Editorial Manager(tm) for Surgical Laparoscopy, Endoscopy & Percutaneous Techniques

Manuscript Draft

Manuscript Number: SLEPT-D-09-00270R

Title: Laparoscopic Excision is an Alterative Method for Rectal Gastrointestinal Stromal Tumor

Article Type: Case Report

Keywords: GIST, rectal, laparoscopy, excision

Corresponding Author: Dr. William Tzu-Liang Chen, M.D

Corresponding Author's Institution: China Medical University Hospital

First Author: Sheng-Chi Chang, M.D.

Order of Authors: Sheng-Chi Chang, M.D.; Tao-Wei Ke, MD; Hua Che Chiang, M.D; Christina Wu, BS; William Tzu-Liang Chen, M.D

Manuscript Region of Origin: TAIWAN

Abstract: Gastrointestinal stromal tumors are rarely found in the anorectum and account for less than 0.3 percent of all rectal malignancies. The major treatment of rectal GISTs is complete resection of the primary tumor with negative microscopic margin. We present an alternative method, laparoscopic-assisted local excision of rectal GIST. This was a patient with a 5 cm x 4 cm x 3 cm GIST located 4 cm above the dentate line in the right rectal wall. The tumor was mobilized by laparoscopic dissection with a clear safe margin and the specimen was removed from anus. The patient had a smooth recovery and no recurrence after 31 months following the procedure. This experience suggests that laparoscopic excision is a safe alternative for rectal GIST, offering the advantage of better visualization of structures and sparing the patient from an unnecessary abdominoperineal resections.

*Copyright Transfer Form 1

Click here to download high resolution image

Surgical Laparoscopy, Endoscopy & Percutaneous Techniques

Lippincott Williams & Wilkins/Wolters Kluwer Health

Authorship Responsibility, Financial Disclosure, and Copyright Transfer

Manuscript Title: Laparoscopic Excision is an alternative Method for Rectal Gastrointestinal including all stromal tumors accompanying digital supplementary content, if any (the "Work")

Corresponding Author: William Tzu Liang Chen

Mailing Address and Telephone/Fax Numbers: 000.5438.2000@gate.com.tw

Fax: 886-4-2202 70 83 Tel: 886-4-22052121-1655

Each author must read and sign the following statements; if necessary, photocopy this document and distribute to coauthors for their original ink signatures. **Completed forms should be submitted to the Editorial Office with the Work or returned to Surgical Laparoscopy, Endoscopy & Percutaneous Techniques, Carol E.H. Conner, M.D., PhD., The University of Iowa College of Medicine, Department of Surgery, 200 Hawkins Drive, #1516 JCP, Iowa City, IA 52242-1086.**

CONDITIONS OF SUBMISSION

RETAINED RIGHTS: Except for copyright, other proprietary rights related to the Work (e.g., patent or other rights to any process or procedure) shall be retained by the authors. To reproduce any text, figures, tables, or illustrations from this Work in future works of their own, the authors must obtain written permission from Lippincott Williams & Wilkins (LWW); such permission cannot be unreasonably withheld by LWW.

ORIGINALITY: Each author warrants that his or her submission to the Work is original and that he or she has full power to enter into this agreement. Neither this Work nor a similar work has been published nor shall be submitted for publication elsewhere while under consideration by this Publication.

AUTHORSHIP RESPONSIBILITY: Each author certifies that he or she has participated sufficiently in the intellectual content, the analysis of data, if applicable, and the writing of the Work to take public responsibility for it. Each has reviewed the final version of the Work, believes it represents valid work, and approves it for publication. Moreover, should the editors of the Publication request the data upon which the work is based, they shall produce it.

DISCLAIMER: Each author warrants that this Work contains no libelous or unlawful statements and does not infringe on the rights of others. If excerpts (e.g., text, figures, tables, illustrations, or audio/video files) from copyrighted works are included, a written release will be secured by the authors prior to submission, and credit to the original publication will be properly acknowledged. Each author further warrants that he or she has obtained, prior to submission, written releases from patients whose names or likenesses are submitted as part of the Work. Should the Editor or LWW request copies of such written releases, authors shall provide them in a timely manner.

PREPRINTS: Upon acceptance of the article for publication, each author warrants that he/she will promptly remove any prior versions of this work (normally a preprint) that may have been posted to an electronic server.

TRANSFER OF COPYRIGHT

AUTHORS' OWN WORK: In consideration of *The Journal*'s publication of the Work, the authors hereby transfer, assign, and otherwise convey all copyright ownership worldwide, in all languages, and in all forms of media now or hereafter known, including electronic media such as CD-ROM, Internet, and Intranet, to LWW. If LWW and the Editor should decide for any reason not to publish an author's submission to the Work, one of them shall give prompt notice of the decision to the corresponding author, this agreement shall terminate, and none of the author, LWW, or the Editor shall be under any further liability or obligation. Each author grants LWW the rights to use his or her name and biographical data (including professional affiliation) in the Work and in its or the Publication's promotion.

***Copyright Transfer Form 2**

Click here to download high resolution image

WORK MADE FOR HIRE: If this Work or any element thereof has been commissioned by another person or organization, or if it has been written as part of the duties of an employee, an authorized representative of the commissioning organization or employer must also sign this form stating his or her title in the organization.

GOVERNMENT EMPLOYEES: If the Work or a portion of it has been created in the course of any author's employment by the United States Government, check the "Government" box at the end of this form. A work prepared by a government employee as part of his or her official duties is called a "work of the U.S. Government" and is not subject to copyright. If it is not prepared as part of the employee's official duties, it may be subject to copyright.

FINANCIAL DISCLOSURE: Each author warrants that he or she has no commercial associations (e.g., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the Work, except as disclosed on a separate attachment. All funding sources supporting the Work and all institutional or corporate affiliations of the authors are acknowledged in a footnote in the Work.

INSTITUTIONAL REVIEW BOARD/ANIMAL CARE COMMITTEE APPROVAL: Each author warrants that his or her institution has approved the protocol for any investigation involving humans or animals and that all experimentation was conducted in conformity with ethical and humane principles of research.

WARRANTIES: Each author warranty above is made for the benefit of LWW and the Editor; each author agrees to indemnify those parties for any breach of such warranties.

"PUBLIC ACCESS POLICY" FUNDING DISCLOSURE

Please disclose below if you have received funding for research on which your article is based from any of the following organizations:

- ☐ National Institutes of Health (NIH)
- ☐ Wellcome Trust
- ☐ Howard Hughes Medical Institute (HHMI)
- ☐ Other: Please List _____

Signature Shang-Chi Chang Printed Name Shang-Chi Chang Date Aug 10, 2007

☑ Author's Own Work ☐ Work for Hire ☐ Government Financial Disclosure Attached

Signature William Chen Printed Name William Tzu Liang Chen Date Aug 10, 2007

☑ Author's Own Work ☐ Work for Hire ☐ Government Financial Disclosure Attached

Signature Hsiu Chi Chiang Printed Name Hsiu Chi Chiang Date Aug 10, 2007

☑ Author's Own Work ☐ Work for Hire ☐ Government Financial Disclosure Attached

Signature Tao Wei Ke Printed Name Tao-Wei Ke Date Aug 10, 2007

Wen-Chien Tang Wen-Chien Tang Aug 10, 2007

*Copyright Transfer Form 3
Click here to download high resolution image

✓Author's Own Work ☐Work for Hire ☐Government Financial Disclosure Attached

COMPLIANCE WITH NIH AND OTHER RESEARCH FUNDING AGENCY ACCESSIBILITY REQUIREMENTS

A number of research funding agencies now require or request authors to submit the post-print (the article after peer review and acceptance but not the final published article) to a repository that is accessible online by all without charge. Within medical research, three funding agencies in particular have announced such policies:

- The U.S. National Institutes of Health (NIH) requires authors to deposit post-prints based on NIH-funded research in its repository PubMed Central (PMC) within twelve months after publication of the final article in the journal.

