

Research Article

Endoscopic submucosal dissection using sodium hyaluronate, a new technique for en bloc resection of a large superficial tumor in the colon

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Abstract. En bloc resection of superficial tumors in the colon is challenging but beneficial for the precise diagnosis and treatment. We have been using a novel technique of endoscopic submucosal dissection with a viscous substance, sodium hyaluronate, and a needle knife in combination with a small-caliber-tip transparent hood and succeeded in the endoscopic en bloc resection of large superficial tumors in the colon. We endoscopically treated superficial tumors larger than 20 mm in diameter of the colon in 166 patients between June 1998 and March 2005. All the lesions were successfully resected endoscopically and en bloc resection was achieved in 77% of them. Even large superficial tumors in the colon can be resected in one piece by using this technique.

Key words: Endoscopic submucosal dissection; Colon tumor; Sodium hyaluronate; Small-caliber-tip transparent hood

1. Introduction

Endoscopic submucosal dissection (ESD) is a newly developed method that enables en bloc resection of large superficial tumors in the GI tract. ESD is widely accepted as a more reliable therapeutic procedure for large superficial gastric cancer in Japan (Yamamoto et al., 2005). However, application of ESD in the colon is considered difficult because the colonic wall is thinner than the gastric wall and piecemeal resection has been widely accepted as a treatment

of superficial tumors in the colon, especially for large lesions with more than 20 mm in diameter, due to the technical difficulties of en bloc resection. We have been performing en bloc resection of large superficial tumors in the colon using sodium hyaluronate and other assisting devices (Yamamoto et al., 1999). Sodium hyaluronate creates the long lasting mucosal protrusion for safety and easiness of mucosal and submucosal incision with a needle knife, which enables en bloc resections of large superficial tumors without relying on a snaring method. This study addressed clinical outcomes of this new technique for large superficial tumors in the colon.

2. Materials and methods

2.1 Patients

ESD was performed for 166 early stage neoplastic lesions of the colon, larger than 20 mm in diameter, between June 1998 and March 2005. ESD using sodium hyaluronate was approved by the ethics committee of Jichi Medical University, and written informed consent was obtained from all the patients.

2.2 Sodium hyaluronate

Sodium hyaluronate solution is thick and has a high viscosity and it has been approved for clinical use in intra-articular injections for osteoarthritis in Japan. During the procedure of ESD, a local injection of sodium hyaluronate creates a more prominent and longer lasting mucosal protrusion than normal saline (Yamamoto et al., 1999). Its other beneficial effects for ESD include ability of locally retaining mixed epinephrine and its harmless nature to the injected tissue because of its isotonicity despite its high viscosity compared with hypertonic solutions such as 50% glucose and glycerol.

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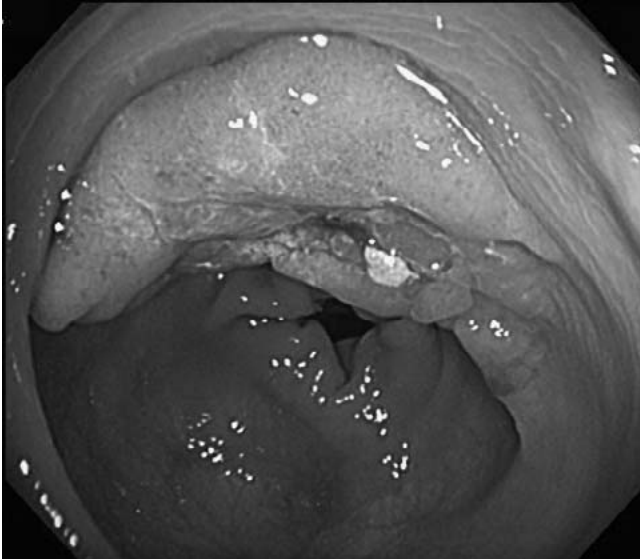


Fig. 1. A large superficial tumor in the colon.

