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Gastrointestinal Stromal Tumor of the Ampulla of Vater: A Narrative Review

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Abstract

Background: Gastrointestinal stromal tumor (GIST) of the ampulla of Vater is a rare occurrence. To the best of our knowledge, there has been no published review on this rare tumor in the English literature so far. ***Summary:*** In this review, we will discuss all the reported details of the published cases, including demography, clinical presentation, imaging, gross pathology and histopathology, immunohistochemical findings, treatment modalities, and outcome of cases with the diagnosis GIST from the ampulla of Vater in the last 20 years. ***Key Message:*** Twenty-five cases of GIST in the ampulla of Vater have been reported in the last 20 years in the English literature. GIST in the ampulla of Vater are usually small tumors (<5 cm) in middle-age patients. The majority of the patients present with lower GI bleeding and abdominal pain. Imaging findings are not characteristic, and most of the patients without biopsy and with no histologic diagnosis were operated with the primary impression of adenocarcinoma, neuroendocrine tumor, and GIST. Perioperative tissue biopsy has been accurate in <70% of the cases. The majority of the reported cases of GISTs in the ampulla of Vater have been low risk with spindle-cell morphology, low mitotic figures, and minimal atypia; reactive for C-KIT and DOG-1; and nonreactive for SMA, desmin, and S100. In the majority of the cases, duodenectomy with or without Whipple's operation has been performed, and most of the cases showed good prognosis.

Introduction

Gastrointestinal stromal tumors (GISTs) are uncommon tumors of the gastrointestinal tract accounting for 1% of all gastrointestinal neoplasms. GISTs are mainly located in the stomach, and duodenal location is rare, accounting only for <4% of all cases. Occurrence of GIST in the ampulla and periampullary region is even more uncommon [1].

To the best of our knowledge, 25 cases of ampullary GIST have been reported in the English literature so far. In this manuscript, we will review the clinicopathologic findings of all the reported ampullary GISTs [1–22].

Materials and Methods

Published case reports and case series in the English literature have been collected by searching in PubMed, Google, and Google Scholar in the last 20 years. The keywords for searching were "Am-

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Table 1. Demographic findings and survival of the reported ampullary GISTs

	Author	Sex/age, years	Clinical presentation	Positive laboratory findings	Tumor size, cm	Mitotic count, /50 HPF	Risk assessment	Surgical procedure	Survival
1	Kocer et al. [1]	M/44	Weight loss	–	9	30	High	Whipple	Disease free after a year
2	Chariyawong and Rakvit [2]	F/65	Lower GI bleeding	–	2.3	1	Low	Sleeve duodenectomy	NR
3	Mou et al. [3]	M/56	Bloating	–	1.6	<3	Low	Endoscopic mucosal dissection	Disease free after 3 months
4	Kwon et al. [4]	M/49	Incidental	–	2.3	nr	Low	Whipple	Alive with no recurrence
5	Aksoy et al. [5]	F/41	Jaundice	Anemia High ALP	1.5	nr	Low	Whipple	nr
6	Marano et al. [6]	F/49	Lower GI bleeding	High ALP	6	nr	High	Robotic resection	Disease free after 4 years
7	Filippou et al. [7]	F/65	Jaundice	High AST, ALT, ALP	5	High	Intermediate	Local resection	Disease free after 2 years
8	Thavaraputta et al. [8]	F/44	Abdominal pain	High ALP	0.4	nr	Low	Whipple	Disease free after 12 months
9	Rotundo and Ahlawat [9]	M/63	Lower GI bleeding	Anemia	2	nr	Low	Resection	nr
10	Behranwala et al. [10]	M/57	Jaundice	Anemia	3.3	5	Low	Whipple	Recurrence after a year
11	Matsushita et al. [11]	M/44	Jaundice	–	8	90	High	Liver transplantation	Liver metastasis, died after 2 months
12	Leung et al. [12]	F/54	Lower GI bleeding	Anemia	3	0	High	Local resection	Recovered well
13	Liao et al. [13]	F/63	Abdominal pain	–	5	20	High	Liver transplantation	Disease free after 13 years, then developed liver metastasis
14	Bagchi et al. [14]	M/48	Jaundice	Anemia	8.8	>10	High	Whipple	Disease free after 7 months
15	Morcos and Al-Ahmad [15]	F/38	Abdominal pain	Anemia	22	1	High	Whipple	Disease free after 34 months
16	Moss et al. [16]	M/57	Lower GI bleeding	Anemia	2.6	4	Low	Whipple	Alive with no recurrence
17	Mouaqit et al. [17]	F/37	Abdominal pain	–	7	nr	High	Whipple	Alive with no recurrence
18	Candanedo-Gonzalez et al. [18]	F/61	Abdominal pain	Anemia	3	0	Low	Whipple	Disease free after 6 months
19	Kim et al. [19]	F/37	Lower GI bleeding	Anemia	5.5	5	Low	Whipple	nr
20	Onal et al. [20]	F/44	Lower GI bleeding	–	2	nr	nr	Surgical resection	nr