- The Howard Hughes Medical Institute (HHMI) requires as a condition of research grants, deposit in PMC, but in its case within six months after publication of the final article.

- The Wellcome Trust requires, as a condition of research grants, deposit in UK PubMed Central within six months after publication of the final article.

As a service to our authors, LWW will identify to National Library of Medicine (NLM) articles that require deposit. This Copyright Transfer Agreement provides the mechanism for identifying such articles. LWW will transmit the post-print of an article based on research funded in whole or in part by one or more of these three agencies to Pub Med Central.
Upon NIH request, it remains the legal responsibility of the author(s) to confirm with NIH the provenance of their manuscript for purposes of deposit.
Author(s) will not deposit their articles themselves.
Author(s) will not alter the post-print already transmitted to NIH.
Author(s) will not authorize the display of the post-print prior to:
(a) 12 months following publication of the final article, in the case of NIH,
(b) 6 months following publication of the final article, in the case of Wellcome Trust and HHMI.

AUTHOR(S) POSTING OF ARTICLES TO AN INSTITUTIONAL REPOSITORY

The Journal will permit the author(s) to deposit for display a "post-print" (the final manuscript after peer-review and acceptance for publication but prior to the publisher's copyediting, design, formatting, and other services) 12 months after publication of the final article on his/her personal web site, university's institutional repository or employer's intranet, subject to the following:

- You may only deposit the post-print.

- You may not update the post-print text or replace it with a proof or with the final published version.

- You may not include the post-print or any other version of the article in any commercial site or in any repository owned or operated by any third party. For authors of articles based on research funded by NIH, Wellcome Trust, HHMI, or other funding agency, see below for the services that LWW will provide on your behalf to comply with "Public Access Policy" guidelines.

- You may not display the post-print until twelve months after publication of the final article.

- You must attach the following notice to the post-print: "This is a non-final version of an article published in final form in (provide complete journal citation)".

- You shall provide a link in the post-print to the *The Journal* website.

Laparoscopic Excision is an Alterative Method for Rectal Gastrointestinal Stromal Tumor

A Case Report

Sheng-Chi Chang, MD, Tao-Wei Ke, MD, Hua-Che Chiang, MD,

Christina Wu, BS, William Tzu-Liang Chen, MD

Division of Colorectal Surgery, Department of Surgery, China Medical University Hospital, Taichung, Taiwan

Corresponding author:
William Tzu-Liang Chen, MD.
Address: No.2, Yu-Der Road, Taichung 404, Taiwan
TEL:0966202253,+886-4-22052121-1638
Fax:+886-4-22029083
E-mail: tzuliang611@yahoo.com

Reprints :
Sheng-Chi Chang, MD.
E-mail : aaa54382000@yahoo.com.tw

Case report

Laparoscopic Excision is an Alterative Method for Rectal Gastrointestinal Stromal Tumor

A Case Report

Abstract:

Gastrointestinal stromal tumors are rarely found in the anorectum and account for less than 0.3 percent of all rectal malignancies. The major treatment of rectal GISTs is complete resection of the primary tumor with negative microscopic margin. We present an alternative method, laparoscopic-assisted local excision of rectal GIST. This was a patient with a 5 cm x 4 cm x 3 cm GIST located 4 cm above the dentate line in the right rectal wall. The tumor was mobilized by laparoscopic dissection with a clear safe margin and the specimen was removed from anus. The patient had a smooth recovery and no recurrence after 31 months following the procedure. This experience suggests that laparoscopic excision is a safe alternative for rectal GIST, offering the advantage of better visualization of structures and sparing the patient from an unnecessary abdominoperineal resections.

Key Wards: GIST, rectal, laparoscopy, excision

Laparoscopic Excision is an Alterative Method for Rectal Gastrointestinal Stromal Tumor

A Case Report

Introduction

The gastrointestinal stromal tumor (GIST) constitutes the largest group of gastrointestinal mesenchymal tumor that is most commonly found in the stomach and small bowel. Anorectal GISTs account for less than 0.3% of all rectal malignancies and comprise approximately 5% of all GISTs. [1] These tumors have a characteristic mutation in the KIT proto-oncogene that results in overexpression of the KIT protein from the interstitial cell of Cajal (ICC).[1]

While the majority of rectal GIST cases are treated with a complete resection of the primary tumor, the best surgical method for rectal GISTs remains controversial. Local excision is suggested in patients with "benign" rectal GISTs (<5 cm in size and <5 mitoses/50 HPF) for the advantage of minimal morbidity and sphincter preservation.[2] Various techniques of local excision have been established, such as the transrectal approach, the transsacral approach and the transvaginal approach. Taking into consideration the magnifying capabilities of laparoscopy when used for visualization of the pelvis cavity, laparoscopic surgery for the rectal tumor can offer adequate surgical margin, less tissue trauma, and thus an alternative method for management of rectal GISTs. In this present case, we performed a laparoscopic-assisted wide excision of rectal GIST on an elderly woman, resulting in a favorable course of recovery as described in this article.

Case Report

Clinical Course

The patient was a 67-year-old female with history of hypertension and cerebrovascular disease. She visited to our gynecologic clinic for a regular Pap smear examination in November 2006. On the initial examination, a 5 cm in diameter mass with smooth surface was palpated in the right lateral wall of the rectum about 4 cm above the dentate line. The rectal mass was firm, immobile, and painless. Tracing back to her symptoms, the patient mentioned a heavy sensation in the lower abdomen along with nocturia and frequent urination for six months. Peripheral blood tests, blood biochemistry tests, and routine urinalysis at the time of the initial examination did not reveal any abnormal findings. Tumor marker tests showed normal levels of carcinoembryonic antigen and carbohydrate antigen 19-9. A urodynamic test reported normal bladder function. Further colonoscopic examination revealed a 5 cm bulging mass with an intact mucosal surface, located at the lower rectal valve (Fig. 1). Pelvic magnetic resonance imaging (MRI) revealed a 5 cm x 4 cm round, smooth mass protruding from the right rectal wall with no invasion of surrounding tissue and no pelvic lymph node enlargement (Fig. 2). A mesenchymal tumor composed of spindle cells with infrequent mitosis was identified during a transrectal needle biopsy (Fig. 3). An immunohistological examination showed strong positive staining for c-kit and CD34 while there was negative staining for smooth muscle actin, desmin, and S-100. Preoperative diagnosis was a 5 cm low-grade malignant GIST originating from the low rectum without lymph node enlargement. Based on these findings, local resection of the tumor via laparoscopy was considered as a viable approach.

