers [9].

Endoscopic therapeutic interventions are usually the initial treatment for vascular malformations, but diffuse lesions might pose limitations. APC is the first-line treatment for angiodysplasia [10]. Other therapeutic interventions include percutaneous embolization via angiography, usually reserved for unstable life-threatening bleedings or when endoscopic and medical therapy have failed. The dual purpose (therapeutic and diagnostic) provides an advantage, but its high risk of complications (up to 10%), mortality rate, and low diagnostic yield when there is no active bleeding makes its use more limited [7,8].

Intraoperative enteroscopy (IOE) is usually reserved for patients with persistent or recurrent life-threatening gastrointestinal bleeding [8]. Diagnostic and therapeutic rates in patients undergoing IOE have been reported to be 58-100% and 79% respectively [11]. In a recent pediatric literature review that included 16 studies with a total of 1210 patients who underwent intraoperative endoscopy from 2000 to 2018, complications rates ranged from 0.3% to 14%. The most frequent complications were bowel perforation, bleeding, and mucosal tear. Mortality ranged between 0.7% and 1.2%. It was concluded that IE can be safe and effective when performed by experienced staff [12]. Intraoperative endoscopy has been used with success for the diagnosis of vascular malformations in an adolescent patient with Turner's with recurrent life-threatening bleeding [4].

Turner syndrome (TS) is a genetic disorder caused by a loss of all or part of the second X chromosome in females. A few small studies and case reports have shown an association between TS and diffuse vascular malformations (DVM), including hemangiomas, telangiectasias, and venous ectasias. The serosa seems to be the most common site of bleeding in patients with Turner's syndrome [2]. A systematic review of 41 cases of pediatric TS with vascular malformations found that the small bowel was the most frequent site of vascular malformation (69% of cases) and the most common malformations were telangiectasias (up to 7%) and dilated veins [3]. Overall, the prognosis of patients who have Turner syndrome associated with vascular malformations appears good, but this is limited due to a small number of case reports [3].

Lack of estrogen has been hypothesized to be one of the causes of these vascular malformations and has also been found to have intrinsic hemostatic properties [2,3]. Proposed mechanisms of action of estrogen include increased coagulation with achievement of stasis in microcirculation, trophic effects on the intestinal mucosa, or direct stabilizing action on the endothelial lining of the abnormal vessels, as observed in the GI lesions of hereditary hemorrhagic telangiectasia (HHT) [2]. Estrogen is not currently recommended for management of angiodysplasia in adults, but there are reports of successful treatment in Osler-Weber-Rendu syndrome and adolescent patients with Turner syndrome and vascular malformations [2-5,10].

Other suggested medical therapies include somatostatin analogs (octreotide) and antifibrinolytic medications such as tranexamic acid, which is a synthetic lysine analog that inhibits conversion of plasminogen to plasmin, and it has been shown to reduce mortality in upper GI bleeds [13]. Other antifibrinolytic therapies include thalidomide, aminocaproic acid, lenalidomide, and tamoxifen, and more novel anti-angiogenic medications such as bevacizumab (monoclonal antibody) have also been utilized, but further studies are needed in young patients with Turner syndrome [10,14,15].

Conclusions

Small bowel bleeding can be life-threatening and should be managed stepwise to minimize unnecessary procedures and maximize diagnostic yield. Intraoperative push enteroscopy appears to be safe and useful for the diagnosis and management of children with obscure gastrointestinal bleed when performed by an experienced surgical team. However, there should be careful risk-benefit assessment and patient selection prior to considering this procedure. Evidence-based guidelines for small bowel bleeding in children are needed to optimize care and outcomes in this population.

Turner syndrome is associated with gastrointestinal vascular malformations, and suspicion for this diagnosis should be high for these patients when presenting with gastrointestinal bleeding. Therapeutic approaches for patients with diffuse vascular malformations are still limited and, although estrogen seems to be a promising therapy in Turner syndrome patient's, further studies should be performed to assess the benefit of this therapy in this population.

Department and Institution Where Work Was Done

This work was performed at the Department of Pediatric Gastroenterology, Hepatology and Nutrition, University of Nebraska Medical Center and Children's Hospital and Medical Center, Omaha, NE, USA.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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