Gastrointestinal stromal tumor (GIST) is the most common mesenchymal tumor in human gastrointestinal (GI) tract, which is considered to arise from the interstitial cells of Cajal (ICC) [10]. Gain-of-function mutation of the receptor tyrosine kinase (RTK) gene, KIT, a stem cell factor receptor, plays a crucial role in the oncogenesis of most GISTs [6]. In this content, 65–80% of GISTs have KIT gene mutation, and the other, approximately 10% of KIT-negative GISTs have activating mutation in the gene of platelet-derived growth factor receptor α (PDGFRα)[9]. The mutation of KIT/PDGFRα may contribute to the occurrence and development of GIST by leading to the activation and autophosphorylation of the downstream signaling pathways [28].

GIST accounts for nearly 2.2% of GI malignancies [35]. Notably, approximately 60–70% of GIST occurs in the stomach, followed by 20–30% in small intestine, 5% in the colon and rectum, and 5% in the esophagus [44]. However, primary GIST can also arise in the following uncommon sites other than GI tract: mesentery, omentum, or retroperitoneum [27], and sporadically in the pancreas [42], gallbladder [30], and liver [13].
nongastrointestinal tumors are defined as extragastrointestinal stromal tumors (EGIST).

The GIST arising in liver as a primary lesion is extremely rare, and thus, reports on hepatic GIST and its clinicopathological features as well as clinical outcomes are limited. Therefore, this study was designed to evaluate the clinicopathological features and prognosis of primary hepatic GIST in order to achieve the optimal treatment strategy.

Materials and Methods

One case of hepatic GIST, which was the only case from May 2010 to March 2015 in our center, and 22 cases of hepatic GIST reported in the literature were enrolled into this study. Literature published from 2001 to 2015 was searched in the databases of MEDLINE and China National Knowledge Infrastructure (CNKI). We found 12 cases of hepatic GIST in English [1, 3, 13, 18, 20–22, 24, 25, 29, 36, 45] and additional 10 cases in Chinese [2, 12, 14, 23, 31, 38–41, 43] by literature search. In addition, clinical and pathological characteristics as well as prognosis of hepatic GIST were compared with those of gastric and small intestinal GIST. All 297 cases of gastric GIST and 59 cases of small intestinal GIST were diagnosed and treated in our center from 2001 to 2015. This study was approved by the Ethics Committee of Xijing Hospital, and written informed consents were obtained from the patients.

The following clinical and pathological data were collected: age, gender, symptoms, primary tumor site, size of the tumor, CT enhancement, tumor size, surgical intervention, histological cell types, mitotic index, Ki-67 expression, gene mutation status, National Institutes of Health (NIH) classification, adjuvant imatinib mesylate therapy, and survival. The GISTs were classified as very low, low, intermediate, and high risk following the modified protocol of NIH risk classification reported by Joensuu et al. [17].

For survival analysis, the exclusion criteria were as follows: (1) GIST in the organs other than hepatic GIST; (2) Patients suffered from other type of malignant tumors in addition to hepatic GIST; (3) Patients had distant metastasis; (4) Patient had tumor rupture during operation; (5) Patient had received neoadjuvant imatinib mesylate therapy; (6) Patient did not receive R0 resection; (7) Patients failed to have follow-up data.

Data was processed using SPSS 22.0 for Windows (SPSS Inc., Chicago, IL). Numerical variables were expressed as mean ± SD. Discrete variables were analyzed using the chi-square test or Fisher’s exact test. Risk factors for survival were identified by univariate analysis and COX regression was employed for multivariate analysis. Disease-free survival (DFS) and disease-specific survival (DSS) were analyzed by the Kaplan–Meier method and differences between the curves were compared using log-rank test. 