Surgical Procedure

A mechanical bowel preparation, achieved by using 90 ml of sodium phosphate (NaP) diluted with a cold clear liquid or water, was given at 6:00-7:00PM before the day of surgery. Broad-spectrum intravenous antibiotics were given preoperatively. The patient was placed in a standard lithotomy position and received general endotracheal anesthesia. A supraumbilical 12 mm trocar was inserted and pneumoperitoneum was maintained at 10-14 mmHg. In addition, four 5 mm trocars were placed in the left lower quadrant, left iliac fossa, right lower quadrant, and right iliac fossa, respectively, under laparoscopic guidance (Fig. 4). A Fujinon flexible laparoscope was used. The surgery began with maneuvering the uterus and suspending it in the abdominal cavity to provide adequate exposure of the pelvis. The whole sigmoid colon was mobilized after dividing the left lateral avascular attachments. The retrorectal space was entered after division of the posterior peritoneal reflection. The bilateral pararectal fascia was then separated along the rectum to develop the retrorectal space between the rectal fascia propria and the presacral fascia. During the presacral dissection, the hypogastric nerve branches should be identified and preserved carefully, also avoiding injury to the presacral venous plexus. Mobilization of the upper and mid-rectum was accomplished after dissecting the anterior wall of rectum via Denonvillier's fascia. Then, the smooth-surfaced tumor was gradually exposed and identified near the right side of the posterior rectal wall (Fig.5). The mass, located at right posterior aspect of the rectal wall, was carefully dissected free from the surrounding areolar tissue with a clear safe margin under direct laparoscopic vision. The tumor was properly mobilized, completely excised with partial rectal mucosa, and then removed via the low rectal wound. Finally, the low rectal wound was repaired with transanal interrupted suturing. The operative procedure was completed in 170 minutes and blood loss volume was 50 ml. No incision

was visible over the abdominal wall aside from the site of trocar insertion.

The tumor was macroscopically encapsulated and measured to be 5 cm x 4 cm x 3 cm in size (Fig.6A). The cut surface was whitish and solid with a homogenous consistency, scattered with blood clots (Fig.6B). The tumor was growing mainly from the tunica muscularis propria toward the lateral tunica serosa. There was no tumor infiltration on the mucosal surface. The histopathological report revealed tumor growth mainly in the subserosal layer and a composition of spindle cells. There were zero mitoses per 50 high-power fields (HPF), and the findings corresponded to those of a low-grade malignant GIST. The section margins were all free of tumor. The immunochemical study revealed positive results for CD 117 and CD 34, and negative results for smooth muscle actin, desmin, and S-100 protein.

After operation, the patient was offered a full liquid diet as the first meal after surgery, but no dietary restrictions thereafter. She was encouraged to ambulate as soon as possible after the procedure. Oral analgesic Diclofenac was used for pain control. The patient experienced a fast and smooth post-operational recovery. There is no complication during post operative course and she was discharged on the fourth day after surgery. No adjuvant chemotherapy was given and the patient was regularly followed-up at our clinics. To date, at 31 months after surgery, there has been no reported recurrence.

Discussion

Gastrointestinal stromal tumors are a mesenchymal tumor derived from the interstitial cells of Cajal. GISTs are most commonly found in the stomach (60%-70%), followed by the small intestine (20%-25%), and only about 5% of all GISTs originate in the rectum.[3] The typical rectal GIST is often located in the submucosa, regardless of its extension into the muscularis propria. and few (10-15%) will spread to the mucosa.[4] In 2001, the National Institutes of Health (NIH) workshop defined the role of KIT immunopositivity in the diagnosis of GISTs and assessing the risk of malignant behavior ranging from very low to high based on tumor size and mitotic count. A rate of ≤ 5 mitoses per 50 HPF is commonly used as a limit for a tumor with expected benign behavior, and has been proven to be a way of distinguishing benign tumors from malignant ones, especially in gastric GISTs.[5]

The key to adequate control of rectal GISTs is complete surgical resection of the primary tumor with negative microscopic margin (R0 resection). Neither radiotherapy nor conventional chemotherapy has any proven efficacy as adjuvant therapy. Unlike adenocarcinoma, GISTs rarely metastasize to local regional lymph nodes and lymphadenectomy is considered only for evident nodal involvement. Although surgical resection of GISTs was widely known as the best choice, the rarity of rectal GISTs makes it difficult to ascertain the extent of surgical resection in such situations. Local excision offers the advantages of minimal morbidity and sphincter preservation while radical surgery, including low anterior resection and abdominoperineal resection, may offer complete removal of the rectal tumor. However, there is no evidence that procedures more extensive than removal of all gross neoplasm prolong survival or delay recurrences.[6] Miettinen et al[2] collected 144 cases of anorectal GISTs and described the tumors in very low-risk group (< 2 cm of size and < 5 mitoses/HPF) have

an indolent behavior and low rates of recurrence, making them suitable candidates for local excision. In the study, the majority of anorectal GISTs with malignant behavior (> 5 cm of size or > 5 mitoses/50 HPF) that had high rates of recurrence or developed metastasis (55-85%) revealed no significant differences in survival rates when comparing types of surgery performed. Currently, en bloc resection of the tumor (R0 resection) and surrounding normal tissue is still the conventional treatment of rectal GISTs, followed by surveillance for metastasis and recurrence.[7] Radical surgery involves anterior or abdominoperineal resection with sacrifice of sphincter function, making it an anatomical resection of the rectum that may provide a better oncologic outcome. Despite the promising results, radical surgery may also result in morbid complications such as anastomotic leakage, sepsis, or incontinence. It is also important to note that patients may not always tolerate the use of a stoma after abdominoperineal resection. Therefore, laparoscopic tumor excision may be an alternative method of surgery, considering its advantages. First, laparoscopic surgery offers better visualization of the structure, especially in narrow anatomic spaces, and allows ease in excising the rectal GIST with an adequate safety margin under laparoscopy. Second, laparoscopic tumor excision results in minimal trauma to the rectum and preserves the sphincter, which reduces the rate of morbidity and mortality. In the present case, R0 resection of the rectal GIST was achieved laparoscopically with no postoperative complications. Neither local recurrence nor distant metastasis was noted even after the 31 month follow-up.

Several minimally invasive treatment options had been published for favorable lesions in the rectum. The transanal approach is most frequently performed for local excision of anorectal tumors, including those within 3 cm from the dentate line.[8] However, this approach is limited by size and position of the tumor and will not ensure

an adequate tumor-free margin if the tumor is too large or too high in the rectum. In this patient, her tumor is relatively large, immobile and in higher position, if transanal approach, might result tumor perforation and unclear cut margin. So transanal excision of the tumor is not favor in this case. Transsacral (transcoccygeal) excision was described by Kraske[9] as a way to resolve higher lesions in the posterior wall of the rectum. Unfortunately, this technique will damage surrounding tissue and is associated with an increased risk of complications such as fecal fistula, anal dysfunction, and poor perineal wound healing.[10] A transsphincteric approach, as originally described by Mason[11], is the usual approach for lower rectal tumors that are too large for a transanal resection, but long-term continence still remains as a main concern after the procedure. Minia et al[12] published a safe alternative method for larger tumors in the rectal wall using the transvaginal approach which resulted in extremely low morbidity rates. This approach still had its limitations of gender and location of the tumor contributing to an unclear margin. As presented in our case, laparoscopic tumor excision can provide both, good visualization to attain an acceptable tumor free margin and no limitations on the lesion site in the rectum. Furthermore, removal of the specimen via the rectum can offer better cosmetic results and decrease postoperative wound pain. Several published case reports[13-15] have discussed the laparoscopic resection of presacral tumors, including sacrococcygeal teratomas, Schwannomas and ganglioneurofibroma. The conclusions of these reports agreed with our results: laparoscopy is a safe and efficient approach for pelvic tumors, providing better visualization of the abdomen and pelvis, especially in narrow anatomic spaces.

The new tyrosine kinase inhibitor, STI571 (imatinib or now known as Glivec), may also be used as a potential treatment for GISTs, in addition to surgical resection. Glivec demonstrated significant activity in the management of unresectable or metastatic

malignant GISTs; effects included≤ 50% shrinkage in size or stabilization of the disease in most patients.[16] Glivec was also approved by US Food and Drug Administration (FDA) for metastatic and unresectable GISTs in 2002. Although the role of adjuvant and neoadjuvent use of Glivec is still undergoing clinical trials, we believe it may change the prognosis and treatment strategies of rectal GISTs in the near future. Currently Glivec for adjuvant treatment is not reimbursed by our National Health Insurance; therefore, we did not give Glivec preoperatively.

