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EPIDEMIOLOGICAL AND CLINICO-PATHOLOGICAL ANALYSIS AND OUTCOMES OF EXTRA-INTESTINAL GIST AT A TERTIARY CARE HOSPITAL IN SOUTH INDIA

Surgery

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ABSTRACT

INTRODUCTION: Extraintestinal GIST (EGIST) is a rare mesenchymal tumor. There is lack of sufficient literature regarding EGISTs. We have undertaken a retrospective observational study to analyze the epidemiology, clinicopathological features and outcomes of EGISTs.
METHODS: All patients with the diagnosis of EGIST in the department of Surgical Gastroenterology, SVIMS from January 2015 to December 2019 were included. Patient's demographics, laboratory and imaging findings, intra-operative findings, tumor pathology and outcomes were analyzed.
RESULTS: Fourteen patients were included. Of these, 8 (57.14%) were males. Mean age was 53.43 years. Most patients (85.71%) presented with abdominal pain. Most common site of EGIST was retroperitoneum (50%). Preoperative imaging was diagnostic of GIST of gastro-intestinal origin in all patients. 71.43% tumors were >10cm in size and 50% had >10 mitotic index. Twelve patients underwent radical surgery. All were advised adjuvant therapy. Mean hospital stay was 7.07 days. Median survival was 38.5 months (range 4-60 months).
CONCLUSION: EGISTs are more likely to be malignant, large in size, with high mitotic rates. Imaging may not be accurate for diagnosis. Owing to low incidence of EGISTs, multi-center studies are required to study their clinical and pathological behavior.

KEYWORDS

Extraintestinal GIST, EGIST, mesenchymal tumors

INTRODUCTION

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors of the gastrointestinal tract. They represent 1-2% of all GI tumors(1). Rarely GIST may arise outside gastrointestinal tract as primary tumor, which is called as Extraintestinal GIST (EGIST). EGISTs can arise from mesentery, omentum, retroperitoneum, liver or pancreas(2).

It is hypothesized that these tumors originate from common precursor cells as GISTs, which differentiate into the Interstitial Cells of Cajal (ICC) type cells outside the gut wall(3). Due to the rarity of EGISTs, the epidemiology, presentation and pathology of such tumors are not well defined. In this retrospective study, we analysed 14 cases of EGIST for clinicopathological findings with correlation of operative findings.

MATERIALS AND METHODS

All patients with a definite histopathological diagnosis of EGIST, in the Department of Surgical Gastroenterology, SVIMS, from January 2015 to December 2019, were included in this retrospective observational study. Retrospective analysis of patient's demographics, laboratory and imaging findings, intra-operative findings, tumor pathology and outcomes were analyzed.

RESULTS

A total of 14 patients of EGIST were included in the study. Mean age at presentation was 53.43 ± 13.15 (Range 33 to 77 years). Eight (57.14%) patients were males.

Most of the patients (12, 85.71%) presented with pain abdomen, followed by palpable lump abdomen (8, 57.14%). Majority were not having any comorbidities, with only 1(7.14%) patient being hypertensive. Ten (71.43%) patients had tumors of more than 10 cm at the time of presentation.

Table 1: Clinicopathological Characteristics Of EGISTs

Characteristics	Parameters	
Age	≤60	11(78.57%)
	>60	3(21.42%)
Gender	Male	8(57.14%)
	Female	6(42.86%)
Symptoms	Abdominal pain	12(85.71%)
	Abdominal mass	8(57.14%)
	Abdominal distension	3(21.43%)
Surgical resection	Complete resection	12(85.71%)
	No surgery	2(14.29%)
Tumor size	<10cm	4(28.57%)
	>10cm	10(71.43%)
Mitotic index	≤5	1(7.14%)
	>5 & ≤ 10	6(42.86%)
	>10	7(50.00%)
Neoadjuvant therapy	Yes	4(28.57%)
	No	10(71.43%)
Adjuvant therapy	Yes	10 (71.43%)
	No	4 (28.57%)

Majority of the EGISTs were located in retroperitoneum (7, 50%), followed by pancreas (3, 21.43%). Other locations were omentum, small bowel mesentery and transverse mesocolon.