Results

General features of the hepatic GIST

Clinical and pathological features of hepatic GISTs are summarized in Table 1. Of the 23 cases, 12 were male (52.2%) and 11 were female (47.8%), and aged from 17 to 79 years (median, 55 years; mean, 52 years). The most common symptom was abdominal discomfort (12/21, 57.1%), followed by abdominal pain (9/21, 42.9%), abdominal mass (5/21, 23.8%), anorexia (3/21, 14.3%), bleeding or anemia (1/21, 4.8%), weight loss (1/21, 4.8%), and other symptoms including dyspnea, fatigue, constipation, vomiting, and abdominal distension (12/22, 54.5%). Incidence of hepatic GIST was higher in the right lobe (10/21, 47.6%) than that in the left lobe (7/21, 33.3%). Majority of the tumors (11/12, 91.7%) were displayed as low density by regular CT examination, followed by light (7/12, 58.3%), moderate (3/12, 25.0%), or high (2/12, 16.7%) density, respectively. Sixteen patients (16/23, 69.6%) underwent complete surgical resection, six patients (6/12, 50%) received imatinib therapy after surgery, one patient was treated with imatinib therapy only, and one patient received radiofrequency ablation therapy.

Size of the tumors ranged from 4.3 to 44.0 cm in diameter (median, 15.0 cm; mean, 14.6 cm). Mitotic index was over 5/50 HPF in 12 out of 16 patients (75.0%) and Ki-67 expression was detected at least in 5% of the cells in all six of the patients (100%) who received Ki-67 examination. Out of 25 hepatic GIST specimens, spindle cell morphology was observed in 18 (85.7%) of them, and mixed morphology in three of the tumor specimens (12.0%) was observed.

Positive CD117 expression in 23 out of 23 (100%) specimens, positive CD34 expression in 11 out of 19 (57.9%) specimens, positive DOG-1 expression in five of six (83.3%) specimens, positive expression of vimentin in nine out of 10 (90.0%), and positive SMA expression in five out of 17 (29.4%) specimens were observed. Genomic mutation was examined in four specimens, and KIT mutation at exon 11 was found in two of the four specimens, while the rest two specimens were without any significant gene mutation. Twenty-two patients were classified as high risk (22/22, 100%) by the NIH risk classification.

Survival of hepatic GIST

Survival data of hepatic GISTs were analyzed and summarized in Table 2. By the inclusion/exclusion criteria, P values were considered to be statistically significant at the 5% level.
described in the methods, the survival rate was analyzed in 11 hepatic GIST patients with range of follow-up from 4 to 108 months (mean, 27.1 months; median, 13 months). Of the 11 cases, two patients had recurrent hepatic GIST and two patients had metastatic GIST in the organs other than liver, three patients died from hepatic GIST. The 5-year median DFS time was 24 months and 5-year DSS rate was 33.3%, respectively.

Comparison among hepatic, gastric, and small intestinal GIST

Next, clinical and pathological feature of 23 hepatic GISTs were compared with that of 297 gastric GISTs and 59 small intestinal GISTs (Table 3). The results showed that tumor size, mitotic index, NIH risk category, and adjuvant therapy were significantly different between hepatic and gastric GISTs (all \( P < 0.05 \)), that is, incidence of tumors with larger size or high-risk tumors was significantly higher in hepatic GIST group compared to that in gastric GIST group. Hepatic GIST group also showed larger size, higher mitotic index, and higher risk category of NIH in comparison with those of small intestinal GIST group (All \( P < 0.05 \)).
In order to analyze the prognosis among hepatic, gastric, and small intestinal GISTs, survivals of 11 hepatic GISTs were compared to those of 217 gastric GISTs and 59 small intestinal GISTs which were enrolled in our center and have complete follow-up data. The results showed that the DFS (5-year median survival time: 24 months vs. 25 months, \( P < 0.001 \), Fig. 1) and DSS (5-year survival rate: 33.3% vs. 89.9%, \( P < 0.001 \), Fig. 2) of hepatic GISTs were significantly worse than those of gastric GISTs. The DFS (5-year median survival time: 24 months vs. 30 months, \( P < 0.001 \), Fig. 1) and DSS (5-year survival rate: 33.3% vs. 84.8%, \( P = 0.004 \), Fig. 2) of hepatic GISTs were significantly worse than those of small intestinal GISTs. Furthermore, univariate and multivariate analysis were performed to evaluate the prognostic value of location (Table 4, 5). The results showed that location was an independent prognostic factor for DFS (stomach vs. liver: \( P = 0.003 \); small intestine vs. liver: \( P = 0.007 \)) of GIST patients. For prognosis of DSS, the location between the stomach and liver was not an independent risk factor (\( P = 0.096 \)), while the location was an independent risk factor for small intestine and liver (\( P = 0.040 \)).

