Endoscopic Removal of Small Gastrointestinal Stromal Tumors: Can We GIST-ify the Risk?

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Background

GISTs are the most common subepithelial tumor of the stomach with a prevalence of 129 per one million [1]. Nearly 500–600 new cases are diagnosed per year in the United States according to the Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute's (NCI) report in 1995 [2]. More recently, including incidental findings, it is estimated that there are 3,000–6,000 new cases per year in the United States [3]. As more of these lesions are found, a strategy to manage these will need to be developed. A recent AGA technical review suggests observation for GISTs less than 3 cm without high risk features [4].

In this month's issue of *Digestive Diseases and Sciences*, Bai et al. present an interesting article on the endoscopic removal of small GIST tumors (<30 mm) [5]. While the authors report a technical success with removal, we should be asking ourselves “should we,” rather than “can we.” To answer this question, we need to have a better understanding of the diagnosis, prognosis, and management of these lesions.

Diagnosis

The diagnosis of GIST is often made after EUS referral for the evaluation of subepithelial lesions. Its diagnostic yield can vary. It can be as low as 68.7% (range 40–100%) without tissue acquisition and as high as 84% (range 73.8–

100%) with tissue acquisition [6]. Unfortunately, even though the diagnosis can be obtained by EUS, predicting its course is not as easy. Although many studies demonstrate features that suggest malignant GISTs on EUS (size >3 cm, irregularity of the extraluminal border, presence of cystic spaces, echogenic foci, and heterogeneity), inter-observer variability is high and results can vary [4, 7, 8].

Outcomes

Two bodies of evidence demonstrate that small gastric GISTs are benign and have a low rate of metastases and progression: resection studies and natural history studies.

We know from a variety of long-term studies of resected GISTs that outcomes and recurrence rates are based upon size, location, and mitotic rate. In a series of 127 patients of surgically resected GISTs by DeMatteo et al., benign outcomes were prognosticated by: size <5 cm, mitotic rate of <5/hpf, and gastric location [9]. These findings were confirmed in a literature review by Miettinen and Lasota where small GISTs of gastric location carry an excellent prognosis [3] (Table 1).

More information on the natural history of GISTs can be gleaned from natural history studies of small GISTs that are not removed [7, 10–12]. Studies by Gill et al. and Chien et al. and have shown that the majority of subepithelial tumors <3 cm including GISTs do not change in size with a mean follow-up of 20.7 and 23 months, respectively [7, 10]. In another longitudinal study with a mean follow-up of 16.5 months (range 5–114), 30% (6/20) of patients with 19 mm (10–32 mm) GISTs had a decrease in tumor size by 1–5 mm, 40% (8/20) had an increase in tumor size by 2–21 mm, and 30% (6/20) remained stable [13]. Other studies have demonstrated similar results. Lachter et al.

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Table 1 Progressive disease in gastric GIST

Tumor size	Mitotic rate	% With progressive disease (risk)
≤2 cm	≤5 per 50 hpf	None (very low)
	>5 per 50 hpf	None (very low)
>2 cm and ≤5 cm	≤5 per 50 hpf	1.9 (very low)
	>5 per 50 hpf	16 (moderate)
>5 cm and ≤10 cm	≤5 per 50 hpf	3.6 (low)
	>5 per 50 hpf	55 (high)
>10 cm	≤5 per 50 hpf	12 (moderate)
	>5 per 50 hpf	86 (high)

Adapted from Miettinen et al. [3]

demonstrated that of 70 patients with 23.2 mm GISTs, only 20% of cases increased in size by more than 2 mm. They also found that the risk for enlargement was related to initial tumor size >17 mm ($P = 0.018$) [14]. These observations are confirmed in several other small studies [11, 12].

In this article, Bai et al. present the management of 25 patients with small gastric GISTs (<30 mm) [5]. Based on resection and natural history studies in the literature and even histologic evaluation of the data of Bai and colleagues, these types of lesions are benign. Therefore, there seems to be no clear medical indication for their removal unless the proposed intervention aimed at their removal is safe and effective.

Management

Currently, the standard of care for GIST removal is surgery. It is well tolerated with little morbidity for tumors <10 cm [2]. In a recent study of laparoscopic resections of GISTs, tumors >2 cm were removed with very little morbidity (1 patient with leak at suture line) and no deaths ($n = 35$). The hospital stay was reasonable with an average of only 7–8 days [15]. This is similar to other published data on laparoscopic resection with a technical success of 98.3–100% and a length of stay of 3.9–7.2 days [16]. These results are certainly acceptable for high risk lesions, but do not seem to be indicated for low risk lesions. Bai et al., in their study, try to find a safer way for the effective removal of the smaller, low risk lesions with a shorter hospital stay. His technique, although effective, is not low risk. His study reports a 28% perforation rate (up to 6 mm in size) leading to a prolonged hospital stay (4.28 days) [5]. This figure is significantly higher than ESD (endoscopic submucosal dissection) done for other indications. For example, in a large Japanese study where ESD is performed for the resection of another type of gastric lesion (early gastric cancer) the overall perforation rate was 4% with low rates

of bleeding and no cases requiring surgery [17]. In another study, reported by a Korean multicenter group, the perforation rate was even lower (1.2%) [18]. The differences can be attributed to the pathology of the lesion being treated. For instance, GISTs emerge from the muscle layer of the stomach and, therefore, would be expected to have a higher perforation rate than gastric neoplasms which are mucosal, allowing for a safer dissection and resection. Clearly, this difference in histopathology would make one hesitate in performing this type of a procedure for these benign lesions.

Conclusions

The endoscopic removal of small GISTs by ESD is technically feasible as demonstrated in the article by Bai et al. [5]. Its use, though, cannot be justified given that it carries a 28% perforation rate along with a potential prolonged hospital stay (4.26 days) for a very benign condition. Therefore, until safer technology becomes available for endoscopic removal of GISTs, the best approach would still be that of watchful waiting for small, low risk GISTs and laparoscopic removal for those that are high risk based on size, location and mitotic rate.

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