Scholars Journal of Medical Case Reports

OPEN ACCESS

Abbreviated Key Title: Sch J Med Case Rep
ISSN 2347-9507 (Print) | ISSN 2347-6559 (Online)
Journal homepage: https://saspublishers.com/sjmcr/

Dual Pathology: Synchronous Existence of Gastrointestinal Stromal Tumour (GIST) of Stomach and Adenocarcinoma of Colon

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DOI: 10.36347/sjmcr.2020.v08i11.003 | **Received:** 23.10.2020 | **Accepted:** 06.11.2020 | **Published:** 09.11.2020

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Abstract **Case Report**

Gastrointestinal stromal tumor (GIST) is a rare cancer of the digestive reported about 0.1%–3.0% of all gastrointestinal neoplasms, 10% of small-bowel tumors, and 10%–15% of all sarcomas. Gastrointestinal Stromal Tumour (GIST) and it's coexistence with adenocarcinoma of colon is one of the rare event to occur and reported in Malaysia. Hereby, we reported a case of 70 years old lady presented with history of passing malaena. Esophagogastroduodenoscopy (OGDS) revealed mass at greater curvature of stomach. Biopsy reported as GIST. Subsequent Computed Tomography (CT) abdomen revealed incidental finding of circumferential bowel thickening at sigmoid colon, colonoscopy revealed circumferential mass at sigmoid colon, in which biopsy reported adenocarcinoma. Patient underwent sleeve gastrectomy and anterior resection however she developed complications from anastomotic leak and succumbed to her illness.

Keywords: Gastrointestinal Stromal Tumors, Adenocarcinoma, Neoplasms, Multiple Primaries.

INTRODUCTION

GIST are mesenchymal tumours arising from the interstitial cells of Cajal, can be present as a set of characteristic features including a spindle cell, epithelioid or, rarely, a pleomorphic morphology. Mutations in the genes for cKIT and platelet-derived growth factor receptor alpha were play a central role in the pathogenesis by tyrosine kinase activation.Co-existence of GIST with other neoplasm is rare. Thus early recognition and prompt diagnosis is needed before the initiation of treatment.

CASE REPORT

A 70 years old lady presented with history of passing out melaena. Oesophagogastroduodenoscopy (OGDS) revealed mass at greater curvature of the stomach with typical central umbilication of which histopathological examination (HPE) from biopsy confirmed as GIST. Subsequent Computed Tomography (CT) abdomen done showed large exophytic mass from greater curvature however incidentally there was evidence of circumferential bowel wall thickening at sigmoid colon, no distant metastasis noted.

We proceeded with colonoscopy revealed circumferential mass at sigmoid colon (30cm from anal verge) of which HPE later confirmed it as an adenocarcinoma.

Patient underwent sleeve gastrectomy and anterior resection in the same setting. Intraoperatively noted a mobile exophytic tumour at greater curvature over the proximal part of stomach and another mobile tumour at sigmoid colon, both showed no evidence of local infiltration. Post-operative HPE of both samples showed GIST of stomach with mitotic rate of 8/50 hpf and moderately differentiated adenocarcninoma of sigmoid colon with no nodal metastasis, pathologically staged as pT3, pN0. Both showed no evidence of lymphovascular or perineural invasion.

Post-operative patient was ventilated and monitored in our Intensive Care Unit (ICU) however on day 10 post operatively patient showed clinical evidence of anastomotic leak and thus underwent laparotomy. Intraoperatively noted there was a small leak about 0.5cm with faecal contamination at the colorectal anastomosis site. Anastomosis was repaired primarily and a diversion ileostomy was created for patient. Unfortunately post operatively patient developed multiorgan failure due to sepsis and patient was succumbed to her illnesses

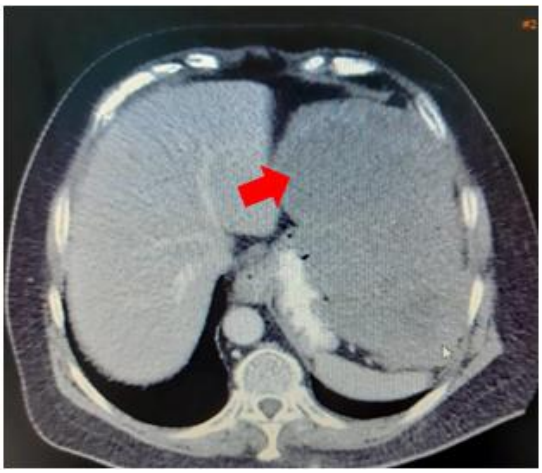

Fig-1: Axial CT scan showed large mass arising from greater curvature of stomach (18.2 x 9.5 x 11.1cm), displacing adjacent stomach, spleen and bowels. (Arrow)

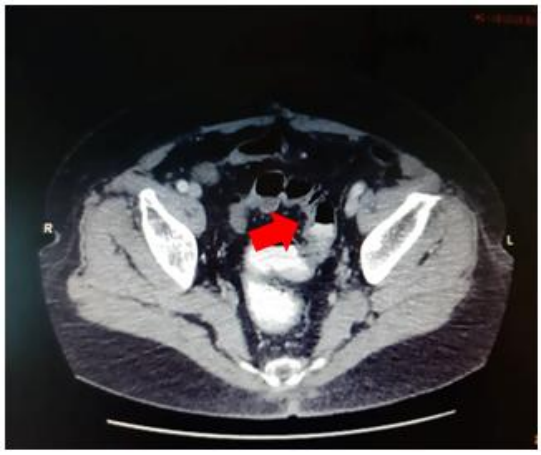

Fig-2: Incidental finding in CT presence of short segment circumferential bowel thickening at the sigmoid colon (arrow)

DISCUSSION

GIST is defined as cellular spindle cell, epithelioid, or pleomorphic mesenchymal tumour of the gastrointestinal (GI) tract. The term gastrointestinal stromal tumour (GIST) was introduced by Mazur and Clark in 1983 to differentiate GISTs from leiomyomas. The origin of these tumours is from the interstitial cells of Cajal, the GI pacemaker cells. Literature reported about 95% of GISTs are positive for expression of the KIT (CD117, stem cell factor receptor) protein and as well as 70-80% of GISTs expressing CD34, the human progenitor cell antigen [1].