In conclusion, the surgical technique and outcomes discussed above indicate the possibility of laparoscopic tumor excision becoming an alternative treatment for such rectal GISTs. As demonstrated in this case, it is a safe and minimally invasive surgical modality that holds promising results. This evidence leads us to believe that the laparoscopic approach of rectal GISTs provides a reasonable alterative and should be consider more often.

Reference

1. Changchien CR, Wu MC, Tasi WS, Tang R, Chiang JM, Chen JS, Huang SF, Wang JY, Yeh CY. Evaluation of prognosis for malignant rectal gastrointestinal stromal tumor by clinical parameters and immunohistochemical staining. Dis Colon Rectum 2004;47:1922-9.
2. Miettinen M, Furlong M, Sarlomo-Rikla M, Burke A, Larsota J. Gastrointestinal stromal tumors, intramural leiomyomas and leiomyosarcomas in the rectum and anus. Am J Surg Pathol 2001;25:1124-33.
3. Tran T, Davila JA, El-Serag HB. The epidemiology of malignant gastrointestinal stromal tumors: an analysis of 1,458 cases from 1992 to 2000. Am J Gastroenterol 2005;100:162-8.
4. Tworek JA, Goldblum JR, Weiss SW. Stromal tumors of the anorectum: a clinicopathologic study of 22 cases. Am J Surg Pathol 1999;23:946-54.
5. Miettinen M, Sarlomo-Rikala M, Lasota J. Gastrointestinal stromal tumors: recent advances in understanding of their biology. Hum Pathol 1999;30:1213-20.
6. Matsushima K, Kayo M. Transsacral Approach for Rectal GIST. Surg Today 2007;37:698–701.
7. Lo SS, Papachristou GI, Finkelstein SD, Conroy WP, Schraut WH, Ramanathan RK. Neoadjuvant Imatinib in gastrointestinal stromal tumor of the rectum: report of a case. Dis Colon Rectum 2005;48:1316–9.
8. Koscinski T, Malinger S, Drews M. Local excision of rectal carcinoma not exceeding the muscularis layer. Colorectal Dis 2003;5:159-63
9. Kraske PZ. Zur Extirpation hechsitzender Mastdarm Krebse. Verh Dtsch Gs Chir 1885;14:465-74.
10. Terkivatan T, Hoed PT, Lange JFM Jr, Koot VCM, Goch JJ, Veen HF. The place of

the posterior surgical approach for the lesions of the rectum. Dig Surg 2005;22:86–90.

11. Mason AY. Surgical access to the rectum—a transsphincteric exposure. Proc R Soc Med 1970;63:91-4.
12. Hellan M, Maker VK. Transvaginal excision of a large rectal stromal tumor: an alternative. Am J Surg 2006;161:121-3.
13. Konstantinidis K, Theodoropoulos GE, Sambalis G, Georgiou M, Vorias M, Anastassakou K, Mpontozoglou N. Laparoscopic resection of presacral Schwannomas. Surg Laparosc Endosc Percutan 2005;15:302-4.
14. Bax NMA, van der Zee DC. The laparoscopic approach to sacrococcygeal teratoma. Surg Endosc 2003;18:128-30.
15. Kohler C, Kuhne-Jeid R, Klemm P, Tozzi R, Schneider A. Resection of presacral ganglioneurofibroma by laparoscopy. Surg Endosc 2003;17:1494-500.
16. Eisenberg BL, Judson I. Surgery and Imatinib in the management of GIST: Emerging approaches to adjuvant and neoadjuvant therapy. Ann Surg Oncol 2004;11:465-75.

FIGURE 1. Colonoscopic image of the 5 cm bulging mass with an intact mucosal surface. The mass was located at the lower rectal valve.

FIGURE 2. The pelvic magnetic resonance imaging (MRI) showed a rectal mass and its anatomic relationship to adjacent structures. A: Axial view B: Sagittal view

FIGURE 3.**A** The tumor was composed of spindle cells arranged in an interlacing pattern (H&E stain). **B** The tumor cells were immunoreactive for CD 117 (immunoperoxidase)

FIGURE 4. Schematic of laparoscopy port placement for excision of rectal GIST

FIGURE 5.Exposure of the rectal gastrointestinal stromal tumor at right side of the posterior rectal wall via laparoscopy

FIGURE 6.A.Grossly, the tumor was encapsulated and measured 5 x 4 x 3 cm in size. B. The cut surface was whitish and solid, with a homogenous consistency and scattered blood clots

Laparoscopic Excision is an Alterative Method for Rectal Gastrointestinal Stromal Tumor

A Case Report

Sheng-Chi Chang, MD, Tao-Wei Ke, MD, Hua-Che Chiang, MD,

Christina Wu, BS, William Tzu-Liang Chen, MD

Division of Colorectal Surgery, Department of Surgery, China Medical University Hospital, Taichung, Taiwan

Corresponding author:
William Tzu-Liang Chen, MD.
Address: No.2, Yu-Der Road, Taichung 404, Taiwan
TEL:0966202253,+886-4-22052121-1638
Fax:+886-4-22029083
E-mail: tzuliang611@yahoo.com

Reprints :
Sheng-Chi Chang, MD.
E-mail : aaa54382000@yahoo.com.tw

Case report

Laparoscopic Excision is an Alterative Method for Rectal Gastrointestinal Stromal Tumor

A Case Report

Abstract:

Gastrointestinal stromal tumors are rarely found in the anorectum and account for less than 0.3 percent of all rectal malignancies. The major treatment of rectal GISTs is complete resection of the primary tumor with negative microscopic margin. We present an alternative method, laparoscopic-assisted local excision of rectal GIST. This was a patient with a 5 cm x 4 cm x 3 cm GIST located 4 cm above the dentate line in the right rectal wall. The tumor was mobilized by laparoscopic dissection with a clear safe margin and the specimen was removed from anus. The patient had a smooth recovery and no recurrence after 31 months following the procedure. This experience suggests that laparoscopic excision is a safe alternative for rectal GIST, offering the advantage of better visualization of structures and sparing the patient from an unnecessary abdominoperineal resections.

Key Wards: GIST, rectal, laparoscopy, excision

Laparoscopic Excision is an Alterative Method for Rectal Gastrointestinal Stromal Tumor

A Case Report

Introduction

The gastrointestinal stromal tumor (GIST) constitutes the largest group of gastrointestinal mesenchymal tumor that is most commonly found in the stomach and small bowel. Anorectal GISTs account for less than 0.3% of all rectal malignancies and comprise approximately 5% of all GISTs. [1] These tumors have a characteristic mutation in the KIT proto-oncogene that results in overexpression of the KIT protein from the interstitial cell of Cajal (ICC).[1]

While the majority of rectal GIST cases are treated with a complete resection of the primary tumor, the best surgical method for rectal GISTs remains controversial. Local excision is suggested in patients with "benign" rectal GISTs (<5 cm in size and <5 mitoses/50 HPF) for the advantage of minimal morbidity and sphincter preservation.[2] Various techniques of local excision have been established, such as the transrectal approach, the transsacral approach and the transvaginal approach. Taking into consideration the magnifying capabilities of laparoscopy when used for visualization of the pelvis cavity, laparoscopic surgery for the rectal tumor can offer adequate surgical margin, less tissue trauma, and thus an alternative method for management of rectal GISTs. In this present case, we performed a laparoscopic-assisted wide excision of rectal GIST on an elderly woman, resulting in a favorable course of recovery as described in this article.