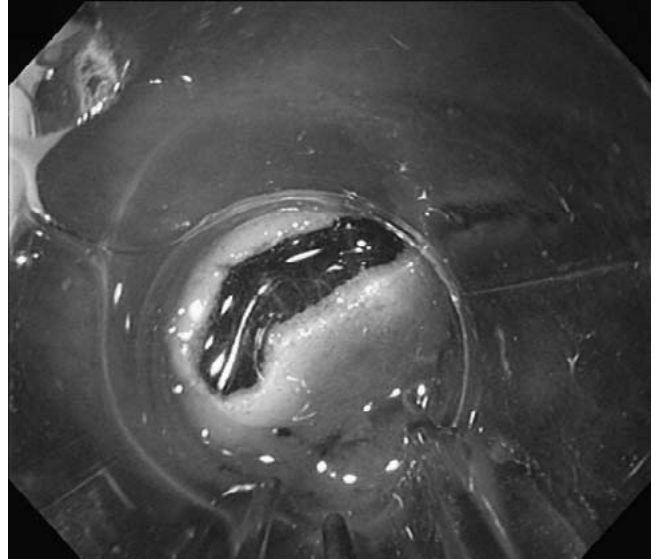


Fig. 3. Mucosal incision.

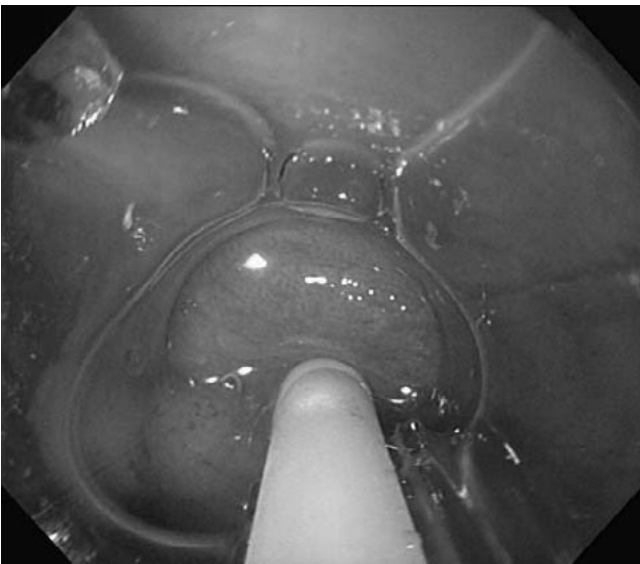


Fig. 2. Injection of sodium hyaluronate.

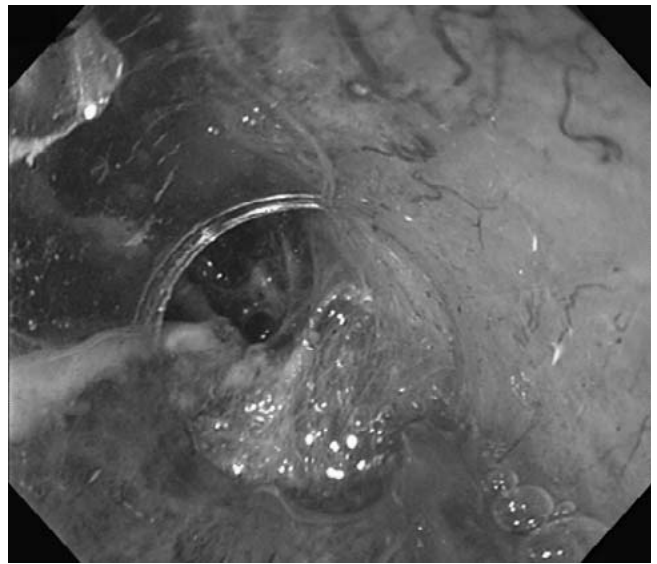


Fig. 4. Blood vessels were pre-coagulated before incision.

2.3 ESD procedure

The detail of the procedure has been described elsewhere (Yamamoto et al., 2004). In brief, normal saline was pre-injected to avoid injections of sodium hyaluronate into the wrong layer because it is more difficult to inject sodium hyaluronate solution into the appropriate submucosal layer of the colon. Sodium hyaluronate (0.5%) was subsequently injected to make a good protrusion of the targeted mucosa. By mixing a small amount of indigo carmine dye into the sodium hyaluronate solution, the injected area of the sodium hyaluronate can be distinguished easily from the non-injected area even after pre-injections of normal saline. A small amount of epinephrine is also mixed with sodium hyaluronate to diminish bleeding during the procedures. Then, mucosal incision around the tumor is made with a needle knife. A cylindrical transparent hood of 8 mm in length attached at the endoscope tip is also helpful for the safety of mucosal incision by halting unintentional movements of the colonic wall toward the needle knife. In most cases, a submucosal incision is

started from the most distant edge of the tumor using a needle knife, by hooking the edge of the tumor with the tip of the transparent hood and opening the incision. After deep incisions of the submucosal layer at the distant and lateral edges of the tumor, submucosal incisions approaching from the nearest edge of the tumor are performed with a needle knife while the incised wound is opened by the tip of the small-caliber-tip transparent hood. The mucosal lesion is exfoliated completely by advancing the submucosal incision while sliding the tip of the endoscope with a hood under the exfoliated mucosa (Matsushita et al., 1997).