Table 1 (continued)

	Author	Sex/age, years	Clinical presentation	Positive laboratory findings	Tumor size, cm	Mitotic count, /50 HPF	Risk assessment	Surgical procedure	Survival
21	Choi et al. [21]	F/54	Lower GI bleeding	Anemia	2.2	1	Low	Partial sleeve duodenectomy	Alive with no recurrence
22		F/67	Lower GI bleeding	–	3.3	1	Low	Partial sleeve duodenectomy	Alive with no recurrence
23		M/28	Lower GI bleeding	–	5.2	2	Intermediate	Partial sleeve duodenectomy	Alive with no recurrence
24		M/61	Lower GI bleeding	–	2.3		Low	Partial sleeve duodenectomy	Alive with no recurrence
25	Kobayashi et al. [22]	M/36	GI bleeding	Anemia	2.2	0	Low	Whipple	Disease free after 1.5 years

GIST, gastrointestinal stromal tumor; ALP, alkaline phosphatase; nr, not reported.

pulla of Vater," "Periampullary," "Ampullary," "Duodenum," "Small intestine," and "Gastrointestinal stromal tumor."

It is worthy to note that the included studies have specifically mentioned the presence of tumor in the ampullary or periampullary region. Twenty-five cases were found in the English literature.

Results

Tables 1 and 2 show the clinicopathologic characteristics of these 25 reported and published cases with ampullary GIST in the English literature [1–22].

Demographic Findings

Fourteen patients were female, and 11 were male (male/female = 11/14). The age range was 28–67 years with a mean of 50.5 [1–22].

Clinical Presentation

The majority of the patients presented with lower GI bleeding either as fresh rectal bleeding or melena. One of these patients presented with unconsciousness secondary to low blood pressure and GI bleeding [22]. Other symptoms were abdominal pain in 6 and jaundice in 5 patients. Other rare gastrointestinal symptoms were also reported such as bloating [3] and weight loss [1] as the primary clinical presentation [3]. One of the patients was incidentally found during investigation and follow-up of gastric adenocarcinoma [4].

Table 2. Summary of the clinicopathologic findings of the 25 reported cases of ampullary GIST

Clinicopathologic findings	
Sex (F/M)	14/11
Age, years	28–67 (50.5±10.7)
Most common clinical presentation	Lower GI bleeding (44%)
Most common laboratory finding	Anemia (24%)
Tumor size, cm	1.5–22 (4.7±4.2)
Mitotic counts, /50 HPF	0–100 (15.4±30)
Most common risk group	Low (60%)
Outcome	Alive with no recurrence and no metastasis after 6 months to 13 years (2.3±3.4 years)

GIST, gastrointestinal stromal tumor.

Laboratory Findings

In the majority of the patients, laboratory tests were normal, except for anemia which was the most common abnormal laboratory finding. Rare isolated reports of abnormal liver function tests and elevated bilirubin, especially high alkaline phosphatase, were also reported [5–8].

Past Medical History and Other Medical Conditions

History of neurofibromatosis type 1 was reported in 3 patients [8–10]. One of the patients with neurofibroma-

tosis and ampullary GIST had also celiac disease and pituitary adenoma [8]. Gastric cancer has been reported in 2 patients; in one, it was found 2 years prior to ampullary GIST diagnosis [4] and in the other, both GIST and gastric cancer were simultaneously diagnosed [7]. In another case, adenocarcinoma of the ampulla of Vater was reported [1]. Also, one of the patients was diagnosed to have pancreatic ductal adenocarcinoma at the time of diagnosis of GIST in the ampulla of Vater [10]. In 2 of the reported cases, simultaneous duodenal neuroendocrine tumor was also diagnosed within the duodenum [1, 8]. Another patient had a past medical history of diverticulitis [2]. Family history in the case report by Leung et al. [12] was positive for breast cancer, colon cancer, coronary artery disease, and stroke. The patient had a history of hypertension, tachycardia, and anxiety disorder.

