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Edited by:
Hillel Naon, M.D.
Acting Division Head, Pediatric Gastroenterology, Hepatology and Nutrition, Children's Hospital Los Angeles, University Southern California, Keck School of Medicine, Los Angeles, USA

Case Report

An Unusual Presentation of a Pediatric Gastrointestinal Stromal Tumor (GIST)

Brigitte Moreau[1]*, Van-Hung Nguyen[2], Sharon Abish[3] and Terry Sigman[4]

[1]*Division of Pediatric Gastroenterology, Sherbrooke University, Canada*
[2]*Division of Pediatric Pathology, McGill University Health Center, Canada*
[3]*Division of Pediatric Oncology, McGill University Health Center, Canada*
[4]*Division of Pediatric Gastroenterology, McGill University Health Center, Canada*

***Corresponding author**
Brigitte Moreau, Division of Pediatric Gastroenterology, Sherbrooke University, 3001 12e avenue Nord, Sherbrooke, Québec, Canada, Tel: 819-346-1110; Fax: 819-564-5398; Email: Brigitte.moreau@usherbrooke.ca

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Abstract

Gastrointestinal stromal tumors (GISTs) are mesenchymal tumors of the gastrointestinal tract. They are rarely seen in children, and the majority of cases occur in the stomach. We report the case of a 17 years old male with a duodenal GIST. He presented with the sole symptom of acute onset fatigue and shortness of breath and on admission was found to have a severe microcytic anemia. An upper endoscopy was performed and a polypoid mass with an adherent clot was identified in the duodenum. No obvious stalk was seen and a biopsy of the mass was taken. Histological findings of the biopsy revealed a spindle cell GIST positive for C-KIT (CD117), a type III tyrosine kinase receptor. Ten days after his admission, the tumor was resected. The mitotic rate was 9/ 50 HPF with negative margins which conferred an intermediate risk according to the NIH consensus. C-KIT positivity was confirmed. Mutation analysis was performed and was positive for mutation in KIT gene exon 11. No mutation was detected in the PDGFRA exons. Typically, gastric GIST is described on endoscopy as a submucosal mass with smooth margins and a normal overlying mucosa. Endoscopic biopsies are often reported as nondiagnostic. In this case, the mass was polypoid and friable in appearance and was suspicious for a polyposis syndrome. This case substantiates the importance of including GIST in the differential diagnosis of a duodenal polypoid mass on endoscopy. Furthermore, it demonstrates the usefulness of endoscopic biopsy in confirming the diagnosis, which can help in the surgical management of these patients.

ABBREVIATIONS

GIST: Gastrointestinal Stromal Tumors; PDGFRA; Platelet Derived Growth Factor Receptor Alpha

INTRODUCTION

Gastrointestinal stromal tumors (GISTs) are mesenchymal tumors of the gastrointestinal tract, which are rarely seen in children. The percentage of patients with GIST occurring below 21 years of age has ranged from 1 to 2.7% [1,2]. The majority of pediatric GIST reported occurred in females and originated from the stomach. Less than 20 cases of pediatric GIST have been reported to occur in the small intestine, and most were

found more distally in the small intestinal tract [3-8]. Clinically, the majority of reported cases of GIST of the small intestine presented with overt gastrointestinal bleeding and secondary anemia, or with intestinal obstruction [3]. Gastrointestinal stromal tumors, which possibly arise from the interstitial cells of Cajal, are usually characterized by a mutation of the tyrosine kinase receptor, either KIT (CD117) or platelet derived growth factor alpha (PDGFRA). Compared to adult GIST, where oncogenic KIT and PDGFRA mutations occur in approximately 88% and 7%[9] respectively, only 15% of pediatric GIST present with KIT and PDGFRA mutations [10]. Other molecular subtypes of GIST include familial cases of GIST in which KIT or PFGFRA mutations have been found, as well as cases of GIST in which no mutation has been associated, including most of the pediatric GIST as well as GIST has been associated with Neurofibromatosis type 1 [1]. The identification of these molecular subtypes is increasingly important, as targeted therapy is now available for some subtypes.

