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Clinical significance of surgery for gastric submucosal tumours with size enlargement during watchful waiting period

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Abstract ***Background:*** The true impact of surgery for small, asymptomatic and biopsy-negative gastric submucosal tumours (SMTs) with size enlargement during 'watchful waiting' period has not been fully understood.

Methods: From 2005 to 2012, 100 patients with gastric SMTs underwent surgery. Twenty-three of them with size enlargement during observation period were enrolled in the retrospective analysis. Data included clinicopathologic findings, genetic findings, operative outcomes and prognoses.

Results: All patients (13 males, 10 females), with median age of 54 (41–71), had their lesions detected by routine health check-up ($n = 21$) or incidentally (2). The tumours were 1.8 (0.5–4.0) cm in size at their initial detection, and enlarged up to 3.2 (2.0–7.0) cm at the operation during 63.0 (14.6–233.7) months. As surgical procedure, laparoscopic partial gastrectomy accounted for the majority (78.3%). Histologic examination revealed gastrointestinal stromal tumour (GIST) (21) and schwannoma (2). Although 16 out of 21 GISTs were categorised into 'Very low' (1), and 'Low' (13) risk according to Fletcher's classification, 'Intermediate' (5) and 'High' (2) risk were identified in the series. No recurrences/metastases were noted in 23.2 (0.9–87) months of postoperative follow-up.

Conclusion: Our study revealed the existence of high mitotic GISTs in asymptomatic, small gastric SMTs with size enlargement, and laparoscopic surgery was safely applied to majority of those cases. Prompt surgical intervention should therefore be considered for those lesions.

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1. Introduction

Gastric submucosal tumour (SMT) originates out of subepithelial, muscular or subserous layer of the stomach and is applied to a mass or bulge covered by normal-appearing gastric mucosa identified during esophagogastroduodenoscopy (EGD). Gastric SMT consists of non-epithelial neoplasia and non-tumour lesion. The former includes mesenchymal tumours (gastrointestinal stromal tumour (GIST), leiomyoma, leiomyosarcoma, and neurogenic tumours), vascular tumours, lipoma, liposarcoma, malignant lymphoma and malignant melanoma. The latter is corresponded to ectopic pancreas, inflammatory fibroid polyp, submucosal cyst and ectopic glands. In addition to such lesions, it is necessary to pay attention to epithelial neoplasia mimicking SMT, such as carcinoid, carcinoma and metastatic carcinoma.[1]

Gastric SMTs are usually found incidentally during GI endoscopy. Contrary to the situation in the United States and Europe, several differences as to those tumours exist in Japan. The first point is the detection rate of gastric SMT in EGD examination. While the incidence of gastric SMT was reported as 0.36% in a Swedish routine endoscopy,[2] it reached up to approximately 3% in Japan.[3] The second point is the size of gastric SMT at detection. Since screening system for gastric cancer by barium study is established as nationwide program in Japan,[4] small gastric SMTs less than 5 cm in size with no clinical symptoms are often detected during routine medical health examinations.[5] On the other hand, in the Western countries, there are no similar screening systems. In general, EGD and/or computed tomography (CT) are/is performed only for patients with clinical symptoms. As a result, large gastric SMTs over 5 cm account for the majority in the Western countries.[6]

In the clinical practice guidelines for GIST in Japan,[1] the operative indication for gastric SMT is 'symptomatic', 'histologically confirmed GIST by biopsy', or 'over 5 cm'. Fig. 1 shows the diagnostic and treatment algorithms for small gastric SMTs according to Japanese guidelines. Solid lines represent 'standard' and/or consensus diagnostic and therapeutic flowcharts of procedures that are recommended in clinical practice, whereas dotted lines are indicative of 'optional' methods. When asymptomatic small gastric SMTs are encountered in daily clinical practice, they are followed closely at least once or twice a year with EGD as 'watchful waiting'. This therapeutic strategy is described as standard arm in these guidelines. However, surgery for small gastric SMTs with size enlargement during watchful waiting period is corresponded to optional arm, since currently there are not sufficient evidences in support of therapeutic strategy. Therefore, investigation research for such tumours is necessary to clarify the biological malignancy of this particular subgroup of patients.

The aim of this study was to assess the clinical significance of surgery for small gastric SMT with size enlargement during watchful waiting period. Clinicopathologic findings, genetic findings, operative outcomes and prognoses were analysed retrospectively to gain insight into the clinical behaviour of such tumours.

2. Patients and methods

2.1. Patients selection criteria

This study was a retrospective study without any study-driven clinical interventions. No material and data were sent to external institutions for protection of privacy. Inclusion criteria of this study were gastric SMTs which met all following items: (1) asymptomatic; (2) with biopsy negative; (3) less than 5 cm in size at detection; (4) with size enlargement for operative indication during watchful waiting period of more than 12 months. Prospectively registered dedicated SMT/GIST database in our institution revealed 100 patients with gastric SMT underwent surgery from 2005 to 2012. Of these 100 patients, 61 patients had any symptom and removed from this study. Of the remaining 39 patients, 11 patients with SMT over 5 cm at detection were excluded. Of 28 patients with biopsy negative SMT less than 5 cm when discovered, 23 patients with tumour size enlargement during watchful waiting period were finally enrolled in this retrospective analysis. The remaining five patients underwent operation for patients' discretion and/or for comorbidity of colon cancer. These eligible patients underwent periodical follow-up with EGD (22 cases) or CT (1 case) once or twice a year as watchful waiting period.

2.2. Clinical and histopathologic features, risk-group stratification

Patient demographics and detailed clinical data including tumour size, tumour location, tumour growth pattern,[7] and imaging findings were obtained from medical records and prospectively registered in a dedicated surgical database on condition of anonymity. Any major operative findings such as clinically malignant factors,[8] achievement rate of complete resection,[1,9] operative procedure, operating time and blood loss were also recorded and included in the database. The histopathologic features, e.g. cell shape, mean number of mitoses per 50 HPF (high-power field) and immunophenotype, were obtained by H&E staining examination and immunohistochemistry, and were registered after thorough review by one of the investigators (S.H.). Patients with GIST were classified according to Fletcher's risk stratification.[10] According to Japanese GIST guidelines, the patients were followed up with routine computed