Cancer Medicine Journal

Case Series | Vol 3 Issue S1

Gastrointestinal Stromal Tumors Incidentalomas: A Case Series

Mina Ferig[1], Sylvia Alarcon Velasco[1], Layla Van Doren[1] and Muhammad Wasif Saif[1,2*]

[1]*Tufts Medical Center, Tufts University School of Medicine, Boston, MA, USA*

[2]*Department of Medical Oncology, Northwell Health Cancer Institute, Donald and Barbara Zucker School of Medicine at Hofstra and Feinstein Institute for Medical Research, USA*

Correspondence should be addressed to Muhammad Wasif Saif, wsaif@northwell.edu

Received Date: September 01, 2020; **Accepted Date:** September 30, 2020; **Published Date:** October 07, 2020

ABSTRACT

BACKGROUND

Gastrointestinal stromal tumors (GISTs) represent approximately 0.2% of all gastrointestinal tumors. GISTs can occur anywhere along the length of the gastrointestinal tract. Most common clinical manifestations of GISTs include GI bleeding, abdominal discomfort, distention and pain. Small lesions can be found incidentally during imaging studies, endoscopy, surgery and post-mortem. The progression of disease from incidentally found indolent to symptomatic disease is unknown.

CASE SERIES

Here we describe a series of cases of incidentally found GIST and their management. The first patient was a 38-years old morbid obese female with an incidentally found GIST in the stomach following an elective laparoscopic vertical sleeve gastrectomy. The second patient was a 69-year-old male who underwent elective sleeve gastrectomy for his obesity and associated refractory acid reflux. On pathologic examination of the gastrectomy specimen, GIST was diagnosed in the gastric fundus.

DISCUSSION

Coexistence of GIST with other malignancies is higher than previously reported and should draw attention of clinicians towards these incidental findings. Prognosis in these patients is usually determined by other malignancy and not significantly influenced by GIST. Therefore, treatment algorithms should be focused on prognostically relevant malignancy.

KEYWORDS

GIST; Obesity; Imatinib; C-kit

INTRODUCTION

Stromal tumors are the major primary non-epithelial tumors of the gastrointestinal tract and are known as gastrointestinal stromal tumors (GISTs). They represent approximately 0.2% of all gastrointestinal tumors. GISTs are mostly found in the gastrointestinal track, with 40%-70% of cases occurring in the stomach, and 20%-50% in the small intestine, however GIST can occur anywhere along the length of the bowel. Even more rarely GIST can occur in extra-visceral sites including the omentum, mesentery, pelvis and retroperitoneum. GIST mesenchymal tumors positive for CD117 (c-kit) and are primarily caused by activating mutations in the KIT or a

Citation: Mina Ferig, Gastrointestinal Stromal Tumors Incidentalomas: A Case Series. Cancer Med J 3(S1): 35-38.

class III receptor tyrosine kinase gene, the PDGFRA which encodes the platelet derived growth factor receptor-alpha receptor tyrosine kinase protein [1,2].

GIST clinical manifestations include GI bleeding, abdominal discomfort, distention and pain. Small lesions can be found incidentally during imaging studies, endoscopy, surgery and post-mortem. The progression of disease from incidentally found indolent to symptomatic disease is unknown. There may be a substantial reservoir of small GIST tumors that do not progress to symptomatic stages. Complete surgical excision with clear margins offers the best curative intent. The use of adjuvant targeted therapy with C-kit inhibitor; Imatinib mesylate has increased the overall survival and progression free survival. The prognosis of GIST is dependent upon the size of the tumor, location and mitotic activity. Here we describe a series of cases of incidentally found GIST and their management [3].

CASE 1

A 38-year-old morbid obese female with an incident found GIST in the stomach following an elective laparoscopic vertical sleeve gastrectomy. Her past medical history included asthma, allergic rhinitis and obstructive sleep apnea. She was a non-smoker. Family history was significant for maternal aunt with breast cancer at the age of 56-years old.

Physical exam was unremarkable. Labs revealed mild anemia. The partial gastrectomy specimen consisted of the lateral margin of the stomach measuring 25 cm in length × 9.0 cm in circumference × 0.8 cm in wall thickness. The surface was smooth and glistening, and remarkable for one round, firm nodule 0.5 cm in diameter, located 1.0 cm from the stapled line. The specimen was longitudinally opened along the stapled line to reveal 60% tan mucosa, and 40% hemorrhagic mucosa, without lesions or masses. The intramural spindle cell lesion was consistent with a GIST, 0.3 cm in greatest dimension. The remaining oxyntic mucosa showed no specific pathologic change. Immunohistochemical stains showed strong and diffusely positive for DOG-1(+) and negative for smooth muscle actin (SMA) consistent with GIST.

Additional testing included ki67, mitotic figures, reconfirmation of negative margins, mutational analysis c-KIT (also called CD117, a receptor tyrosine kinase (RTK) expressed exon) and platelet-derived growth factor receptor alpha (PDGFR-alpha), endoscopic ultrasound, and CT chest, abdomen pelvis, and PET scan. The GIST was confirmed to be no more than 3 mm, completely excised with no mitotic figures seen. Mutational analysis showed mutational hot spots with surrounding negative exons for PDGFRA (exons 12, 14, 15, 18). Upper endoscopy/EUS confirmed the findings of the CT and PET scans, there were no other abnormalities. The GIST was an incidental finding, and no further treatment was needed.

CASE 2

A 69-year-old morbidly obese male presented with long-standing acid reflux refractory to dietary lifestyle changes. He underwent esophagogastroduodenoscopy (EGD) with random gastric biopsies showing evidence of mild chronic inactive inflammation and intestinal metaplasia. He was started on omeprazole twice daily with some improvement in symptoms. Repeat EGD and gastric biopsy five weeks later showed reactive gastropathy in a background of active chronic gastritis. *H. pylori* organisms were not present. Distal esophageal biopsy showed squamous esophageal and cardiac mucosa with chronic carditis with no intestinal metaplasia.

