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Gastrointestinal Stromal Tumor: A Rare Tumor of Childhood

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Gastrointestinal stromal tumors (GISTs) arise from the myenteric ganglion cells, also known as interstitial cells of Cajal, found in the gastrointestinal tract.[1] This tumor is the most frequent mesenchymal tumor at this site.[2] While GISTs are normally found in the stomach, they have been identified in other areas of the gastrointestinal tract as well as beyond it.[1-4] Overall, reported incidence rates in the UK National Registry of Childhood range from 6.5 to 14.5 cases per million per year, with a rate of 0.02 per million for children under 14 years of age.[3] Children and adolescents only account for up to 2% of diagnosed GIST cases.[2] The pediatric form of GIST is distinct from the adult form, with different clinical and pathological characteristics, tumor biology, and patient outcomes.[1,5] Pediatric patients with GIST appear to have a relatively benign clinical course compared to adults. In addition, KIT or platelet derived growth factor receptor-alpha (PDGFRA) mutations have been reported less frequently in children (<15%) compared to adults (>90%).[3,6] Gastrointestinal stromal tumors have been associated with Carney triad syndrome, Carney–Stratakis syndrome, familial GISTs, and type 1 neurofibromatosis.[1,3,4,7] Most children typically experience symptoms during the second decade of life (with a median age of 13 years), and there is a higher prevalence rate among females (2.5 : 1).[1,3,4,8] In terms of clinical presentation, pediatric GISTs often manifest as gastrointestinal bleeds, which may be caused by their inclination toward the stomach in younger patients. Other symptoms may include abdominal discomfort (such as pain, changes in appetite, early satiety, bloating, vomiting, constipation, or obstipation), weight loss, and anemia.[1,2,4] In this article, we present a case of GIST, as a rare pediatric solid tumor.

A 16-year-old male patient presented to the emergency department with a complaint of hematemesis and was scheduled for elective upper gastrointestinal endoscopy once the patient's hematocrit and hemodynamics were stable. During the endoscopy, a hyperemic mass lesion with a large diameter, originating from the incisura angularis and extending from the pylorus to the bulbus, was observed in the stomach antrum (Figure 1A). A mucosal biopsy was taken, and the procedure was then terminated. Pathology showed superficial gastric mucosa without atypia. There were no signs of metastasis during the abdominal and thorax computed tomography (CT) examination. The pediatric oncology evaluation did not provide any further preoperative recommendations. Two units of erythrocyte suspension were administered to the patient, whose preoperative hemoglobin level was 8.5 g/dL with a hematocrit of 29.4%, before the scheduled surgery. During surgery, through a median incision above the umbilicus, a 4 × 5 × 6 cm mass was observed in the prepyloric region of the anterior gastric wall. The mass was completely excised using Ligasure (Covidien-Medtronic, USA), with a surgical margin of 2 cm around it (Figure 1B and 1C). The stomach wall was closed in 2 layers, and omentopexy was performed. The postoperative period was uneventful. The pathology presented as a mixed spindle and epithelioid type of GIST. Surgical margins were found to be intact and 0-1 mitoses were present in 50 high power fields (HPFs). The tumor was immunohistochemically positively stained with DOG-1, C kit (CD117), and CD34, while Ki67 amounted to 1% (Figure 1D and 1E). No genetic syndrome was investigated. Adjuvant therapy was not deemed necessary for the patient, who was followed in the

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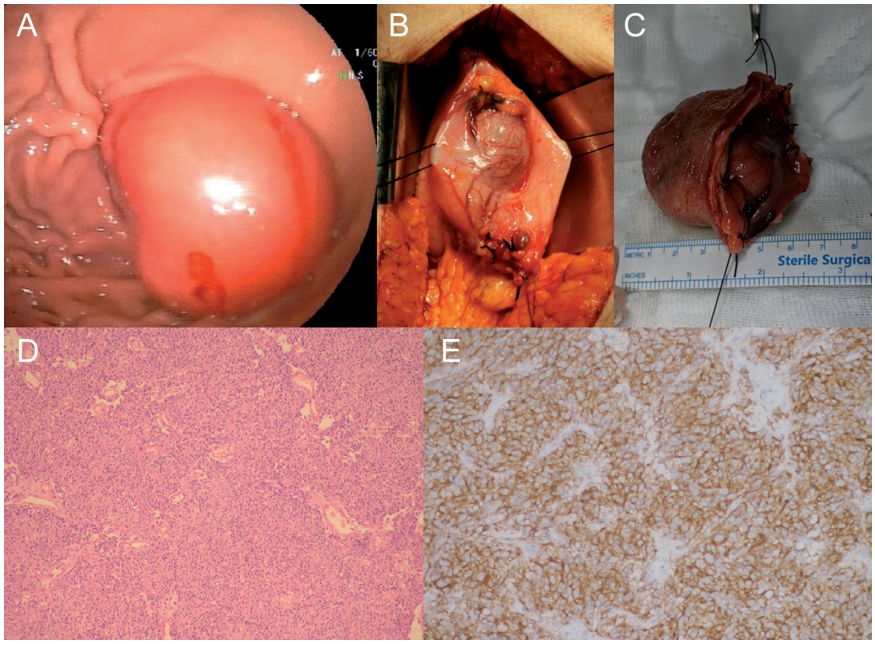