### Table 3. Comparison of selected clinicopathological parameters among hepatic, gastric, and small intestinal GISTs.

| Characteristics         | Liver (N = 23) | Stomach (N = 297) | Small intestine (N = 59) | \( P \)-value | \( P \)-value |
|-------------------------|---------------|-------------------|--------------------------|-------------|-------------|
| Age                     |               |                   |                          | 0.688       | 0.877       |
| ≤60                     | 14 (60.9%)    | 168 (56.6%)       | 37 (62.7%)               |             |             |
| >60                     | 9 (39.1%)     | 129 (43.4%)       | 22 (37.3%)               |             |             |
| Gender                  |               |                   |                          | 0.099       | 0.557       |
| Male                    | 12 (52.2%)    | 155 (52.2%)       | 35 (59.3%)               |             |             |
| Female                  | 11 (47.8%)    | 142 (47.8%)       | 24 (40.7%)               |             |             |
| Tumor size              |               |                   |                          | <0.001      | <0.001      |
| ≤2 cm                   | 0             | 96 (32.3%)        | 4 (6.9%)                 |             |             |
| 2.1–5 cm                | 1 (4.3%)      | 107 (36.0%)       | 26 (44.8%)               |             |             |
| 5.1–10 cm               | 8 (34.8%)     | 72 (24.2%)        | 17 (29.3%)               |             |             |
| >10 cm                  | 14 (60.9%)    | 22 (7.4%)         | 11 (19.0%)               |             |             |
| Morphology              |               |                   |                          | 0.222       | 0.696       |
| Spindle                 | 18 (85.7%)    | 275 (92.6%)       | 51 (89.5%)               |             |             |
| Epithelioid/mixed       | 3 (14.3%)     | 22 (7.4%)         | 6 (10.5%)                |             |             |
| Mitotic index           |               |                   |                          | 0.020       | 0.043       |
| ≤5                      | 4 (25.0%)     | 163 (54.9%)       | 29 (53.7%)               |             |             |
| >5                      | 12 (75.0%)    | 134 (45.1%)       | 26 (46.3%)               |             |             |
| NIH risk category       |               |                   |                          | <0.001      | 0.003       |
| Very low                | 0             | 83 (27.9%)        | 0 (4.7%)                 |             |             |
| Low                     | 0             | 58 (19.5%)        | 17 (31.5%)               |             |             |
| Intermediate            | 0             | 87 (29.3%)        | 0                        |             |             |
| High                    | 22 (100%)     | 69 (23.2%)        | 33 (61.1%)               |             |             |
| Adjuvant therapy        |               |                   |                          | 0.044       | 0.531       |
| Yes                     | 6 (50.0%)     | 68 (23.1%)        | 36 (61.0%)               |             |             |
| No                      | 6 (50.0%)     | 226 (76.9%)       | 23 (39.0%)               |             |             |

NIH, National Institute of Health.

**Figure 1.** Comparison of disease-free survival (DFS) between hepatic, gastric, and small intestinal GISTs. Liver versus Stomach: \( P < 0.001 \); Liver versus Small intestine: \( P < 0.001 \). Vertical axes: percent of survival; horizontal axes: time (months). GIST, gastrointestinal stromal tumor.

**Discussion**

In this study, we summarized clinical and pathological features of 23 cases of hepatic GIST. Of the 23 cases,
one case was diagnosed and treated in our center and the rest 22 cases were literature searched in MEDLINE for English and CNKI for Chinese publications. We further analyzed prognosis of hepatic GIST in comparison with that of gastric and small intestinal GIST. It was found that most common clinical symptoms for hepatic GIST were abdominal discomfort and abdominal pain, majority of the tumors were low density by CT examination, and fibroblast-like spindle cell shape was predominant by histology. In addition, hepatic GIST had poorer prognosis compared to gastric GIST and small intestinal GIST.

