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Case Report

Gastrointestinal Stromal Tumours in Stomach - A Cause of Occult Anaemia

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Abstract

Gastrointestinal stromal tumours (GISTs) are rare mesenchymal tumours of the gastrointestinal tract, first described by Mazur and Clark in 1983. At present GISTs represents 1–3% of all gastrointestinal malignancies, making it a diagnostic challenge. Lesions are frequently located in stomach and proximal small intestine but rarely elsewhere in the abdomen. They are believed to result from mutations of proto-oncogenes c-Kit or platelet-derived growth factor receptor alpha polypeptide, this increase tyrosine kinase receptor activity, leading to uncontrolled proliferation of stem cells that differentiate into cells of Cajal, autonomic nerve related gastrointestinal pacemaker cells that regulate intestinal motility. They can occur at any age but predominantly in middle-aged people and in elderly. We report the case of a 60-year-old woman presented to our hospital with upper gastrointestinal bleeding and black tarry loose stool, findings in diagnostic image studies suggested a GIST in proximal part of stomach without evidence of distant metastasis; therefore subtotal gastrectomy was performed. Cytology and immunohistochemistry analysis confirm diagnosis of GISTs.

Keywords: Gastrointestinal stromal tumours (GISTs), CD117 antigen, Proto-oncogene c-Kit

Introduction

GISTs are stromal or mesenchymal tumours that affect the gastrointestinal tract typically appear as subepithelial neoplasms and are often discovered during endoscopy done for various complaints. The most common is GIST, which arises from mesenchymal stem cells programmed to differentiate into interstitial cells of Cajal in the myenteric plexus.[1] The cells of Cajal form a complex cell network within the gastrointestinal tract (GIT) wall where they function as a pacemaker system. The GIST can arise from anywhere into the GIT and are frequently located in stomach (66%) and small intestine (30%) particularly in duodenum, as well as in oesophagus, colon, rectum and anus (<10%).[2] They can even occur in extra-digestive tube, by example in omentum, mesentery or peritoneum.[3]

Case Report

A 60-year-old woman presented to primary care physician with colicky upper abdominal pain, occasional non-bilious coffee ground vomiting, moderate anaemia, anorexia with significant weight loss. She had a history of occasional black tarry loose stool, had no history of smoking, alcohol consumption and recently not used any non-steroidal anti-inflammatory drug (NSAID) or steroid. On examination, the patient was ill looking and anxious, afebrile and haemodynamically stable. Her abdomen was scaphoid in shape, soft but tender on epigastria region and there was no organomegaly and palpable mass lesion. Other systemic examination reveals no abnormalities. Venous blood tests revealed a haemoglobin level of 7g/dl then 2 units of whole blood was transfused.

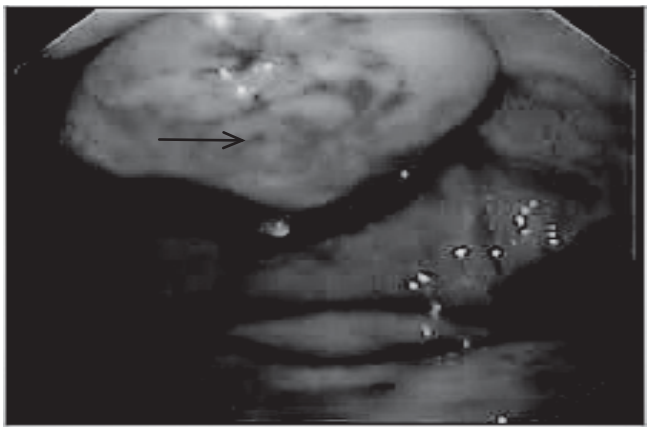

Figure-1 Endoscopy of upper GIT (black arrow to the mass).

After resuscitation and stabilization, she underwent to upper GI endoscopy with biopsy. A hidden bleeding point with regular gastric mass was identified along the greater curvature of the Proximal stomach. Later, the patient was transferred to general surgery department, following this; she was brought under to contrast enhanced CT scan of abdomen. The images showed a homogeneous pattern attenuation range of soft tissue and a well-defined dumb-bell shaped 5.4×6.5 cm mass arising from the greater curvature of proximal stomach and well attached at it. There was no evidence of distant lesions (see Figs. 1 and 2).

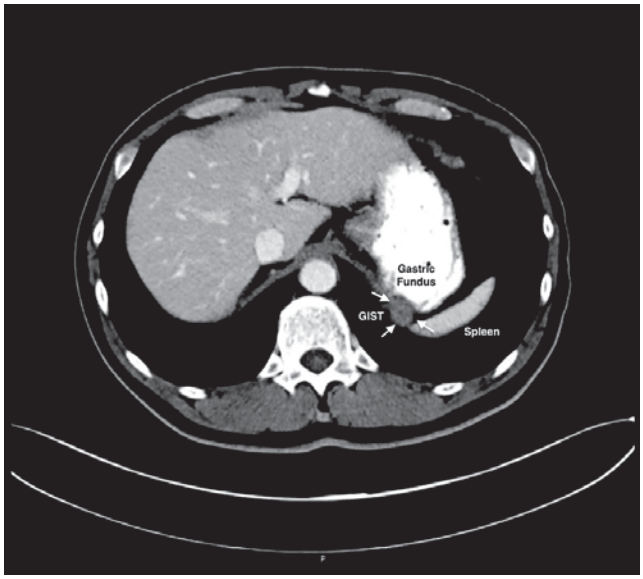

Figure-2 Contrast enhanced CT scan of abdomen (white arrow to the mass)

