

Jejunal Leiomyosarcoma in a Young Adult: Distinguishing from Gastrointestinal Stromal Tumor through Radiographic, Histologic, and Epidemiologic Analysis – A Case Report

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Keywords

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Abstract

Introduction: Primary small intestinal malignancies are rare with an incidence of less than 5% of all gastrointestinal malignancies and are more common in the middle-aged and elderly population. They are comprised either an adenocarcinoma, neuroendocrine tumor, gastrointestinal stromal tumor (GIST), lymphoma, and/or sarcoma. **Case Presentation:** Here we exhibit the case of a 23-year-old who presented with progressive nausea, weight loss, abdominal pain, and iron deficiency anemia and was diagnosed with leiomyosarcoma of the jejunum. **Conclusion:** We distinguish a GIST from leiomyosarcoma based on radiographic, histologic, and epidemiologic evidence and review the significance of prompt, accurate diagnosis as related to treatment.

Introduction

Primary malignancies of the small bowel are relatively rare compared with other malignancies of the gastrointestinal tract. Although incidence can vary across countries and patient populations, primary small bowel cancers account for less than 5% of all gastrointestinal tract malignancies with an overall incidence of 2–3 per 100,000 individuals annually [1] and median age of 66 years [2]. Multiple hypotheses have attempted to explain the lower incidence of small intestinal malignancies, including a rapid transit time leading to decreased exposure to toxins and carcinogens; enzymes in the small intestine reducing the production of free radicals; and lymphoid tissue aiding in surveillance against neoplastic growth [3].

The differential of small bowel malignancies (in decreasing frequency) includes adenocarcinoma, neuroendocrine tumor, gastrointestinal stromal tumor (GIST), lymphoma, and sarcoma. Risk factors of small intestinal malignancies include alcohol, tobacco, familial syndromes, inflammatory conditions (e.g., Crohn and celiac disease) and immunocompromised states (e.g., EBV in

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Fig. 1. Coronal (left) and axial (right) computed tomography (CT) views identifying a markedly thickened heterogeneous jejunal loop up to 3 cm along an affected segment measuring up to 7 cm in the left hemiabdomen, identified by blue arrows.



HIV-infected patients, transplant patients, congenital immunodeficiency) [3–6]. This case demonstrates the diagnosis of leiomyosarcoma of the jejunum in a young adult.

Case Presentation

A 23-year-old Caucasian male with a recent diagnosis of gastroesophageal reflux disorder presented with 5 months of persistent abdominal pain, intermittent nausea, intermittent non-bloody emesis, and a 20-pound weight loss. His vital signs revealed a heart rate of 97 beats per minute, blood pressure of 119/71, respiratory rate of 17, and temperature of 98.3 F. Physical exam was remarkable for conjunctival pallor with epigastric tenderness to palpation. Serology demonstrated an iron deficiency anemia (hemoglobin: 5.8 g/dL; MCV: 67.8 fL; iron: <10 µg/dL; ferritin: 2 ng/mL), hemoccult-positive stool and negative carcinoembryonic antigen, cancer antigen 19–9 and AFP tumor markers. HIV antigen antibody and EBV-PCR were nonreactive. Computed tomography (CT) of the abdomen and pelvis with contrast revealed markedly thickened heterogeneous jejunal loop in the left hemiabdomen with associated mesenteric adenopathy and small volume pelvic ascites (shown in Fig. 1). Gastroenterology was consulted with subsequent esophagogastroduodenoscopy with push enteroscopy revealing a single, malignant appearing and ulcerated mass measuring 45 mm × 45 mm in the proximal jejunum (shown in Fig. 2). Pathology was concerning for a high-grade malignancy neoplasm. Fluorescence in situ hybridization analysis was normal. Positron emission tomography-CT demonstrated a hypermetabolic, multilobulated, ill-defined mass involving multiple loops of jejunum (shown in Fig. 3).