Common presentations were gastrointestinal bleeding including either hematemesis, hematochezia, melena or a positive stool blood test (55.8%), abdominal pain (38.5%), weight loss, or a general feeling of weakness and dizziness (each 13.5%) [2].

In a single center retrospective studying association of GIST with other malignancies showed that carcinomas of the gastrointestinal tract were observed most frequently (52.6%). Others tumors of the urogenital tract (21.1%) and the mammary gland (18.4%). [2] The number and site of malignant neoplasia and comparison with other literatures are shown in Figure 3.

		Our cohort number of tumors, *n* (%)	Pandurengan et al. [1], 2010, *n* (%)	Agaimy et al. [41], 2006, *n* (%)
Carcinoma of the urogenital tract	All	8 (21.1)	62 (33)	111 (23)
	Prostate cancer	6 (15.8)	28 (15)	43 (9)
	Kidney cancer	1 (2.6)	12 (6.5)	27 (6)
	Urothelial cancer	1 (2.6)	7 (3.8)	10 (2)
Carcinoma of the gastrointestinal tract	All	20 (52.6)	48 (26)	228 (47)
	Colorectal cancer	10 (26.3)	18 (9.7)	109 (22)
	Pancreatic cancer	3 (7.9)	5 (2.7)	11 (2)
	Gastric cancer	6 (15.8)	5 (2.7)	95 (19)
	Gallbladder cancer	1 (2.6)	1 (0.5)	4 (1)
Breast cancer		7 (18.4)	15 (8)	34 (7)
Hematologic neoplasia	Lymphoma/ leukemia	2 (5.3)	12 (6.5)	36 (7)
Malignant peripheral nerve sheath tumor		1 (2.6)	NA	NA
Total number of additional malignancies		38 (100)	186 (100)	518 (100)

Fig-3: Aghdassi et al. 2018 comparing secondary maglinancies reported in GIST with other literatures

Meanwhile other case studies of 86 patients with GIST in a centre at Germany showed that thirty-seven patients (43%) were identified with non-GIST malignancy. 13.5% of them (5 of the 37 patients) suffered from more than one other malignancy in addition to GIST. Commons site reported for localisation of GIST was the stomach (24 cases, 65%) followed by the small intestine (11 cases, 30.6%), oesophagus (1 case, 2.7%) and rectum (1 case, 2.7%) [3].

The concurrence of GIST with other neoplasms posed a dilemma in studying such occurrence. Either it was coincidental or whether both

are relatively related to each other. However, less known about the etiology of this event.

In a study, Au et al. proposed that the coexistence of a GIST with renal papillary carcinoma may result from mutation of protooncogenes coding tyrosine kinases, c-KIT and c-MET, respectively [4]. This phenomenon also reported to be observed in case of multiple endocrine neoplasia (MEN 2A) of which there is analogous c-RET protooncogene mutation. Relation between frequent c-KIT and c-MET coexpression in solid tumour suggest there are common regulatory mechanim coexist each other [4].

Another study in a centre of 25 patients with small cell lung cancer (SCLC) showed about 88% of their patient (22 out 25 patients) existence of coexpression between c-MET and c-KIT mRNA in SCLC [5].

In term of treatment, surgery remains the main therapy for both non-metastatic GISTs and colorectal cancer (CRC), it might differ from the operative strategies and extents of resection. In case of GIST, routine lymphadenectomy is not routinely recommended due to its rarity in lymph node involvement. In contrast, in case of CRC, curative resection requires the inclusion of lymphatic dissection as well adequate margins dissection [6].

As far it was, conventional chemotherapy and radiation appear to have no effect on the natural history of GISTs. Main focus of treatment is toward molecular targeting; imatinib mesylate. Imatinib is one of a selective tyrosine kinase competitive inhibitor that appears to be an effective drug in treatment of GIST.

In other hand, no evidence stating the role of Imatinib mesylate in the treatment of CRC, the lack of evidence might contribute from the lacking role of c-Kit in the pathogenesis of CRC and the rarity of c-Kit mutation in these tumour of which does not support the use of Imatinib in treatment of CRC.

There are lack of data and studies relating the concurrent treatment of imatinib mesylate in GIST with chemotherapy and radiotherapy for CRC. As for our patient, we were unable to do follow up treatment as patient succumbed to her illnesses post operatively before starting adjuvant treatment.

There was a case report regards of concurrent treatment of imatinib mesylate and chemotherapy regime – FOLFOX in combination with dexamethasone showed there were no side effects occurred in the case. One of the possibilities reported is that due to the drug interaction. Imatinib plasma concentration may decrease when administered with dexamethasone [1].

CONCLUSION

Here we reported a case of synchronous existence of GIST with colorectal adenocarcinoma of which rarely to be reported in Malaysia. Synchronous existence of GIST with other malignancies remains a challenge in term of diagnosing, surgery and follows up treatment. It required a prompt and timely diagnosis before initiating the treatment. More valuable data and studies should be carry out in order to obtain optimal data in treating synchronous existence of GIST with other type of malignancies.

ACKNOWLEDGEMENT

The authors would like to thank the Director General of Health, Malaysia for permission to publish this case report.

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