Discussion

GISTs are subepithelial tumours, initially referred to as leiomyoma, leiomyosarcoma or leioblastoma. However, with the availability of electron microscopy and immunohistochemical staining, Mazur and Clarks were able to distinguish GISTs as a separate gastrointestinal neoplasm with distinct features.[2] GISTs represent 1-3% of gastrointestinal malignancies with an incidence of seven per million per year[3]. GISTs originate from CD34-positive stem cells residing within the wall of the gut, which can then differentiate incompletely toward the interstitial cells of Cajal (ICC) phenotype. More than 95% of GISTs exhibit KIT (CD117). Expression of CD34 is not specific for GISTs but is noted to be a poor prognostic indicator as most cases of malignant GIST are CD34 positive. Five present of GIST cells are not caused through activation and aberrant signalling of the KIT receptor, but rather through mutational activation of the structurally related kinase known as the platelet-derived growth factor receptor- alpha (PDGFRA). Definitive diagnostic criteria for CD117-negative true GIST are currently obscure. The DOG1 gene, which encodes for chloride channel protein actin 1 (independent of KIT and PDGFRA), was discovered in 2004 and is specific for GIST in appropriate clinical and pathological context. Expression of CD117 could be heterogenous, and biopsy could be false negative. True leiosarcomas express smooth muscle actin and desmin but are negative for CD117. Schwannomas are positive for neural antigen S100. GIST tumours are classified into three types based on histopathologic appearance: spindle cell type (70%), epithelioid type (20%) or mixed type (10%).[4, 5] GISTs have a wide variety of clinical presentations depending on the site of involvement. The most common site is the stomach (60-70%), followed by the small intestine (20-30%), colon, rectum (5%), and oesophagus (<5%).[6] Small GISTs may be asymptomatic and are discovered incidentally during endoscopy. Oesophageal GISTs may present with dysphagia,[7] and stomach or small intestinal GISTs may present with overt or occult gastrointestinal bleeding.[8] Colonic GISTs may present with acute abdomen, perforation, pain or obstruction.[9] Large tumours may present as an abdominal mass or symptoms of paraneoplastic syndrome. Consumptive hypothyroidism caused by marked overexpression of the thyroid hormone-inactivating enzyme type 3 iodothyronine deiodinase (D3) within GISTs has been reported.[10] Malignant GISTs may present with metastasis most commonly in the liver and peritoneum.

The diagnosis of GIST is often suspected on contrast-enhanced CT or magnetic resonance imaging (MRI) showing an abdominal mass. Imaging can also evaluate the extent of the tumour and assess for the presence of metastasis.[11] Endoscopy can be done to evaluate a luminal involvement by the mass. However, an endoscopic ultrasound (EUS) can differentiate intramural and extramural lesions and can further

characterize the mass by identifying its layer of origin and allowing ultrasound-directed fine needle aspiration (FNA) biopsy to be obtained for definitive diagnosis. Usually GISTs are well-demarcated, hypoechoic lesions arising from the fourth layer of the gastrointestinal tract (muscularis propria), although small lesions may arise from the second layer (muscular mucosae).[12,13] GISTs may have different clinical behaviors depending on the site and mitotic activity. In the stomach the benign lesions outnumber the malignant ones, in contrast to the oesophagus and colon where most of the GISTs are malignant. Tumours with low mitotic activity, five or fewer mitoses per 50 HPF, usually have a benign behaviour as compared to those with more than five per 50 HPF are described as malignant. Tumours with more than 50 mitoses per 50 HPF are described as high-grade malignant.[14]

Treatment for GIST depends on the tumour size and location. Oesophageal GISTs greater than 2 centimeters need to be excised,[15] however for those smaller than 2 centimeters different guidelines recommend different management; there is a conservative approach with follow up with repeat esophagogastroduodenoscopy (EGD) and removal if there is an increase in size. Another approach recommends removal of the tumour for fear of the risk of metastasis.[16] For gastric GISTs, submucosal lesions <1 cm with EUS findings suggestive of benign tumour may be followed conservatively. Management of gastric lesions between 1 and 2 cm is controversial and lesions greater than 2 cm should be excised.[17] For duodenal GISTs, excision is advised whether endoscopically or surgically with pancreaticoduodenectomy.[18] For GISTs in the colon and rectum, excision of the tumour is advised, however sometimes it is challenging especially in the rectum. So preoperative imatinib is advised to downsize the tumour and achieve better surgical outcomes.[19]

Conclusion

GISTs comprise only 0.5-1% of gastric neoplasms. Clinical features and management depend on the location, size, appearance and characteristics on EUS. Tumours with benign features can be monitored, while large tumours should be excised, with neoadjuvant chemotherapy to downsize the tumour prior to resection. Our patient presented with abdominal pain, occult anaemia and weight loss, which is a common symptom of many pathologic conditions. It is important to consider GISTs as one of the differential diagnoses, when patients present with similar symptoms, as early stage diagnosis improves outcome and long-term prognosis.

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