3. Results

We have successfully resected all of the 166 superficial tumors in the colon endoscopically by using ESD technique using sodium hyaluronate. Mean diameter of these lesions

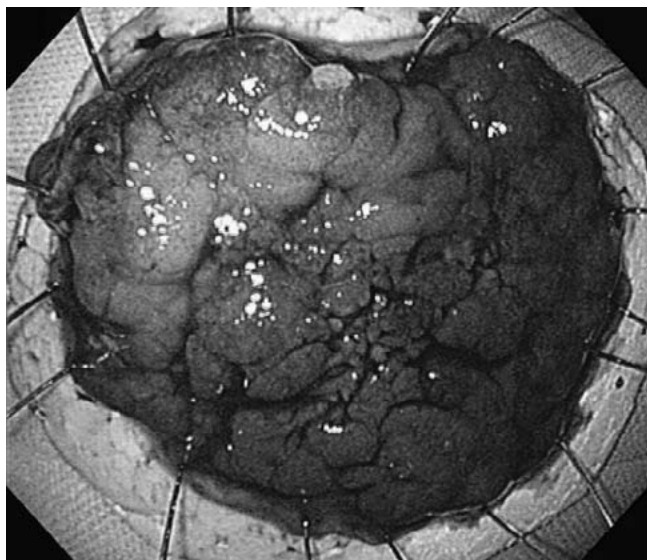


Fig. 5. Resected specimen. The lesion was resected en bloc.

was 33 mm and mean procedure time for the resection was 102 min. Macroscopic feature of the tumors include granular type in 109 lesions and non-granular type in 46 lesions. All the lesions were successfully resected endoscopically and en bloc resection was successful in 77% of them. Complications of the treatments included bleeding, which required further endoscopic examination or treatment like clip placement, in 3 patients and perforation in 7 patients, respectively. Bleeding was endoscopically controlled in all 3 patients and perforation was treated endoscopically using clip devices in 5 patients, laparoscopically in one patient and conservatively in one patient. No other complications required laparotomy.

4. Discussion

Large superficial tumors in the colon have little tendency of vertical growth despite their lateral extension. Therefore, they are best removed endoscopically (Saito et al., 2001). However, they sometimes invade deeply into the submucosal layer without showing a definite endoscopic sign of invasion. Accurate histopathologic assessment of the resected specimens is essential to ensure the curability, because significant amount of submucosal invasion of the tumor suggests considerable risk of lymph node metastasis, which necessitates additional surgery. Due to the technical difficulties of en bloc EMR, piecemeal EMR has been accepted as a treatment for large superficial tumors in the colon especially for lesions larger than 20 mm in diameter (Tanaka et al.,

2001). However, re-constructions of the resected specimens are sometimes difficult and an accurate histopathologic assessment can be ruined. Moreover, higher rates of residual and recurrent lesions are reported with piecemeal EMRs than with en bloc EMRs in the stomach (Matsushita et al., 1997).

We use several devices to overcome the difficulty and have made it feasible in the colon as well (Yamamoto et al., 2001). Submucosal injection of sodium hyaluronate is used to maintain a sufficient thickening of the submucosal tissue and a small caliber tip or regular cylindrical transparent hood is used to open up the incised mucosa as a substitute for a counter traction. In this method, not only the lateral margin, the vertical margin of the resection can also be determined precisely because submucosal incision is carried out under direct visualization of the submucosal tissue. In our study, we have successfully achieved en bloc resection of the tumor in most of the cases. En bloc resection, however, was unsuccessful in 23% of them. There are several factors that can affect the success rate of en bloc resection, including tumor size, location and nature of the tumor. In our study, the average size of the 33 lesions that we have failed to achieve en bloc resection was 37 mm, larger than the overall average. These 33 lesions were located more frequently in the sigmoid colon, transverse colon, and ascending colon compared with 129 lesions that have been successfully resected en bloc. It is plausible that the tumor located in the sigmoid colon or transverse colon is more difficult to resect due to the anatomical reason. Finally, the rate of the non-granular type is higher in these 33 lesions. It should also be noted that learning curve also is another important factor for en bloc resection. In conclusion, ESD using sodium hyaluronate and needle knife is feasible even for a large superficial tumor in the colon.

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