Imaging Studies

In >20 reported cases of ampullary GIST, imaging studies were reported, consisting of ultrasonography, CT scan, and MRI. The most important imaging finding was common bile duct and/or pancreatic duct dilatation. In ultrasonography, GISTs in the ampulla are hypoechoic masses. CT scan of the mass reported hypervascular uniformly or peripherally enhanced masses with or without central necrosis. Ampullary GIST is reported as a well-defined mass with pushing border and indentation of adjacent organs without significant invasion. MRI of ampullary GIST has been reported to show low signal intensity on T1-weighted images and high signal intensity on the T2-weighted image [7–15].

Main differential diagnosis by imaging modalities is adenocarcinoma of the ampulla of Vater or pancreatic ductal adenocarcinoma in the pancreatic head. The only way for the best diagnosis is histology and biopsy before surgery [10–15].

Endoscopic Findings

In 16 cases, endoscopic findings have been reported as round to oval submucosal or subserosal mass or masses with overlying mucosal ulceration arose from the duodenal wall, without intraluminal projection. Some tumors showed minimal invasion to the adjacent pancreatic head as well [11, 16].

In 8 cases, presurgical biopsies have been taken which was correctly diagnosed in 5 patients [1, 2, 7, 12, 17], and other 3 cases were either nondiagnostic (normal mucosa) or incorrectly diagnosed as carcinoma [2, 16, 17]. In most of the patients without perioperative histology, the clinical impression has been carcinoma of the ampulla of Vater/head of pancreas, neuroendocrine tumor, and GIST.

Microscopic Findings

Twenty-one out of 25 reported cases of GISTs in the English literature showed pure spindle-cell morphology with fascicular and storiform patterns. Only 4 cases showed focal epithelioid morphology [1, 7, 18, 20]. Skenoid fibers were reported in 2 cases [15, 18]. In the case reported by Candanedo-Gonzalez et al. [18], focal collections of skenoid fibers with osteoid-like material and focal aneurysmal bone cyst-like areas were seen. Six ampullary GISTs reported to have bizarre and atypical spindle-shaped cells [1, 7, 11, 14, 20].

Most of the reported cases of ampullary GIST are categorized as low risk, that is, the number of mitosis was low (<5/50 HPF), and the tumors were mostly small (<5 cm). Only 5 cases have been reported with large size, that is, >5 cm [1–22].

The main differential diagnosis in these cases is spindle-cell tumors of the gastrointestinal tract, mostly schwannoma, leiomyoma, leiomyosarcoma, malignant peripheral nerve sheath tumors, and desmoid tumors. Immunohistochemistry can be helpful for the definite diagnosis [10–21].

Immunohistochemistry and Molecular Studies

All the reported GISTs in the ampullary lesion were reactive with CD34. CD117 was negative in 2 cases [2, 15]. Also, all of the reported DOG-1 were positive. Smooth muscle actin has been stained in 9 cases, and 7 of them (77.8%) were negative and 2 were positive [13, 20]. Desmin has been stained in 6 cases; only one has been positive, and all the other 5 cases were negative [13].

In 8 out of 9 cases with reported S100, the antibody was nonreactive, and in only 1 case, S100 was positive [15]. In Liao et al.'s [13] case, they have done genetic studies, and the tumor showed KIT N822K gene mutation in exon 17.

Treatment

In 13 patients, Whipple's operation was performed. In 4 patients, duodenectomy and resection were done [7, 9, 12, 14]. In 5 patients, sleeve duodenectomy was the procedure [2, 21]. Two patients developed liver metastasis, and liver transplantation and Whipple were the procedures to resect the tumor and the metastasis [11, 13].

In only 1 case endoscopic mucosal dissection was done to resect the tumor [3]. In 1 case, duodenal sparing robotic resection has been performed [6]. All of the above surgical procedures have been performed in association

with imatinib (tyrosine kinase inhibitor) administration [1–22].

Outcome

Liver metastasis has been reported in 2 ampullary GISTs [11, 13]. Also, lymph node metastasis has been reported in 1 case [11]. In 1 patient, local recurrence was developed [10]. All of the other 21 patients were free of any recurrence or metastasis.

Conclusions

Ampullary GIST is a rare tumor, mostly present with lower GI bleeding and small size. The imaging in this tumor is not specific, and perioperative biopsies are not so accurate (because of the submucosal location). The majority show low mitoses and are reactive with C-KIT and DOG-1. Ampullary GISTs can be treated effectively with imatinib and surgical resection. Findings of GIST in the ampulla of Vater are very similar to our previous experiences in regard to the demographic findings, pathologic characteristics, and outcome [23–25].

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Bita Geramizadeh: idea of the project, searching the literature, and writing the manuscript. Alireza Shojazadeh: searching the literature and writing the manuscript.

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