Table 2: Location Of EGISTs

Location	Parameters
Retroperitoneum	7 (50.00%)
Pancreas	3 (21.43%)
Small bowel mesentery	2 (14.29%)
Transverse mesocolon	1 (7.14%)
Greater Omentum	1 (7.14%)

All patients were nutritionally well preserved at the time of presentation, with mean haemoglobin of 12.81 ± 1.69 gm/dl and mean albumin of 3.79 ± 0.43 gm/dl.

Preoperative imaging was diagnostic of GIST in all of the patients, but incidentally, all tumors were reported to be originating from the gastrointestinal tract.

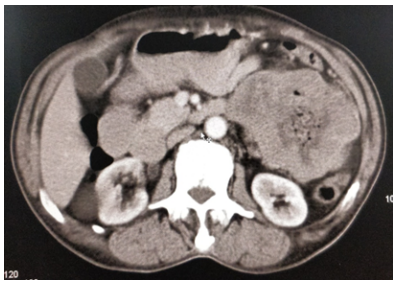

Image 1: CT Scan Showing Egist Of Distal Pancreas

Out of 14 patients, 10 (71.43%) underwent upfront radical surgery. Four (28.6%) patients were subjected to neoadjuvant Imatinib after pathological confirmation as they were locally advanced. After neoadjuvant treatment, 2 (14.29%) patients underwent radical resection. The remaining 2 (14.29%) patients expired during chemotherapy and within 6 months of diagnosis. Of the 12 (85.7%) patients who underwent surgery, 1 (7.15%) patient underwent multi-visceral resection, 2 (14.29%) patients underwent distal pancreatectomy with splenectomy, 1 (7.15%) patient underwent Whipple's pancreaticoduodenectomy and the rest underwent radical resection of tumor masses.

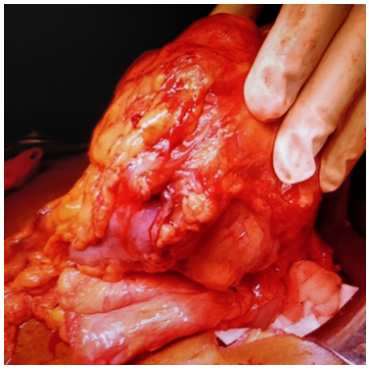

Image 2: Intra-operative Photo Of Distal Pancreas Egist

Postoperative course was uneventful in 10 (71.43%) patients. One (7.15%) patient who underwent multivisceral resection had delayed gastric emptying and 1 (7.15%) patient had surgical site infection. Mean hospital stay was 7.07±1.44 days. There was no post-operative mortality.

All 12 patients who underwent surgery were started on adjuvant chemotherapy. Two patients were lost to follow-up. Median survival was 38.5 months, with a range of 4 to 60 months.

DISCUSSION

EGISTs are defined as tumors identical phenotypically to gastric (classical) GIST, both by clinicopathological features and by molecular characteristics, but originating outside the GIT(4). They comprise about 5-10% of all GISTs. It has been suggested that EGISTs originated from a common precursor that differentiated into ICC-like cells outside of the GIT(3). In the study by Cho et al(5), the most common site for EGISTs was found to be mesentery (45.1%) followed by intra-abdominal (34.3%), pelvis (9.8%), retroperitoneum (3.9%) and abdominal wall (3.9%). EGISTs have also been found to originate from pancreas, gall bladder, pharynx, myocardium, mediastinum, urinary bladder(3), and female reproductive system including vulvo-vaginal and recto-vaginal septae(6). Even though pancreas is a very rare site of EGIST in literature, we had 3 (21%) patients with EGIST arising from pancreas, all diagnosed on post-operative histopathology.

EGISTs have generally been found to occur in younger age groups compared to classical GISTs. In the current study, the mean age at presentation was 53.4 years, which was lower than that in Western studies but higher than in another Indian study by Vij et al which included all types of GIST (50.4 years)(7). There was a male preponderance in our study. However, various studies show different ratios of gender distribution.