Figure 1. (A) Endoscopic view of solid mass originating from the incisura angularis. (B) Intraoperative negative gross margins of mass. (C) Resected material 4 × 5 × 6 cm in size. (D) Hematoxylin and eosin staining, cells with eosinophilic cytoplasm with occasional palisaded, eosinophilic cytoplasm, indistinct cytoplasmic borders, and monotonous nuclei (10× magnification). (E) Immunohistochemically membranous DOG-1 positivity (20× magnification).

oncology evaluation and the 1-year follow-up was uneventful. The diagnosis of GIST in children can be difficult clinically due to the non-specific and slow-developing symptoms, as well as the unusual occurrence of the disease. A lesion caused by GIST will typically manifest itself as a submucosal lump with smooth edges, pushing the overlying mucosa outward, with occasional associated necrosis or hemorrhaging visible during endoscopy.[1] There are no published guidelines for the management of children with GISTs, and these recommendations are based on non-analytic case series and expert opinion, taking into account the available published literature.[7]

In our patient, thorax and abdominal CT were normal outside of the gastric lesion. In the management of GISTs, excision with wedge resection is the standard approach, as obtaining negative gross margins is indicated.[2,4,5,7] Typically, a macroscopic margin of 1 cm is sufficient to achieve microscopically negative margins.[4] High mitotic index, tumor size greater than 5 cm, and spindle morphology were all associated with poor patient outcomes.[8] Gastric GISTs carry a better prognosis than tumors of the small intestine.[9] Weldon et al[10] reported that the only significant predictors of disease progression were tumor mitotic rate and metastasis at presentation. We carried out a full excision and left a margin of 2 cm around the tumor. The mitotic rate of our patient was low, and there was no evidence of metastasis. Tumor spread to lymph node basins is much more common in pediatric GIST than in the adult counterpart and it is recommended to investigate all lymph node basins that drain the primary tumor and remove any nodes that appear suspicious.[3,5,7] Our patient has shown no evidence of metastasis to lymph nodes. Gastrointestinal stromal tumors present 3 distinct morphologies: spindle cell, epithelioid cell, and mixed cell types. Pediatric GISTs are more commonly associated with epithelioid and mixed cell morphologies, with epithelioid being the most common, followed by an equal distribution of spindle and mixed morphology.[1,4,7,8] In pediatric patients, spindle cell morphology was associated with a poorer prognosis.[8] The pathology in our patient was presented as a mixed cell type of GIST. In abdominal locations, solitary fibrous tumors (SFT) can mimic other soft tissue neoplasm and also show spindle to ovoid cells arranged in fascicles or randomly distributed. CD34 expression is common in both GISTs and SFTs. However, GISTs are positive for CD117 and DOG1 while STAT6 is always negative.[11] Immunohistochemistry showed positive staining for CD34, CD117, and DOG1 in our patient, which led to a differential diagnosis. In cases of localized disease where complete resection is achieved and no tumor spillage is observed during surgery, no adjuvant therapy is necessary.[4,5] For non-localized disease, tyrosine kinase inhibitors (TKI) are the mainstay of therapy, with adult GISTs exhibiting excellent response to TKI treatment.[4] Unfortunately, most cases of pediatric GIST do not exhibit these mutations in KIT and PDGFRA and consequently have been less responsive to conventional TKI treatment.[5,7] As our patient underwent an R0 resection and no metastases were observed, genetic testing was not performed. No further adjuvant treatment was given following the oncologic evaluation. Currently, no published data suggest an optimal follow-up protocol for GIST patients.[4] As metastases outside the abdomen are very rare, abdominal and pelvic magnetic resonance imaging is suitable for the conventional follow-up of GIST patients. Herzberg et al[3] recommended a biannual follow-up for completely resected tumors and asymptomatic unresectable tumors. The patient continues to be followed radiologically regularly. In conclusion, pediatric GIST is a rare condition that requires a multidisciplinary approach involving radiology, pathology, gastroenterology, oncology, and surgical teams. Differential diagnosis necessitates histopathological morphology, immunophenotypic analysis, and molecular testing. Since

GISTs have the potential to metastasize, it is essential to perform complete surgical resection and monitor the patient's progress over the long term.

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