It has been reported that GIST is considered to originate from interstitial cells of Cajal (ICC), the pacemaker of gastrointestinal tract [19]. Furthermore, a subset of “ICC-like” interstitial cells were observed in organs outside of the gastrointestinal tract, which was similar in structure and function to ICCs [16]. Recently, the existence of intrahepatic ICCs in the portal spaces and septa was demonstrated through the immunohistochemistry in human specimens [33]. Additionally, Rusu et al.[32] found the evidence that ICCs also existed in human embryonic liver presented as the distinctively precursor/progenitor cells. While the distribution of ICCs in the liver remains to be defined, existence of ICCs in hepatic tissue may contribute to the development of hepatic GISTs. In this study, the incidence of GIST in each lobe was comparable indicating ICCs may exist in both lobes. However, the role of ICCs in the development of GIST remains to be further investigated.

Previous studies indicated that liver is the most popular organ for metastasis of GIST originated from gastrointestinal tract [5]. Size of the metastatic GIST in liver is usually large and often found in both lobes [46]. In fact, CT findings of metastatic GIST are similar to those of primary GIST [11]. Vanel et al.[37] reported that the imaging feature of liver metastatic GIST was

![Figure 2. Comparison of disease-specific survival (DSS) between hepatic, gastric, and small intestinal GISTs. Liver versus Stomach: \(P < 0.001\); Liver versus Small intestine: \(P = 0.004\). Vertical axes: percent of survival; horizontal axes: time (months). GISTs, gastrointestinal stromal tumors.](image)

| Characteristics                        | \(\beta\) | Hazard ratio (95% CI) | P-value  |
|----------------------------------------|----------|-----------------------|---------|
| DFS                                    |          |                       |         |
| Age                                    | -0.727   | 0.483 (0.156–1.502)   | 0.209   |
| Gender                                 | -0.437   | 0.646 (0.234–1.778)   | 0.397   |
| Tumor size                             | 2.110    | 8.251 (3.611–18.851)  | <0.001  |
| Morphology                             | 1.092    | 2.981 (0.662–13.416)  | 0.155   |
| Mitotic index                          | 1.521    | 4.579 (1.270–16.504)  | 0.020   |
| NIH risk category                      | 1.723    | 5.600 (1.983–15.816)  | 0.001   |
| Adjuvant therapy                       | 1.730    | 5.638 (1.947–16.331)  | 0.001   |
| Location                               |          |                       | <0.001  |
| Stomach vs. liver                      | -3.979   | 0.019 (0.005–0.076)   | <0.001  |
| Small intestine vs. liver              | -2.928   | 0.054 (0.012–0.233)   | <0.001  |
| DSS                                    |          |                       |         |
| Age                                    | 0.912    | 2.488 (0.696–8.889)   | 0.161   |
| Gender                                 | 0.164    | 1.179 (0.339–4.098)   | 0.796   |
| Tumor size                             | 0.783    | 2.188 (1.072–4.466)   | 0.031   |
| Morphology                             | 1.734    | 5.663 (1.164–27.543)  | 0.032   |
| Mitotic index                          | 2.305    | 10.020 (1.244–80.697) | 0.030   |
| NIH risk category                      | 1.419    | 4.131 (1.213–14.068)  | 0.023   |
| Adjuvant therapy                       | 0.600    | 1.822 (0.508–6.538)   | 0.357   |
| Location                               |          |                       | 0.001   |
| Stomach vs. liver                      | -2.683   | 0.068 (0.016–0.296)   | <0.001  |
| Small intestine vs. liver              | -2.337   | 0.097 (0.016–0.589)   | 0.011   |

DFS, disease-free survival; DSS, disease-specific survival; NIH, National Institute of Health.