He subsequently underwent an exploratory laparotomy with resection of a proximal jejunal mass (10 × 8 × 7 cm), mesenteric lymphadenectomy, and jejunojunctionostomy creation. Pathology demonstrated high-grade spindle cell malignancy with extensive necrosis centered in the muscularis propria, bulging to the mucosa and serosa. Spindle cells were atypical with enlarged hyperchromatic nuclei and a mitotic rate up to 37 mitoses/10 high-power fields. Immunohistochemical stains of the spindle cells were strongly and diffusely positive for caldesmon and EMA, patchy

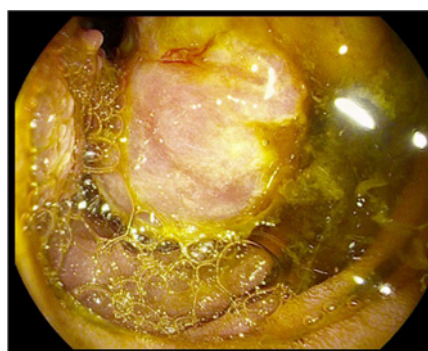


Fig. 2. Endoscopic visualization of a single, malignant appearing and ulcerated mass measuring 45 mm × 45 mm in the proximal jejunum.

positive for SMA, BCL2, and desmin and negative for MSA, CD117, DOG1, consistent with leiomyosarcoma, FNCLCC grade 3 (of 3) with 40% tumor necrosis (shown in Fig. 4). Lymph nodes were negative for malignancy. He was diagnosed with leiomyosarcoma (pT2aN0MoG3) and was initiated on continuous infusion with cyclophosphamide and doxorubicin.

Discussion

Leiomyosarcomas are soft tissue sarcomas arising from either bone, tendon, blood vessels, or muscle with a spectrum of disease that can range from low-grade cutaneous lesions to aggressive lesions of internal organs with significant potential for metastatic disease [7]. Small intestine tumors tend to have nonspecific symptoms, such as weight loss, nausea, vomiting, abdominal pain, and anemia, often leading to delayed diagnosis, which can progress to bowel obstruction, perforation, or bleeding [8]. This is particularly true in stromal tumors

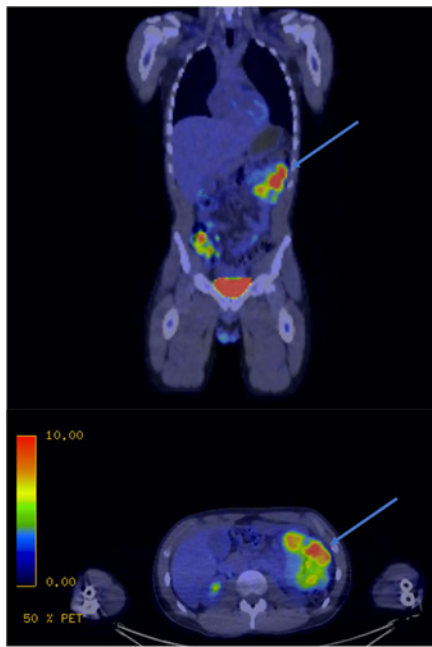


Fig. 3. Coronal (top) and axial (bottom) positron emission tomography-CT views demonstrating a hypermetabolic, multi-lobulated, ill-defined mass involving multiple loops of jejunum, identified by blue arrows.

as they originate from the muscular wall of the intestine, allowing them to grow significantly large before causing symptoms.

Blanchard et al. [9] performed a review of all available case reports and case series of smooth muscle tumors of the small intestine between 1881 and 1996, identifying 1,074 leiomyomas and 1,689 leiomyosarcomas. However, it should be noted that these types of tumors in the older medical literature are actually GISTs since definitive tools to discriminate leiomyosarcomas from GIST were not introduced until the late 1990s. Therefore, a review of the literature from 2000–2012 identified only 56 cases of gastrointestinal leiomyosarcoma in adults [10] with a peak incidence between the ages of 55–59 years, the most common chief complaint was gastrointestinal bleeding. The jejunum was found to be the most frequent location and notably had larger tumors, and specifically tumors of 5–9 cm were more often malignant than smaller tumors [9]. Our patient was significantly younger (23 years old) than typically seen but otherwise presented with nonspecific symptoms of nausea, abdominal pain, and anemia with a malignant tumor of relatively large size.

Identification of the mass is most often made via CT, which reveals a well-circumscribed soft tissue density

mass with an adjacent thickened wall, potentially with enhancement and areas of low attenuation from hemorrhage, necrosis, or cyst formation following intravenous contrast. Magnetic resonance imaging depicts heterogeneous tumors with low intermediate signal intensity on T1-weighted images and heterogeneous high signal intensity on T2-weighted images [11]. Endoscopic sampling, when possible, is preferable to transcutaneous biopsy due to the lower risk of abdominal cavity seeding.