CASE PRESENTATION

We report the case of 17 years old male with a duodenal GIST. He presented with the sole symptom of acute onset fatigue and shortness of breath and was found to have a severe microcytic anemia (Hemoglobin 48 g/dL and MCV 64.3 fl) requiring a blood transfusion. His stools were reported as normal with no evidence of melena or hematochezia; however, a fecal occult blood test was found to be positive. An upper endoscopy was performed and a polypoid mass with an adherent clot was seen in the duodenum (Figure 1). No obvious stalk was seen and a biopsy of the mass was taken. Barium imaging and wireless capsule endoscopy confirmed a unique polyploid mass in the duodenum. Histological findings of the biopsy revealed a spindle cell GIST positive for C-KIT (Figure 2). No association with syndromic GIST, such as type 1 neurofibromatosis or familial GIST syndrome, was found by clinical examination or family history. There was no evidence of metastatic disease on examination or imaging. Ten days after his admission, the tumor was resected and the surgical specimen showed a polypoid tumor (2.5 x 2.0 x 1.8 cm) arising from the muscle wall with an irregular shape and an ulcerated surface. The mitotic rate was 9 per 50 high power fields with negative margins which conferred an intermediate risk according to the NIH consensus criteria [4]. Immunohistochemical analysis for CD34, desmin, S-100 and keratin AE1/AE3 were negative. C-KIT positivity was confirmed and staining was also positive for vimentin in addition to some focal staining for smooth muscle actin and caldesmon. Mutation analysis was performed and was positive for mutation in KIT gene exon 11 (deletion/substitution WKV 557-59 C). No mutations were detected in other KIT exons or in the PDGFRA exons. Because of the presence of the KIT mutation, he was treated with Imatinib mesylate therapy, which specifically targets tyrosine kinase receptors. The patient completed 3 years of treatment and a recent imaging of the abdomen has shown no disease recurrence.

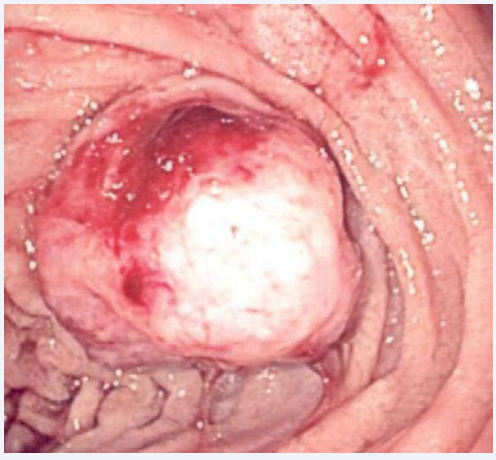

Figure 1 Endoscopic view of the polypoid mass.

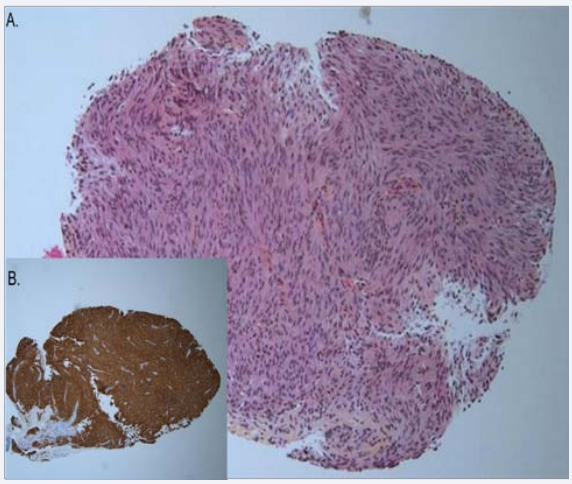

Figure 2 Endoscopic biopsy.
(A) Presence of spindle cell, (B) C-kit positivity staining in brown.