He then underwent elective sleeve gastrectomy for his obesity and associated refractory acid reflux. On pathologic examination of the gastrectomy specimen, there was a low-grade spindle cell type GIST with

negative margins and Ki67 <2%, oxyntic stomach with chronic inactive gastritis. The GIST was 0.6 cm in greatest dimension in the gastric fundus. It was unifocal, mitotic rate 0/5 mm^2, without necrosis, and histologic grade G1. The margins were uninvolved by the GIST. Immunohistochemical studies were positive for c-KIT, DOG1 (ANO1), and SMA weakly positive. Because nodal metastasis is so rare at diagnosis, the general consensus is nodal dissection is not necessary.

Additional testing to better evaluate the GIST consisted of reconfirmation of negative margins, c-KIT mutation analysis, and platelet-derived growth factor receptor alpha (PDGFR-alpha), EUS, CT chest, abdomen, pelvis, and PET scan. The GIST was confirmed to be no more than 0.6 cm in size; it was completely excised and had no mitotic figures. Mutational analysis showed mutational hot spots and surrounding exons for PDGFRA (exons 9, 11) were negative. There was no other abnormality by imaging.

DISCUSSION

GIST can be present anywhere in the GI tract but it is most commonly found in the stomach and small intestine and rarely on extra-visceral sites. Symptoms can vary upon location, size and growth rate. Small lesions usually asymptomatic are incidentally found as a result of imaging, endoscopy, pathologic specimens following surgery for another cause and post-mortem [4]. The natural history of these incidental tumors and the frequency of progression to symptomatic disease are unknown.

There may be a substantial reservoir of small GIST tumors that do not progress to symptomatic stages. In a series of 98 consecutive systematic autopsies on adults who died of unrelated causes revealed grossly recognizable gastric tumors, 22.5% of them were histologically confirmed to be GISTs. DNA analysis performed in 24 patients showed c-KIT mutations in 11 cases (46%) and PDGFRA mutations in 1 case (4%) [5,6].

Sporadic GIST tumorlets of the proximal stomach are common in the general population over the age of 50-years and frequently show somatic c-KIT mutations. GIST tumorlets probably represent the grossly recognizable counterpart of sporadic ICC hyperplasia caused by somatic c-KIT or PDGFRA mutations. Early hyalinization and calcification seem to confer limited growth potential, and complete regression of such lesions is common. GIST tumorlets likely represent preclinical (preneoplastic) lesions that need additional stimuli to evolve into clinical GISTs, raising the possibility of a hyperplasia-neoplasia sequence in the development of sporadic GISTs [7].

GIST should be included in the differential diagnosis of any intra-abdominal non-epithelial malignancy. Diagnostic interventions may include the following Computed tomography (CT), upper GI endoscopy, and 18F-FDG PET (fluorine F 18-fludeoxyglucose positron emission tomography). Endoscopic ultrasound with fine-needle aspiration biopsy is useful in the detection of GIST in the upper GI tract because most tumors arise below the mucosal layer and grow in an endophytic fashion [8].

Standard management of GISTs includes complete surgical resection followed by adjuvant imatinib as per current guidelines after risk assessment of the tumor. Because nodal metastasis is so rare at diagnosis there is general agreement that nodal dissection is not needed. High risk futures will need a closer follow up imaging (CT scan or PET/CT scan) every 3 months - 6 months as per current NCCN guidelines [9].

In summary, detailed understanding about GIST as a notable GI tract tumor is important in the treatment of this rare disease entity that is known to have a high recurrence

rate. Surveillance continues to be the key for early detection among patients with prior history.

REFERENCES

1. Agaimy A, Wünsch PH, Hofstaedter F, et al. (2007) Minute gastric sclerosing stromal tumors (GIST tumorlets) are common in adults and frequently show c-KIT mutations. The American Journal of Surgical Pathology 31(1): 113-120.
2. Sashidharan P, Matele A, Matele U, et al. (2014) Gastrointestinal stromal tumors: A case report. Oman Medical Journal 29(2): 138-141.
3. Morcos B, Al-Ahmad F (2011) A large gastrointestinal stromal tumor of the duodenum: A case report. Journal of Medical Case Reports 5(1): 1-3.
4. Franzini C, Alessandri L, Piscioli I, et al. (2008) Extra-gastrointestinal stromal tumor of the greater omentum: Report of a case and review of the literature. World Journal of Surgical Oncology 6(1): 1-5.
5. Poveda A, García Del Muro X, López-Guerrero JA, et al. (2017) GEIS guidelines for gastrointestinal sarcomas (GIST). Cancer Treatment Reviews 55: 107-119.
6. Lai EC, Lau SH, Lau WY (2012) Current management of gastrointestinal stromal tumors-a comprehensive review. International Journal of Surgery 10(7): 334-340.
7. Gold JS, DeMatteo RP (2006) Combined surgical and molecular therapy: The gastrointestinal stromal tumor model. Annals of Surgery 244(2): 176-184.
8. Nishida T, Blay JY, Hirota S, et al. (2016) The standard diagnosis, treatment, and follow-up of gastrointestinal stromal tumors based on guidelines. Gastric Cancer 19(1): 3-14.
9. Agaimy A, Wünsch PH, Hofstaedter F, et al. (2007) Minute gastric sclerosing stromal tumors (GIST tumorlets) are common in adults and frequently show c-KIT mutations. The American Journal of Surgical Pathology 31(1): 113-120.