	Current study	Reith et al(8)	Yamamoto et al(9)	Feng et al(1)
Mean age	53.4	58	59	57
Male distribution	57.14%	33.33%	38.46%	51.2%
MC symptom – Abdominal pain	85.71%	NA	NA	27.8%
Tumor size ≥10cm	71.43%	77.08%	76.92%	63.4%
Complete resection	85.71%	NA	NA	91%
Mitotic Index ≥5	92.86%	40.62%	56.41%	58.8%
Neoadjuvant therapy	28.57%	NA	NA	NA
Adjuvant therapy	71.43%	NA	NA	61%

Earlier, most EGISTs were identified clinically as abdominal lumps or diagnosed radiologically as GIST of intestinal origin or underwent exploratory surgery for undiagnosed masses, and were all later identified retrospectively as being EGISTs. With current imaging modalities like multi-detector CT scan and PET-CT, EGISTs are being diagnosed in the pre-operative stage more frequently. The 'Embedded Organ sign' is a useful sign to identify the site of origin of GIST on CT scan(10).

As seen both in the current study and earlier studies, most of the EGISTs are diagnosed late and most of them measure more than 10cm at the time of diagnosis itself. But unlike GISTs, the tumor size is not a reliable prognostic parameter in EGISTs and it has been noted that tumor size has different clinical implications at different anatomical sites(4). Hence, the original tumor location should be taken into consideration along with the tumor size and mitosis to classify the risk of malignancy or recurrence. The study by Cho et al has proposed that male gender, age and stage should be also considered as factors for risk stratification of EGISTs, along with tumor necrosis, mucosal and vascular invasion. This study has also shown that EGISTs are more likely to be malignant and have higher risk of recurrence as per NIH grading, when compared to classical GISTs(5).

Surgery gives the best chance of cure for GISTs at any location. However, as EGISTs are usually diagnosed later in the disease process with larger tumor size, higher mitotic rate and local infiltration to adjacent organs, it has been advised that EGISTs if diagnosed preoperatively, be given neoadjuvant therapy with Imatinib for 6 to 12 months, though there are no randomized trials regarding the same. NCCN guidelines recommend tumor biopsy for confirmation of the diagnosis before initiating Imatinib treatment(10–12). 4 (28%) of our patients were given neoadjuvant therapy after diagnosing advanced EGIST by imaging and biopsy. Most studies show less than 10% partial pathological response and less than 1% complete response with neoadjuvant Imatinib(12).

In spite of complete surgical resection, most studies have shown that overall survival for EGISTs is lower than that of classical GISTs due to unfavorable prognostic factors, such as tumors of large size, higher mitotic index, higher incidence of lymph node or distant metastasis. However, the recurrence-free survival was similar with both GISTs and EGISTs(3).

Adjuvant therapy for EGIST has been advocated on similar lines to conventional GIST, though it is not supported by sufficient evidence. EGISTs need to be followed up rigorously as most recurrences occur within first two years of primary surgery. In low-risk patients, an annual CT is recommended for 5 years, and in high risk patients and those on adjuvant therapy, CT is done every 6 months. Once Imatinib is stopped, CT is repeated every 3-4 months for the first 2 years and every 6-12 months for 10 years.

In conclusion, EGISTs are usually large in size at diagnosis, with high mitotic rates, and higher risk of malignancy. Most cases detected in the fifth decade with probable male preponderance. They may be asymptomatic for longer times, thus being advanced at the time of diagnosis. Cross-sectional imaging may not be accurate in diagnosing the site of origin. Pre-operative tumor biopsy and neoadjuvant therapy are recommended for locally advanced tumors. Adjuvant therapy is recommended for all EGISTs. Owing to the low incidence of these tumors, multi-center studies will be beneficial in identifying true epidemiological trends, in ascertaining benefit of neoadjuvant and adjuvant therapy, and to study the biology of EGISTs at different locations.

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