DISCUSSION

Pediatric case reports suggest that pediatric GIST characteristics are most often different from those in adults [2,3,11,12]. They seem to occur predominantly in females and appear mostly in the stomach. Histologically, a higher proportion of pediatric GIST are classified as epithelioid cell or mixed epithelial and spindle cell and only rarely is a C-KIT or PDGFRA gene mutation found. Our case, however, is a 17 years old male with a duodenal GIST composed of spindle cells that expresses C-KIT mutation, and thus has features more characteristic of adult GIST. These characteristics, similar to the 19 small intestinal pediatric GIST (age range birth to 18 years) reported in the literature [3,8], support the observation that most pediatric small intestinal GIST show features of adult GIST.

On endoscopy, gastric GIST is usually described as a submucosal mass with smooth margins, normal overlying mucosa and only occasionally is a central ulceration seen. There are rare endoscopic descriptions of pediatric GIST in the literature. In 2008, Bauer [13] described endoscopic findings of a large submucosal mass protruding into the lumen of the proximal jejunum. This mass presented with a central ulceration and a visible vessel, but due to acute angle of the endoscope, a biopsy was unable to be obtained. The mass was surgically resected and immunostaining showed diffuse CD 117 positivity and the presence of an exon 11 mutation on the KIT gene [13]. In the same year, an ileocolonoscopy revealed an ovoid 3 cm

mass projecting intraluminally at the ileocecal valve, overlaid by an ulcerated mucosa with intermittent ileal invagination. Endoscopic biopsies were obtained but were inconclusive [14]. The tumor was surgically resected and tumor cells showed a strong cytoplasmic CD117 staining and CD34 was found to be expressed in the majority of the tumor tissue. Only one pediatric small intestinal GIST, diagnosed by endoscopic biopsy, has been reported in the literature [15]. A 14 years old female presented with iron deficiency anemia and was found to have occult blood in stool. Two upper endoscopies and colonoscopies failed to reveal any abnormality. Meckel scan suggested a Meckel diverticulum; however, surgical laparoscopy did not reveal any abnormality. Video Capsule Endoscopy revealed a regular submucosa mass in the proximal jejunum. A push enteroscopy was performed and a 2 cm jejunal ulcerated bleeding mass, 30 cm beyond the ligament of Treitz, was found and the biopsy was suspected for GIST [15].

Since endoscopic biopsies are often reported as nondiagnostic, endoscopic ultrasound with fine needle aspiration has been suggested to be the most reliable and useful tool in the histological diagnosis of submucosal tumors such as GIST [16], however, the use of transperitoneal biopsies, is not accepted by all experts because of the theoretical risk of tumor dissemination and risk of bleeding [17]. In pediatrics, 2 patients have had confirmed diagnoses using endoscopic ultrasound to obtain histologic material; the first was an 11 years old girl with a gastric mass with failure to obtain tissue using standard endoscopic forceps [7] and the other was a 10 years old boy with a duodenal mass [8]. Another study suggests that the jumbo biopsy unroofing technique, which seems effective to get histologic material, should be considered as an initial diagnostic strategy for gastric submucosal masses found during upper endoscopy [18]. Although no pediatric cases have been reported using this technique to date, it may be a useful means of diagnosis in older children.

The mass described in our case report was polypoid and friable in appearance, and was suspicious for a polyposis syndrome at the time of endoscopy. Since a polyp stalk was not clearly visible we were not able to perform polypectomy using a polypectomy snare. An endoscopic biopsy was done with the surgeon present in order to help us decide on further diagnostic workup. It was this endoscopic biopsy, which provided the diagnosis of a GIST tumor and thus was crucial in guiding the surgeons at the time of surgical resection. This case substantiates the importance of including GIST in the differential diagnosis of a duodenal polypoid mass on endoscopy. Furthermore, it demonstrates the usefulness of endoscopic biopsy in confirming the diagnosis of small intestinal GIST, which can be crucial to planning further surgical management of these patients.

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