Case Report

Clinical Course

The patient was a 67-year-old female with history of hypertension and cerebrovascular disease. She visited to our gynecologic clinic for a regular Pap smear examination in November 2006. On the initial examination, a 5 cm in diameter mass with smooth surface was palpated in the right lateral wall of the rectum about 4 cm above the dentate line. The rectal mass was firm, immobile, and painless. Tracing back to her symptoms, the patient mentioned a heavy sensation in the lower abdomen along with nocturia and frequent urination for six months. Peripheral blood tests, blood biochemistry tests, and routine urinalysis at the time of the initial examination did not reveal any abnormal findings. Tumor marker tests showed normal levels of carcinoembryonic antigen and carbohydrate antigen 19-9. A urodynamic test reported normal bladder function. Further colonoscopic examination revealed a 5 cm bulging mass with an intact mucosal surface, located at the lower rectal valve (Fig. 1). Pelvic magnetic resonance imaging (MRI) revealed a 5 cm x 4 cm round, smooth mass protruding from the right rectal wall with no invasion of surrounding tissue and no pelvic lymph node enlargement (Fig. 2). A mesenchymal tumor composed of spindle cells with infrequent mitosis was identified during a transrectal needle biopsy (Fig. 3). An immunohistological examination showed strong positive staining for c-kit and CD34 while there was negative staining for smooth muscle actin, desmin, and S-100. Preoperative diagnosis was a 5 cm low-grade malignant GIST originating from the low rectum without lymph node enlargement. Based on these findings, local resection of the tumor via laparoscopy was considered as a viable approach.

Surgical Procedure

A mechanical bowel preparation, achieved by using 90 ml of sodium phosphate (NaP) diluted with a cold clear liquid or water, was given at 6:00-7:00PM before the day of surgery. Broad-spectrum intravenous antibiotics were given preoperatively. The patient was placed in a standard lithotomy position and received general endotracheal anesthesia. A supraumbilical 12 mm trocar was inserted and pneumoperitoneum was maintained at 10-14 mmHg. In addition, four 5 mm trocars were placed in the left lower quadrant, left iliac fossa, right lower quadrant, and right iliac fossa, respectively, under laparoscopic guidance (Fig. 4). A Fujinon flexible laparoscope was used. The surgery began with maneuvering the uterus and suspending it in the abdominal cavity to provide adequate exposure of the pelvis. The whole sigmoid colon was mobilized after dividing the left lateral avascular attachments. The retrorectal space was entered after division of the posterior peritoneal reflection. The bilateral pararectal fascia was then separated along the rectum to develop the retrorectal space between the rectal fascia propria and the presacral fascia. During the presacral dissection, the hypogastric nerve branches should be identified and preserved carefully, also avoiding injury to the presacral venous plexus. Mobilization of the upper and mid-rectum was accomplished after dissecting the anterior wall of rectum via Denonvillier's fascia. Then, the smooth-surfaced tumor was gradually exposed and identified near the right side of the posterior rectal wall (Fig.5). The mass, located at right posterior aspect of the rectal wall, was carefully dissected free from the surrounding areolar tissue with a clear safe margin under direct laparoscopic vision. The tumor was properly mobilized, completely excised with partial rectal mucosa, and then removed via the low rectal wound. Finally, the low rectal wound was repaired with transanal interrupted suturing. The operative procedure was completed in 170 minutes and blood loss volume was 50 ml. No incision

was visible over the abdominal wall aside from the site of trocar insertion.

The tumor was macroscopically encapsulated and measured to be 5 cm x 4 cm x 3 cm in size (Fig.6A). The cut surface was whitish and solid with a homogenous consistency, scattered with blood clots (Fig.6B). The tumor was growing mainly from the tunica muscularis propria toward the lateral tunica serosa. There was no tumor infiltration on the mucosal surface. The histopathological report revealed tumor growth mainly in the subserosal layer and a composition of spindle cells. There were zero mitoses per 50 high-power fields (HPF), and the findings corresponded to those of a low-grade malignant GIST. The section margins were all free of tumor. The immunochemical study revealed positive results for CD 117 and CD 34, and negative results for smooth muscle actin, desmin, and S-100 protein.

After operation, the patient was offered a full liquid diet as the first meal after surgery, but no dietary restrictions thereafter. She was encouraged to ambulate as soon as possible after the procedure. Oral analgesic Diclofenac was used for pain control. The patient experienced a fast and smooth post-operational recovery. There is no complication during post operative course and she was discharged on the fourth day after surgery. No adjuvant chemotherapy was given and the patient was regularly followed-up at our clinics. To date, at 31 months after surgery, there has been no reported recurrence.

Discussion

Gastrointestinal stromal tumors are a mesenchymal tumor derived from the interstitial cells of Cajal. GISTs are most commonly found in the stomach (60%-70%), followed by the small intestine (20%-25%), and only about 5% of all GISTs originate in the rectum.[3] The typical rectal GIST is often located in the submucosa, regardless of its extension into the muscularis propria. and few (10-15%) will spread to the mucosa.[4] In 2001, the National Institutes of Health (NIH) workshop defined the role of KIT immunopositivity in the diagnosis of GISTs and assessing the risk of malignant behavior ranging from very low to high based on tumor size and mitotic count. A rate of ≤ 5 mitoses per 50 HPF is commonly used as a limit for a tumor with expected benign behavior, and has been proven to be a way of distinguishing benign tumors from malignant ones, especially in gastric GISTs.[5]

The key to adequate control of rectal GISTs is complete surgical resection of the primary tumor with negative microscopic margin (R0 resection). Neither radiotherapy nor conventional chemotherapy has any proven efficacy as adjuvant therapy. Unlike adenocarcinoma, GISTs rarely metastasize to local regional lymph nodes and lymphadenectomy is considered only for evident nodal involvement. Although surgical resection of GISTs was widely known as the best choice, the rarity of rectal GISTs makes it difficult to ascertain the extent of surgical resection in such situations. Local excision offers the advantages of minimal morbidity and sphincter preservation while radical surgery, including low anterior resection and abdominoperineal resection, may offer complete removal of the rectal tumor. However, there is no evidence that procedures more extensive than removal of all gross neoplasm prolong survival or delay recurrences.[6] Miettinen et al[2] collected 144 cases of anorectal GISTs and described the tumors in very low-risk group (< 2 cm of size and < 5 mitoses/HPF) have

an indolent behavior and low rates of recurrence, making them suitable candidates for local excision. In the study, the majority of anorectal GISTs with malignant behavior (> 5 cm of size or > 5 mitoses/50 HPF) that had high rates of recurrence or developed metastasis (55-85%) revealed no significant differences in survival rates when comparing types of surgery performed. Currently, en bloc resection of the tumor (R0 resection) and surrounding normal tissue is still the conventional treatment of rectal GISTs, followed by surveillance for metastasis and recurrence.[7] Radical surgery involves anterior or abdominoperineal resection with sacrifice of sphincter function, making it an anatomical resection of the rectum that may provide a better oncologic outcome. Despite the promising results, radical surgery may also result in morbid complications such as anastomotic leakage, sepsis, or incontinence. It is also important to note that the use of a stoma after abdominoperineal resection may not always be tolerated by patients. Therefore, laparoscopic tumor excision may be an alternative method of surgery, considering its advantages. First, laparoscopic surgery offers better visualization of the structure, especially in narrow anatomic spaces, and allows ease in excising the rectal GIST with an adequate safety margin under laparoscopy. Second, laparoscopic tumor excision results in minimal trauma to the rectum and preserves the sphincter, which reduces the rate of morbidity and mortality. In the present case, R0 resection of the rectal GIST was achieved laparoscopically with no postoperative complications. Neither local recurrence nor distant metastasis was noted even after the 31 month follow-up.