Table 4. Univariate analysis of variables associated with DFS and DSS in patients with hepatic, gastric, and small intestinal GISTs.
Hepatic GIST

Table 5. Multivariate analysis of prognostic factors for DFS and DSS in patients with hepatic, gastric, and small intestinal GISTs.

| Characteristics | β     | Hazard ratio (95% CI) | P-value |
|-----------------|-------|-----------------------|---------|
| **DFS**         |       |                       |         |
| Tumor size      | 1.760 | 5.811 (2.325–14.524)  | <0.001  |
| Location        | 0.007 |                       |         |
| Stomach vs. liver | −2.336 | 0.097 (0.020–0.457)  | 0.003   |
| Small intestine vs. liver | −2.181 | 0.113 (0.023–0.548)  | 0.007   |
| **DSS**         |       |                       |         |
| Age             | 1.437 | 4.208 (0.953–18.585)  | 0.058   |
| NIH risk category | 1.366 | 3.918 (1.077–14.254)  | 0.038   |
| Location        | 0.078 |                       |         |
| Stomach vs. liver | −1.317 | 0.268 (0.057–1.261)  | 0.096   |
| Small intestine vs. liver | −2.397 | 0.091 (0.009–0.901)  | 0.040   |

DFS, disease-free survival; DSS, disease-specific survival; NIH, National Institute of Health.

heterogeneous hypodense lesions with progressive and concentric enhancement. In this study, majority of the primary hepatic GISTs were in large size, comparably found in both lobes, and showed as low density with variety degrees of enhancement on image examination, which was similar to the feature of liver metastatic GISTs as described above. Thus, differential diagnosis of primary and metastatic hepatic GISTs is difficult, but it is important to differentiate them from the point view of therapy. In this regard, imaging examinations including computed tomography (CT), ultrasound (US), esophagogastroduodenoscopy (EGD), and colonoscopy are generally used to differentiate the primary and metastatic liver GISTs. However, Luo et al. (Miettinen et al.) reported discrepancies of contrast-enhanced ultrasound (CEUS) and enhanced CT examination findings in the distinct vascular architecture of primary and metastatic liver GISTs. Thus, intraoperative inspection is also often applied to confirm origination of GISTs [10, 26].

Preoperative diagnosis of extragastrointestinal stromal tumors (EGISTs) is also relatively difficult due to the deeper location and lack of mucosal connection, which could potentially lead to misdiagnosis [8]. In this content, differential diagnosis of GISTs in liver may involve the poorly differentiated carcinomas, epithelioid angiomylipoma and leiomyoscaroma, or malignant melanoma [44]. In these instances, the ultrasound-guided fine needle aspiration biopsy (US-FNAB) ought to be performed in order to make a definite diagnosis after which different treatment strategies will be applied to primary or metastatic liver GISTs.

Due to variety kinds of clinical presentation of the GIST, treatment and prognosis of this tumor is variable [4, 7]. It has been reported that approximately 10%–30% of GISTs were regarded as clinically malignant [15]. In this study, clinical and pathological characteristics of hepatic GISTs were analyzed in comparison with gastric GISTs. It was found that tumor size and NIH risk category were significantly higher in hepatic GISTs than that in gastric GISTs. While it has also been reported that tumor size and mitotic index are the most efficient prognostic factors in determining malignancy of GISTs [4], this study, could not predict the survival rate from tumor size and mitotic index due to the limit of sample size of hepatic GISTs.

Original site of a primary GIST is also an independent predictor for the prognosis of GISTs [34]. In the NIH risk classification system, GIST is classified as gastric or nongastric GIST, and hepatic GIST is not included yet. Thus, we compared the prognosis of hepatic GISTs with gastric and small intestinal GISTs from our center. The results showed that the DFS and DSS of hepatic GISTs were significantly worse than those of gastric and small intestinal GISTs. However, the multivariate analysis showed that location was an independent prognostic factor for DFS (stomach vs. liver; small intestine vs. liver) of GIST patients. For prognosis of DSS, the location between small intestine and liver was an independent risk factor, while the location was not an independent risk factor for stomach and liver. This contrary results of DSS may attribute to the limitation of our sample size and the less tumor-related death of GISTs. Furthermore, it is unavoidable that the low incidence of adjuvant therapy of Imatinib in this study would lead to bias during the survival analysis. Thus, the actual prognosis of hepatic GISTs may be more favorable than that in this study.

