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Case Report

Gastrointestinal Stromal Tumor (GIST) Presenting as Unexplained Chronic Anemia in an Adolescent Boy

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Case Presentation

A 14-year-old boy was investigated in another Hospital for the occurrence of pallor and mild weakness in the last months. His family history was significant for Crohn's disease in the mother and he had had a surgical removal of a Meckel diverticulum at 2 years of age. Hematologic data showed severe iron deficiency anemia (IDA) (Hb 7.7 g/dl, ferritin 3.43 mg/dl). He was successfully treated with oral iron administration, but a few months later anemia relapsed. Further evaluation showed normal hemoglobin distribution, negative celiac disease serology and negative fecal occult blood tests. The boy was then referred to our Hospital for further gastrointestinal evaluation. A positive H. pylori fecal antigen was found but, even if H. pylori infection has been associated with IDA, and in spite of the absence of digestive symptoms, we preferred to perform a gastroscopic evaluation. EGD showed the presence of 2 ulcerated protruding submucosal lesions of the greater curvature and the gastric antrum (Figure 1a,1b), suggestive for submucosal tumors. An endoscopic ultrasound-guided needle aspiration sampling of the mass (Figure 2) showed aggregated sheets with scant interposed stroma of fusiform cells of mesenchymal type, suggestive for a Gastrointestinal stromal tumor (GIST). Abdominal NMR showed the presence of 2 ovular lesions located at the VII and VIII liver segment, with a max diameter of 1 cm, characterized by low signal intensity on T1-weighted and mild high signal intensity on T2-weighted imaging, and moderate contrast enhancement. Cytological evaluation of the largest lesion confirmed the same neoplastic picture described in the stomach.

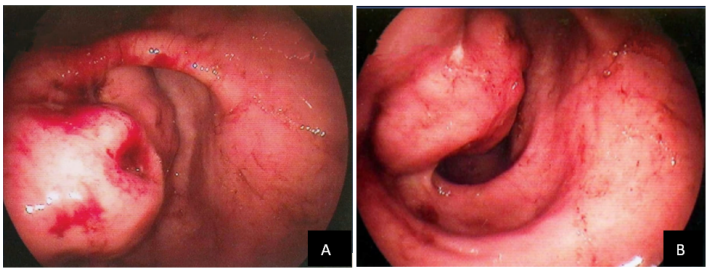

Figure 1: Endoscopic appearance of the stomach. A. A large, ulcerated, volcano-like mass protruding from the greater curvature. B. A second mass involving the antrum and the pre-pyloric region.

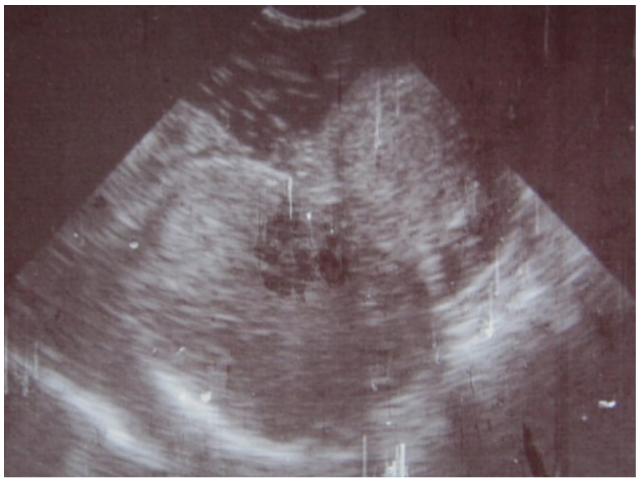

Figure 2: Ultrasound endoscopy showed a echo-poor pattern, homogeneous and well demarcated solid tumor.

The patient was submitted to subtotal gastrectomy and histologic evaluation of the multiple nodular tumors of the anterior gastric wall. The biggest (12 cm of diameter) mass of the antrum revealed the presence of a multicentric, malignant gastrointestinal stromal tumor (GIST), constituted by epithelioid cells with neuronal (synaptophysin positive), but not muscular (α-actin and desmin negative) markers. At immunohistochemistry specimens were found positive for CD117 (KIT), CD34 with a Mib1 of 5%. Metastatic involvement was found in 5 of 7 and 1 of 6 lymph nodes of the lesser and greater gastric curvatures.