Several minimally invasive treatment options had been published for favorable lesions in the rectum. The transanal approach is most frequently performed for local excision of anorectal tumors, including those within 3 cm from the dentate line.[8] However, this approach is limited by size and position of the tumor and will not ensure

an adequate tumor-free margin if the tumor is too large or too high in the rectum. In this patient, her tumor is relatively large, immobile and in higher position, if transanal approach, might result tumor perforation and unclear cut margin. So transanal excision of the tumor is not favor in this case. Transsacral (transcoccygeal) excision was described by Kraske[9] as a way to resolve higher lesions in the posterior wall of the rectum. Unfortunately, this technique will damage surrounding tissue and is associated with an increased risk of complications such as fecal fistula, anal dysfunction, and poor perineal wound healing.[10] A transsphincteric approach, as originally described by Mason[11], is the usual approach for lower rectal tumors that are too large for a transanal resection, but long-term continence still remains as a main concern after the procedure. Minia et al[12] published a safe alternative method for larger tumors in the rectal wall using the transvaginal approach which resulted in extremely low morbidity rates. This approach still had its limitations of gender and location of the tumor contributing to an unclear margin. As presented in our case, laparoscopic tumor excision can provide both, good visualization to attain an acceptable tumor free margin and no limitations on the lesion site in the rectum. Furthermore, removal of the specimen via the rectum can offer better cosmetic results and decrease postoperative wound pain. Several published case reports[13-15] have discussed the laparoscopic resection of presacral tumors, including sacrococcygeal teratomas, Schwannomas and ganglioneurofibroma. The conclusions of these reports agreed with our results: laparoscopy is a safe and efficient approach for pelvic tumors, providing better visualization of the abdomen and pelvis, especially in narrow anatomic spaces.

The new tyrosine kinase inhibitor, STI571 (imatinib or now known as Glivec), may also be used as a potential treatment for GISTs, in addition to surgical resection. Glivec demonstrated significant activity in the management of unresectable or metastatic

malignant GISTs; effects included≤ 50% shrinkage in size or stabilization of the disease in most patients.[16] Glivec was also approved by US Food and Drug Administration (FDA) for metastatic and unresectable GISTs in 2002. Although the role of adjuvant and neoadjuvent use of Glivec is still undergoing clinical trials, we believe it may change the prognosis and treatment strategies of rectal GISTs in the near future. Currently Glivec for adjuvant treatment is not reimbursed by our National Health Insurance; therefore, we did not give Glivec preoperatively.

In conclusion, the surgical technique and outcomes discussed above indicate the possibility of laparoscopic tumor excision becoming an alternative treatment for such rectal GISTs. As demonstrated in this case, it is a safe and minimally invasive surgical modality that holds promising results. This evidence leads us to believe that the laparoscopic approach of rectal GISTs provides a reasonable alterative and should be consider more often.

Reference

1. Changchien CR, Wu MC, Tasi WS, Tang R, Chiang JM, Chen JS, Huang SF, Wang JY, Yeh CY. Evaluation of prognosis for malignant rectal gastrointestinal stromal tumor by clinical parameters and immunohistochemical staining. Dis Colon Rectum 2004;47:1922-9.
2. Miettinen M, Furlong M, Sarlomo-Rikla M, Burke A, Larsota J. Gastrointestinal stromal tumors, intramural leiomyomas and leiomyosarcomas in the rectum and anus. Am J Surg Pathol 2001;25:1124-33.
3. Tran T, Davila JA, El-Serag HB. The epidemiology of malignant gastrointestinal stromal tumors: an analysis of 1,458 cases from 1992 to 2000. Am J Gastroenterol 2005;100:162-8.
4. Tworek JA, Goldblum JR, Weiss SW. Stromal tumors of the anorectum: a clinicopathologic study of 22 cases. Am J Surg Pathol 1999;23:946-54.
5. Miettinen M, Sarlomo-Rikala M, Lasota J. Gastrointestinal stromal tumors: recent advances in understanding of their biology. Hum Pathol 1999;30:1213-20.
6. Matsushima K, Kayo M. Transsacral Approach for Rectal GIST. Surg Today 2007;37:698–701.
7. Lo SS, Papachristou GI, Finkelstein SD, Conroy WP, Schraut WH, Ramanathan RK. Neoadjuvant Imatinib in gastrointestinal stromal tumor of the rectum: report of a case. Dis Colon Rectum 2005;48:1316–9.
8. Koscinski T, Malinger S, Drews M. Local excision of rectal carcinoma not exceeding the muscularis layer. Colorectal Dis 2003;5:159-63
9. Kraske PZ. Zur Extirpation hechsitzender Mastdarm Krebse. Verh Dtsch Gs Chir 1885;14:465-74.
10. Terkivatan T, Hoed PT, Lange JFM Jr, Koot VCM, Goch JJ, Veen HF. The place of

the posterior surgical approach for the lesions of the rectum. Dig Surg 2005;22:86–90.

11. Mason AY. Surgical access to the rectum—a transsphincteric exposure. Proc R Soc Med 1970;63:91-4.
12. Hellan M, Maker VK. Transvaginal excision of a large rectal stromal tumor: an alternative. Am J Surg 2006;161:121-3.
13. Konstantinidis K, Theodoropoulos GE, Sambalis G, Georgiou M, Vorias M, Anastassakou K, Mpontozoglou N. Laparoscopic resection of presacral Schwannomas. Surg Laparosc Endosc Percutan 2005;15:302-4.
14. Bax NMA, van der Zee DC. The laparoscopic approach to sacrococcygeal teratoma. Surg Endosc 2003;18:128-30.
15. Kohler C, Kuhne-Jeid R, Klemm P, Tozzi R, Schneider A. Resection of presacral ganglioneurofibroma by laparoscopy. Surg Endosc 2003;17:1494-500.
16. Eisenberg BL, Judson I. Surgery and Imatinib in the management of GIST: Emerging approaches to adjuvant and neoadjuvant therapy. Ann Surg Oncol 2004;11:465-75.

FIGURE 1. Colonoscopic image of the 5 cm bulging mass with an intact mucosal surface. The mass was located at the lower rectal valve.

FIGURE 2. The pelvic magnetic resonance imaging (MRI) showed a rectal mass and its anatomic relationship to adjacent structures. A: Axial view B: Sagittal view

FIGURE 3.**A** The tumor was composed of spindle cells arranged in an interlacing pattern (H&E stain). **B** The tumor cells were immunoreactive for CD 117 (immunoperoxidase)

FIGURE 4. Schematic of laparoscopy port placement for excision of rectal GIST

FIGURE 5.Exposure of the rectal gastrointestinal stromal tumor at right side of the posterior rectal wall via laparoscopy

FIGURE 6.A.Grossly, the tumor was encapsulated and measured 5 x 4 x 3 cm in size. B. The cut surface was whitish and solid, with a homogenous consistency and scattered blood clots

China Medical University Hospital
Sheng-Chi Chang MD, Department of Colorectal Surgery
2, Yuh-Der Road, Taichung 404, Taiwan
Tel: 886-4-22052121 ext. 1638 FAX:886-4-22029083 E-mail: aaa5438@ms16.hinet.net

February 02, 2010

Maurice E. Arregui MD

Carol EH Scott-Conner MD PhD

Editors in Chief

Surgical Laparoscopy, Endoscopy & Percutaneous Techniques

Re : SLEPT-D-09-00270
Entitled "Laparoscopic Excision is an Alterative Method for Rectal Gastrointestinal Stromal Tumor"

Dear Editor Arregui:

Thank you very much for your review of this manuscript. We are gratified about your substantial comments, and we made the following corrections were based on the pages and paragraph of revised manuscript.