There are some limitations in this study. First, this study is a retrospective analysis and lacks systematic and prospective data. Second, sample size of the hepatic GIST was small. Third, due to the limited number of duodenal or rectal GIST cases in our center, these types of GISTs were not included in this study.

Conclusions

Majority of the primary hepatic GISTs are large in size and highly malignant. Clinical and pathological features of hepatic GIST are significantly different from that of gastric and small intestinal GIST. Prognosis of the primary hepatic GISTs is very poor and worse than that of gastric and small intestinal GISTs.

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Conflict of interests

There are no financial or other relations that could lead to a conflict of interest.

References

1. Bhoy, T., S. Lalwani, J. Mistry, V. Varma, V. Kumaran, S. Nundy, et al. 2014. Primary hepatic gastrointestinal stromal tumor. Trop. Gastroenterol. 35:252–253.
2. Cai, S., Y. Jing, and Q. Li. 2013. Misdiagnosis of extragastrointestinal stromal tumor in liver: a case report. Chin. J. Trauma Disability Med. 21:449–450.
3. de Chiara, A., V. de Rosa, S. Lastoria, R. Franco, G. Botti, V. R. Iaffaioli, et al. 2006. Primary gastrointestinal stromal tumor of the liver with lung metastases successfully treated with STI-571 (imatinib mesylate). Front Biosci. 11:498–501.
4. Dematteo, R. P., J. S. Gold, L. Saran, M. Gonen, K. H. Liau, R. G. Maki, et al. 2008. Tumor mitotic rate, size, and location independently predict recurrence after resection of primary gastrointestinal stromal tumor (GIST). Cancer 112:608–615.
5. Dematteo, R. P., J. J. Lewis, D. Leung, S. S. Mudan, J. M. Woodruff, and M. F. Brennan. 2000. Two hundred gastrointestinal stromal tumors: recurrence patterns and prognostic factors for survival. Ann. Surg. 231:51–58.
6. Feng, F., Z. Liu, X. Zhang, M. Guo, G. Xu, G. Ren, et al. 2015. Comparison of Endoscopic and Open Resection for Small Gastric Gastrointestinal Stromal Tumor. Transl. Oncol. 8:504–508.
7. Feng, F., Y. Tian, Z. Liu, G. Xu, S. Liu, M. Guo, et al. 2016. Clinicopathologic Features and Clinical Outcomes of Esophageal Gastrointestinal Stromal Tumor: evaluation of a Pooled Case Series. Medicine (Baltimore) 95:e2446.
8. Gao, Y. N., G. Q. Jiang, J. X. Liu, W. S. Tang, and L. Z. Chen. 2005. Preoperative misdiagnosis of extragastrintestinal stromal tumors as ovarian cancer: report of three cases with literature review. Zhonghua Fu Chan Ke Za Zhi 40:339–341.
9. Heinrich, M. C., C. L. Corless, A. Duensing, L. McGreevey, C. J. Chen, N. Joseph, et al. 2003. PDGFRA activating mutations in gastrointestinal stromal tumors. Science 299:708–710.
10. Hodges, K., L. Kennedy, F. Meng, G. Alpini, and H. Francis. 2012. Mast cells, disease and gastrointestinal cancer: a comprehensive review of recent findings. Transl. Gastrointest. Cancer 1:138–150.