Our patient's tumor was initially described as having markedly thickened and heterogenous appearance of a loop of jejunum, consistent with the typical radiographic features. Although uncommon and not present in our patient, intra-abdominal metastatic spread of soft tissue sarcomas must be ruled out with the primary site most frequently originating in the lower extremities and spreading to the mesentery or retroperitoneum, with infrequent small bowel involvement [12]. Additional consideration in female patients is to eliminate metastasis from uterine leiomyosarcoma, representing 5% of uterine malignancies and the most common uterine pure mesenchymal tumor [13]. Gastrointestinal metastasis from extra-abdominal sites is exceedingly rare with few case reports detailed metastasis to the small bowel [14]; however, immunohistochemical analysis will demonstrate higher detected rates of estrogen receptor (48 vs. 12%), PR (62 vs. 21%), desmin (79 vs. 50%), and EMMPRIN (69 vs. 45%) in uterine leiomyosarcoma compared with extra-uterine leiomyosarcoma, respectively [15].

Once identified, a key is to distinguish GISTs and leiomyosarcomas as treatment options are vastly different. GIST is the most common mesenchymal neoplasm of the gastrointestinal tract, postulated to arise from the interstitial cells of Cajal and is prognostically categorized into three categories based on size, mitotic index, and more recently location [16], ranging from very low risk to high risk. GIST harbor KIT or PDGFRA gene mutations in 85% with approximately 95% positive for CD117 on immunohistochemistry [17]. A mouse monoclonal antibody, DOG1.1, has superior sensitivity and specificity than CD117 and CD34, particularly in KIT-negative GIST [16, 18]. With the development of tyrosine kinase inhibitors, the treatment of GISTs has been revolutionized, particularly for metastatic or inoperable tumors, though the decision for surgery is a complicated decision based on numerous factors. Our patient's histology was notably negative for CD117 and DOG1. Leiomyosarcoma originates from smooth muscle cells and is composed of spindle-shaped cells