I. The patients in this study had never been reported in other previous publications

II. For Reviewer #1:

- Common 1: Schematic of laparoscopy port placement was added as Figure 4.
- Common 2: Our postoperative care information was added on p.6, 2nd paragraph till p.6 17th line.
- Common 3: The pathologic report of specimen margin was added on P6,

9th line

III. For Reviewer #2:

- Common 1: The discussion for transanal tumor excision was described on p.8, 2nd paragraph till p.9 4th line. Because the tumor size was 5*4 in size, immobile and firm. Transanal was not favor after thorough discussion in our service meeting. The reasons were: 1. This is a relatively large tumor, if via transanally, might iatrogenically perforate the tumor. 2. Our surgeons believe transanally remove that tumor might result of inadequate surgical margin. 3. Our laparoscopic team is well established, and techniques were standardized for colorectal surgery, so we choice laparoscopic approach for this patient without any hesitation.
- Common 2: The discussion for adjuvant Glivec use was described on p.9, 2nd paragraph till p.10 7th line.
- Comment 3: All mentioned grammar had been alerted.

We have made above corrections. I want to thank all of you again in reviewing this paper.

Sincerely yours,

William Tzu-Liang Chen, MD
Division of Colorectal Surgery
Department of Surgery
China Medical University Hospital,
Taichung, Taiwan

Sheng-Chi Chang, MD.
Department of Surgery
China Medical University Hospital
Address: No.2, Yu-Der Road, Taichung 404,Taiwan
TEL:0966202253,
+886-4-22052121-1638
Fax:+886-4-22029083 Aug.10, 2009

Dr. Carol E. H. Scott-Conner,
The Editor-in Chief of
Surgical Laparoscopy, Endoscopy & Percutaneous Techniques

Dear Dr. Carol E. H. Scott-Conner

Enclosed are hard copies of a manuscript entitled "Laparoscopic Excision is an Alterative Method for Rectal Gastrointestinal Stromal Tumor". The manuscript represents our experience of laparoscopic surgery for rectal lesion. All authors have participated in the work to take responsibility for the appropriateness of the method, design, collection, analysis, and interpretation of the data. All have reviewed and approved submission of the final version of the manuscript. The manuscript has not been published in whole or in part and is not being considered for publication elsewhere.

All authors transfer the copyright to their article to Surgical Laparoscopy, Endoscopy & Percutaneous Techniques effective if and when the article is accepted for publication. The copyright covers the exclusive and unlimited rights to reproduce and distribute the article in any form of reproduction (printing, electronic media or any other form); it also covers translation rights for all languages and countries.

Please consider this paper for publication in the "Surgical Laparoscopy, Endoscopy & Percutaneous Techniques". Thank you.

Sincerely,

Sheng-Chi Chang, MD

Tzu-Liang Chen,MD

Hua-Che Chiang, MD.