11. Hong, X., H. Choi, E. M. Loyer, R. S. Benjamin, J. C. Trent, and C. Charrasvangavej. 2006. Gastrointestinal stromal tumor: role of CT in diagnosis and response evaluation and surveillance after treatment with imatinib. Radiographics 26:481–495.
12. Hu, X. 2008. Primary hepatic gastrointestinal stromal tumor: a case report. Chin. J. Dig. Surg. 7:77.
13. Hu, X., J. Forster, and I. Damjanov. 2003. Primary malignant gastrointestinal stromal tumor of the liver. Arch. Pathol. Lab. Med. 127:1606–1608.
14. Hu, Z., Y. Wei, H. Zhu, X. Yang, Z. Deng, and M. You. 2007. A case of giant malignant hepatic gastrointestinal stromal tumor. Chin. J. Pract. Surg. 27:417.
15. Huang, R. X., P. Xiang, and C. Huang. 2014. Gastrointestinal stromal tumors: current translational research and management modalities. Eur. Rev. Med. Pharmacol. Sci. 18:3076–3085.
16. Huizinga, J. D., and M. S. Faussone-Pellegrini. 2005. About the presence of interstitial cells of Cajal outside the musculature of the gastrointestinal tract. J. Cell Mol. Med. 9:468–473.
17. Joensuu, H. 2008. Risk stratification of patients diagnosed with gastrointestinal stromal tumor. Hum. Pathol. 39:1411–1419.
18. Kim, H. O., J. E. Kim, K. S. Bae, B. H. Choi, C. Y. Jeong, and J. S. Lee. 2014. Imaging findings of primary malignant gastrointestinal stromal tumor of the liver. Jpn. J. Radiol. 32:365–370.
19. Kindblom, L. G., H. E. Remotti, F. Aldenborg, and J. M. Meis-Kindblom. 1998. Gastrointestinal pacemaker cell tumor (GIPACT); gastrointestinal stromal tumors show phenotypic characteristics of the interstitial cells of Cajal. Am. J. Pathol. 152:1259–1269.
20. Li, Z. Y., Q. L. Liang, G. Q. Chen, Y. Zhou, and Q. L. Liu. 2012. Extra-gastrointestinal stromal tumor of the liver diagnosed by ultrasound-guided fine needle aspiration cytology: a case report and review of the literature. Arch. Med. Sci. 8:392–397.
21. Lin, X. K., Q. Zhang, W. L. Yang, C. H. Shou, X. S. Liu, J. Y. Sun, et al. 2015. Primary gastrointestinal stromal tumor of the liver treated with sequential therapy. World J. Gastroenterol. 21:2573–2576.
22. Louis, A. R., S. Singh, S. K. Gupta, and A. Sharma. 2014. Primary GIST of the liver masquerading as primary intra-abdominal tumour: a rare extra-gastrointestinal stromal tumor (EGIST) of the liver. J. Gastrointest. Cancer 45:392–394.
23. Lu, Y., and S. Guo. 2013. One case: primary malignant stromal tumor of the liver. Journal of Practical Radiology 29:1368–1369.
24. Luo, X. L., D. Liu, J. J. Yang, M. W. Zheng, J. Zhang, and X. D. Zhou. 2009. Primary gastrointestinal stromal tumor of the liver: a case report. World J. Gastroenterol. 15:3704–3707.
25. Mao, L., J. Chen, Z. Liu, C. J. Liu, M. Tang, and Y. D. Qiu. 2015. Extracorporeal hepatic resection and autotransplantation for primary gastrointestinal stromal tumor of the liver. Transplant. Proc. 47:174–178.
26. Mastoraki, A., E. Toliaki, E. Chrisovergi, S. Mastoraki, I. S. Papanikolaou, N. Danias, et al. 2015. Metastatic Liver Disease Associated with Gastrointestinal Stromal Tumors: controversies in Diagnostic and Therapeutic Approach. J. Gastrointest. Cancer 46:237–242.