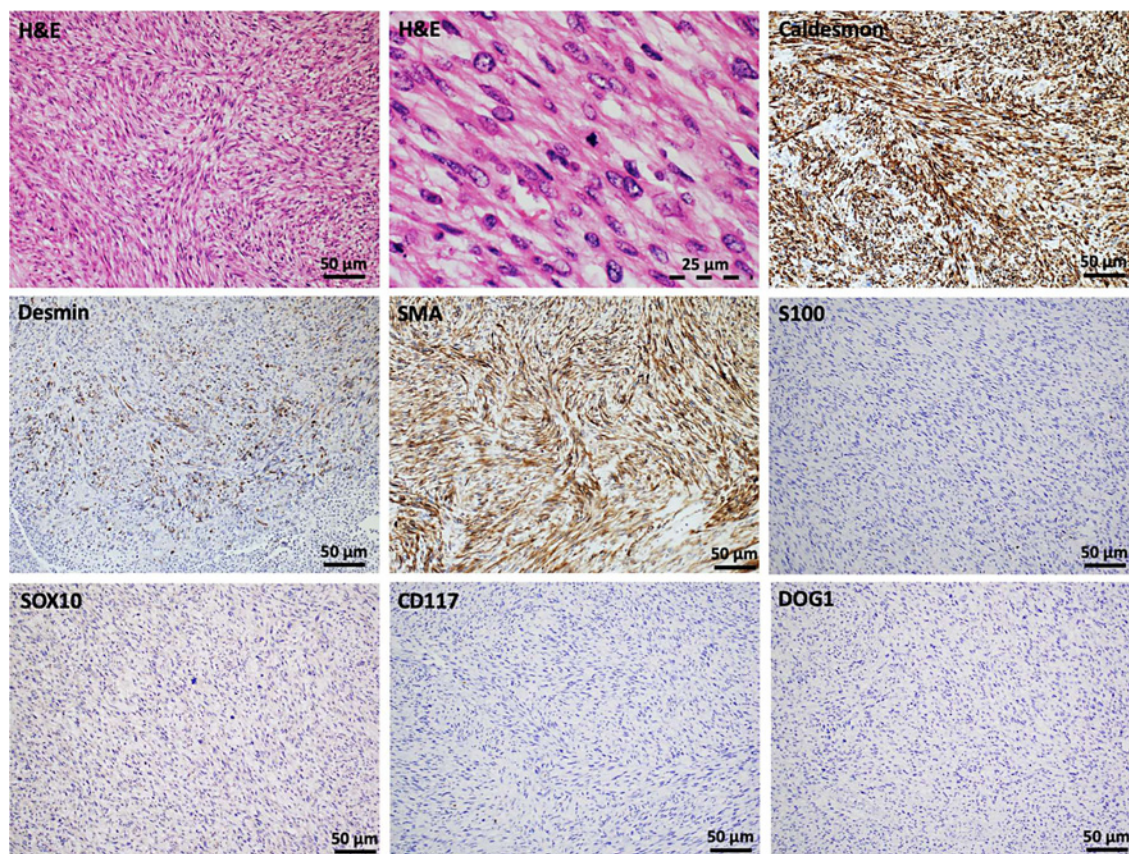


Fig. 4. Histological sections demonstrate a high-grade spindle cell malignancy forming long fascicles with herringbone growth pattern. The spindle cells are atypical with enlarged, hyperchromatic nuclei and occasional bizarre forms. Mitotic rate is up to 37 mitoses/10 high-power fields. Tumor necrosis is present accounting for approximately

40% of the tumor volume. Immunohistochemical stains show the spindle cells are strongly and diffusely positive for caldesmon and SMA, patchy positive for desmin, and are negative for S100, SOX10, CD117, DOG1, myogenin (image not shown), MSA (image not shown), and MUC4 (image not shown).

demonstrating elongated nuclei and eosinophilic cytoplasm. Diagnosis is based on immunohistochemical positivity for SMA, desmin, h-caldesmon and negativity for CD117, CD34, and DOG1.1, notably lacking KIT and PDGFRA mutations [10]. Our patient's histologic staining fits this clinical picture with strongly positive caldesmon, patchy positive SMA, and desmin with negative CD117 and DOG1. Various predisposing factors for leiomyosarcoma have been identified, including a history of retinoblastoma and immunocompromised patients with Epstein-Barr virus or HIV [5, 19], none of which were present in our patient. Treatment involves surgical resection and a cost-benefit analysis of adjuvant chemotherapy with an oncologist specializing in the treatment of sarcomas.

Aggarwal et al. reviewed the outcome data of 18 small bowel leiomyosarcomas, finding 11 patients survived

5 years or more. Although statistical analysis was precluded due to sample size, there was a trend to suggest smaller tumor size and low mitotic count favorable prognostic factors. The average tumor size of the survival group was 9.3 cm versus 13.8 cm for those who died with mitotic activity of 6/10 HPFs compared with 11/HPF, respectively [10]. This is vastly different than the survival data for localized GIST with the estimated 5-year and 15-year recurrence-free survival rates treated with surgery alone 70.5% and 59.9%, respectively [20], though median survival for advanced metastatic GIST is lower at 51–57 months [21]. Based on the Memorial Sloan Kettering Sarcoma nomogram, which indicated a 48% chance of sarcoma-related death at 4 years without adjuvant chemotherapy, his young age, and high mitotic activity, the decision was made to initiate adjuvant chemotherapy [22].

Conclusion

We present a case following the presentation and the diagnosis of a rare gastrointestinal malignancy in a patient without predisposing factors, such as immunocompromised states, and well outside the typical age of presentation. We review the clinical presentation, histology, and importance of distinguishing between GIST and leiomyosarcoma due to the differing prognosis and treatment options. We hope this case adds to the limited, though growing body of literature describing gastrointestinal leiomyosarcoma and highlights the need for standardized histologic evaluation to ensure timely, accurate diagnosis.

Statement of Ethics

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. Ethical approval is not required for this study in accordance with local or national guidelines.

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Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

As per ICMJE criteria for authorship: Blake H. Bentley designed the article and contributed to conception and literature search. Abigail L. Ellington contributed to article design and literature search. Alyssa A. Guo procured case details and contributed to literature search. Haiyan Lu procured pathology photographs. William C. Lippert contributed to literature search and final proofreading.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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