As this case presented all features of highly malignant GIST (tumor size, multifocality, multinodularity, dissemination to liver and lymph nodes), a first-line systemic treatment for metastatic disease with Imatinib mesylate (STI571, GleevecTM, Novartis Pharmaceuticals) at a dose of 400 mg/day was started.

Eighteen months later, due to the progression of disease with liver and thoracic and axillary lymph nodes involvement, therapy with Sunitinib malate (SutentTM, Pfizer) at a dose of 50 mg/day, was started. Twenty years after diagnosis of malignant and disseminated GIST, the patient is live and he became an happy father.

Discussion

Iron deficiency anemia (IDA) is a frequent disease at all pediatric ages, affecting up to 25% of school-age children and adolescents [1]. The most common causes of iron deficiency in children include insufficient intake, impaired intestinal absorption and blood gastrointestinal losses. If insufficient intake and malabsorption have been excluded and there is poor response to oral iron treatment or relapsing anemia, blood loss should be promptly considered as the underlying cause [2]. We described here a case of disseminated GIST in an adolescent boy, where IDA was the only presenting feature. IDA was responsive to oral iron treatment, but relapsed shortly after discontinuation. Interestingly, in spite of the presence of ulcerated gastric lesions, the fecal blood occult test resulted persistently negative. This is not surprising, because of the well-known low sensitivity of routine fecal tests for blood originated from the upper digestive system [3]. Another point to debate is the occurrence of anemia in association of H. pylori infection [4,5]. To date, some well-conducted studies showed that there is no evidence for a causal relationship between IDA and H pylori infection. Probably previous data showing an association between concomitant IDA and H pylori infection have been biased by the high frequency of both these conditions and the sharing risk factors (low-income countries of origin, poor hygiene, and nutritional deficiency in the first years of life). In agreement with the most recent ESPGHAN guidelines, we think that "Noninvasive testing for H pylori is not recommended as part of the initial investigation of IDA in children." [4,5]. For this reason, we preferred to look for a digestive source of occult gastrointestinal bleeding and, even if the boy didn't show any digestive symptom, we submitted him to esophagogastroduodenoscopy.

Although gastrointestinal stromal tumors (GISTs) are the most common mesenchymal neoplasms of the digestive tract, their occurrence in children is very rare. Overall incidence rates of 6.5–14.5/million per year and 0.02 per million children below the age of 14 years in the UK National Registry of Childhood have been reported [6]. Pediatric-type of GIST are more frequently seen in females, and the median age of the patients included in a representative pediatric review was 13 years (range, 1 day–21 years). GIST in children either occur sporadically or are associated with other tumor syndromes, such as Neurofibromatosis Type-1 (NF1), Carney Triad and Carney–Stratakis Syndrome [7]. In our case no other tumor or phenotypic picture suggesting a syndromic form of GIST have been found and no other family member has been affected by mesenchymal tumors, excluding a Familial GIST. Sporadic pediatric-type of GIST tend to be frequently located in the stomach, with metastasis to lymph nodes (29%) and liver (25%) [5,6], as in our case. Looking at the treatment of GIST, surgery to achieve local excision with microscopic free margins is the most important aspect. In our case the choice to perform subtotal and not partial gastrectomy was due to the multinodularity and large size of tumors. Adjuvant treatment with RTK inhibitors are recommended in children and adolescents with extensive GIST and accordingly, our patient was treated with imatinib and, on relapse, with sunitinib with a long-time remission [6,7].

This case report demonstrates the importance that in any case of severe anemia any effort to find an organic cause should be done. Moreover, negative fecal blood tests don't exclude upper digestive bleeding and such tests do not be used for this indication. Search for H. pylori infection for IDA is not supported, as stated by the most recent Guidelines on this topic. Poor response of disseminated pediatric-type of GIST to one RKT inhibitor drug doesn't exclude successive response to another similar agent.

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