27. Miettinen, M., J. M. Monihan, M. Sarlomo-Rikala, A. J. Kovatich, N. J. Carr, T. S. Emory, et al. 1999. Gastrointestinal stromal tumors/smooth muscle tumors (GISTs) primary in the omentum and mesentery: clinicopathologic and immunohistochemical study of 26 cases. Am. J. Surg. Pathol. 23:1109–1118.

28. O’Brien, K. M., I. Orlow, C. R. Antonescu, K. Ballman, L. McCall, R. Dematteo, et al. 2013. Gastrointestinal stromal tumors, somatic mutations and candidate genetic risk variants. PLoS ONE 8:e62119.

29. Ochiai, T., T. Sonoyama, S. Kikuchi, H. Ikoma, T. Kubota, M. Nakanishi, et al. 2009. Primary large gastrointestinal stromal tumor of the liver: report of a case. Surg. Today 39:633–636.

30. Ortiz-Hidalgo, C., B. De Leon Bojorge, and J. Albores-Saavedra. 2000. Stromal tumor of the gallbladder with phenotype of interstitial cells of Cajal: a previously unrecognized neoplasm. Am. J. Surg. Pathol. 24:1420–1423.

31. Ren, S., Z. Huang, and B. Dong. 2006. Primary hepatic gastrointestinal stromal tumor: a case report. Natl. Med. J. China 86:3311.

32. Rusu, M. C., I. Duta, A. C. Didilescu, A. D. Vrapciu, S. Hostiuc, and E. Anton. 2014. Precursor and interstitial Cajal cells in the human embryo liver. Rom. J. Morphol. Embryol. 55:291–296.

33. Rusu, M. C., F. Pop, S. Hostiuc, G. C. Curca, and A. Streinu-Cercel. 2011. Extrahepatic and intrahepatic human portal interstitial Cajal cells. Anat. Rec. (Hoboken) 294:1382–1392.

34. Rutkowski, P., Z. I. Nowecki, W. Michej, M. Debiec-Rychter, A. Wozniak, J. Limon, et al. 2007. Risk criteria and prognostic factors for predicting recurrences after resection of primary gastrointestinal stromal tumor. Ann. Surg. Oncol. 14:2018–2027.

35. Sheppard, K., K. M. Kinross, B. Solomon, R. B. Pearson, and W. A. Phillips. 2012. Targeting PI3 kinase/AKT/mTOR signaling in cancer. Crit. Rev. Oncog. 17:69–95.

36. Su, Y. Y., N. J. Chiang, C. C. Wu, and L. T. Chen. 2015. Primary gastrointestinal stromal tumor of the liver in an anorectal melanoma survivor: a case report. Oncol. Lett. 10:2366–2370.

37. Vanel, D., M. Albiter, L. Shapeero, A. le Cesne, S. Bonvalot, C. le Pechoux, et al. 2005. Role of computed tomography in the follow-up of hepatic and peritoneal metastases of GIST under imatinib mesylate treatment: a prospective study of 54 patients. Eur. J. Radiol. 54:118–123.

38. Wang, J., Q. Li, Y. Sun, H. Zheng, Y. Cui, H. Li, et al. 2009. Clinicopathologic features between multicentric occurrence and intrahepatic metastasis of multiple hepatocellular carcinomas related to HBV. Surg. Oncol. 18:25–30.

39. Wu, P. 2012. A giant hepatic gastrointestinal stromal tumor: a case report. Med. J. Natl. Defending Forces in Southwest China 22:197.

40. Xiao, D., and H. Zhao. 2006. The CT-guided misdiagnosis of gastrointestinal stromal tumor in liver: a case report. Chin. J. Misdiagnositics 6:2140–2141.

41. Xue, Y., and X. He. 2013. Primary gastrointestinal stromal tumor of the liver: one case report. J. Chin. Oncol. 19:159–160.

42. Yamaura, K., K. Kato, M. Miyazawa, Y. Haba, A. Muramatsu, K. Miyata, et al. 2004. Stromal tumor of the pancreas with expression of c-kit protein: report of a case. J. Gastroenterol. Hepatol. 19:467–470.

43. Yang, J., F. Feng, M. Li, L. Sun, L. Hong, L. Cai, et al. 2013. Surgical resection should be taken into consideration for the treatment of small gastric gastrointestinal stromal tumors. World J. Surg. Oncol. 11:273.

44. Zhao, X., and C. Yue. 2012. Gastrointestinal stromal tumor. J Gastrointest Oncol. 3:189–208.

45. Zhou, B., M. Zhang, S. Yan, and S. Zheng. 2014. Primary gastrointestinal stromal tumor of the liver: report of a case. Surg. Today 44:1142–1146.

46. Zhu, J., Y. Yang, L. Zhou, M. Jiang, and M. Hou. 2010. A long-term follow-up of the imatinib mesylate treatment for the patients with recurrent gastrointestinal stromal tumor (GIST): the liver metastasis and the outcome. BMC Cancer 10:199.

Supporting Information

Additional supporting information may be found in the online version of this article:

Table S1: Clinicopathological features of hepatic GISTs