Tao-Wei Ke, MD

Wen-Chien Ting, MD

Figure 1

Click here to download high resolution image

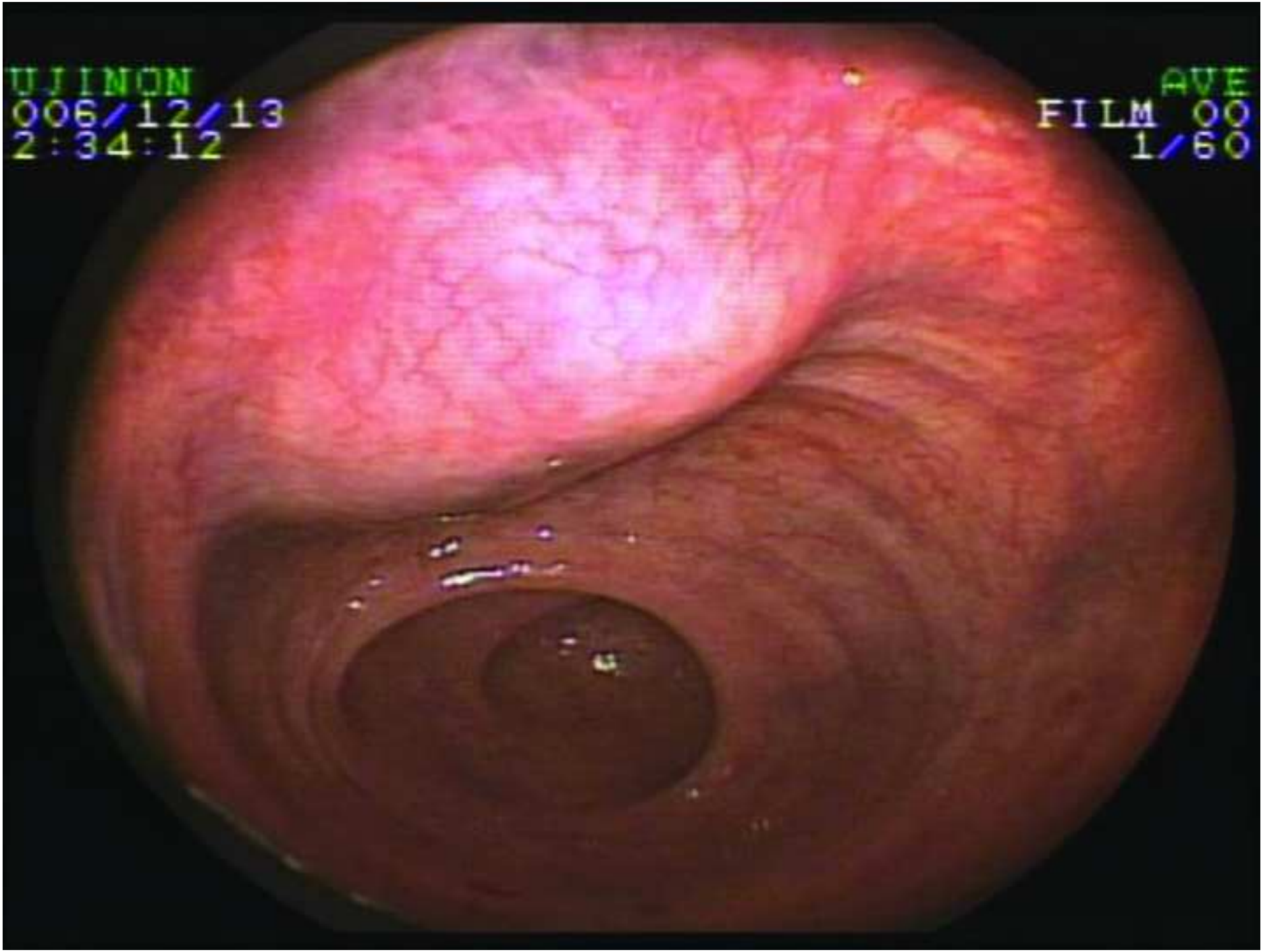


Figure 2A

Click here to download high resolution image

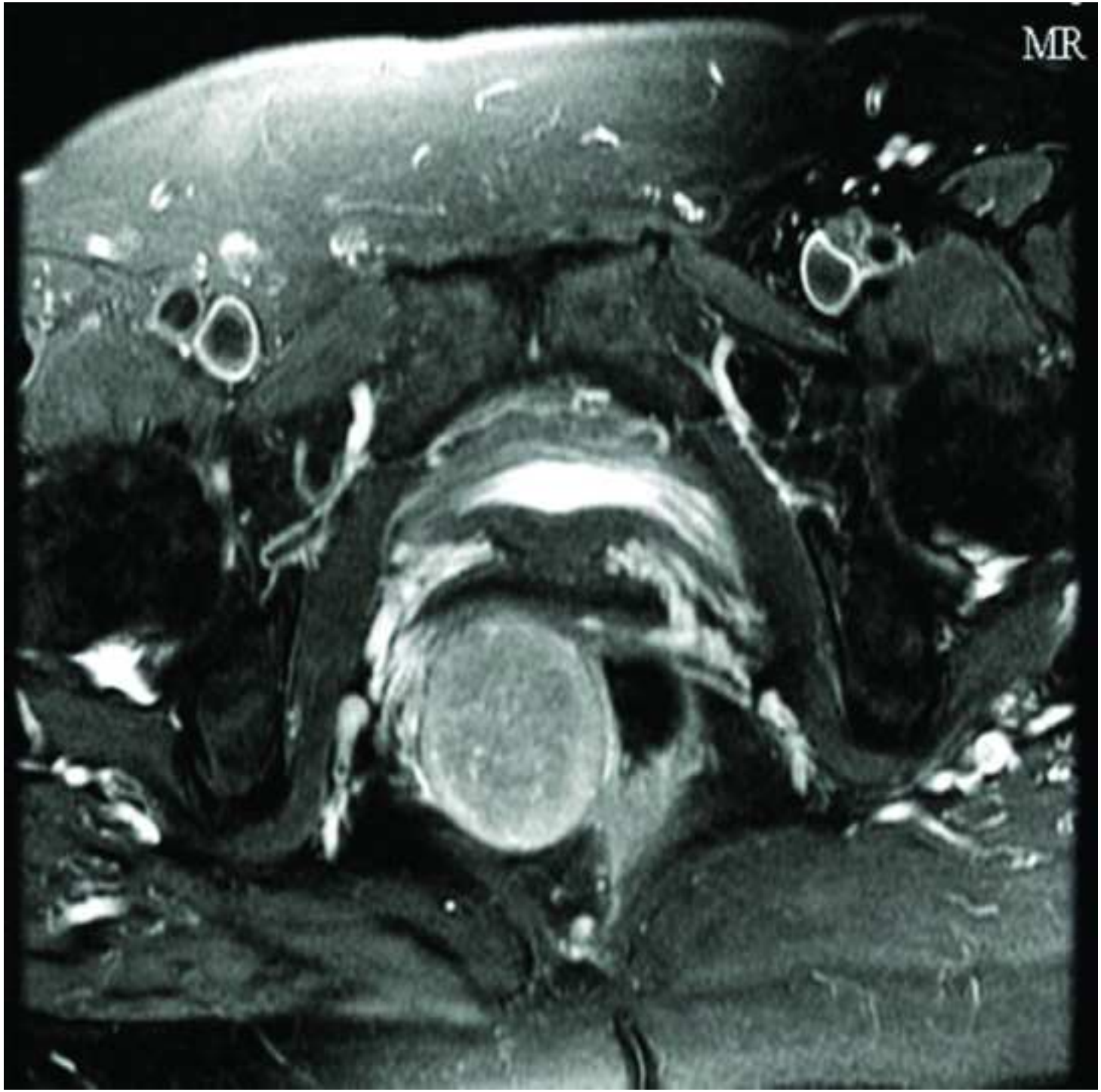


Figure 2B

Click here to download high resolution image

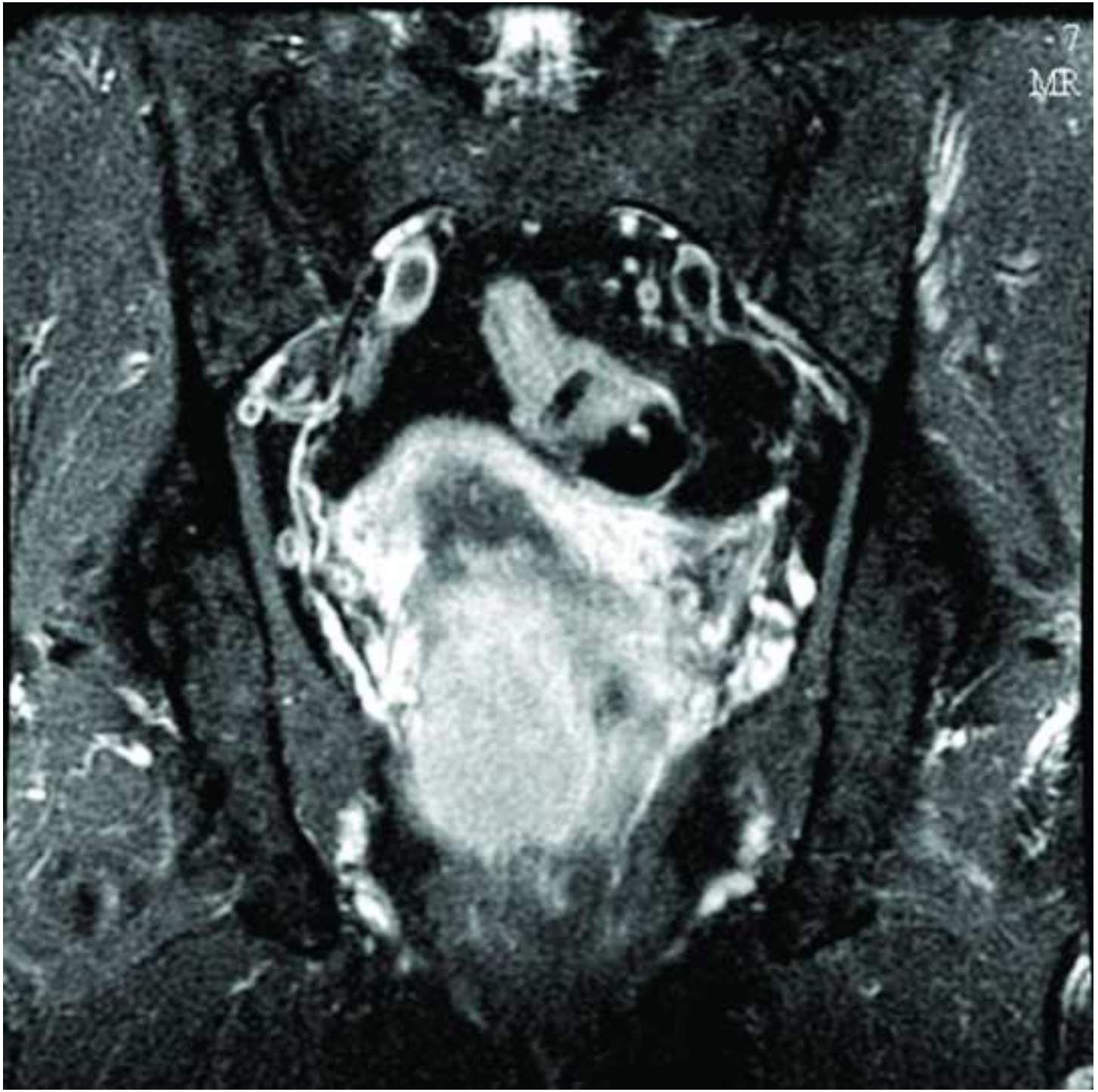


Figure 3A

Click here to download high resolution image

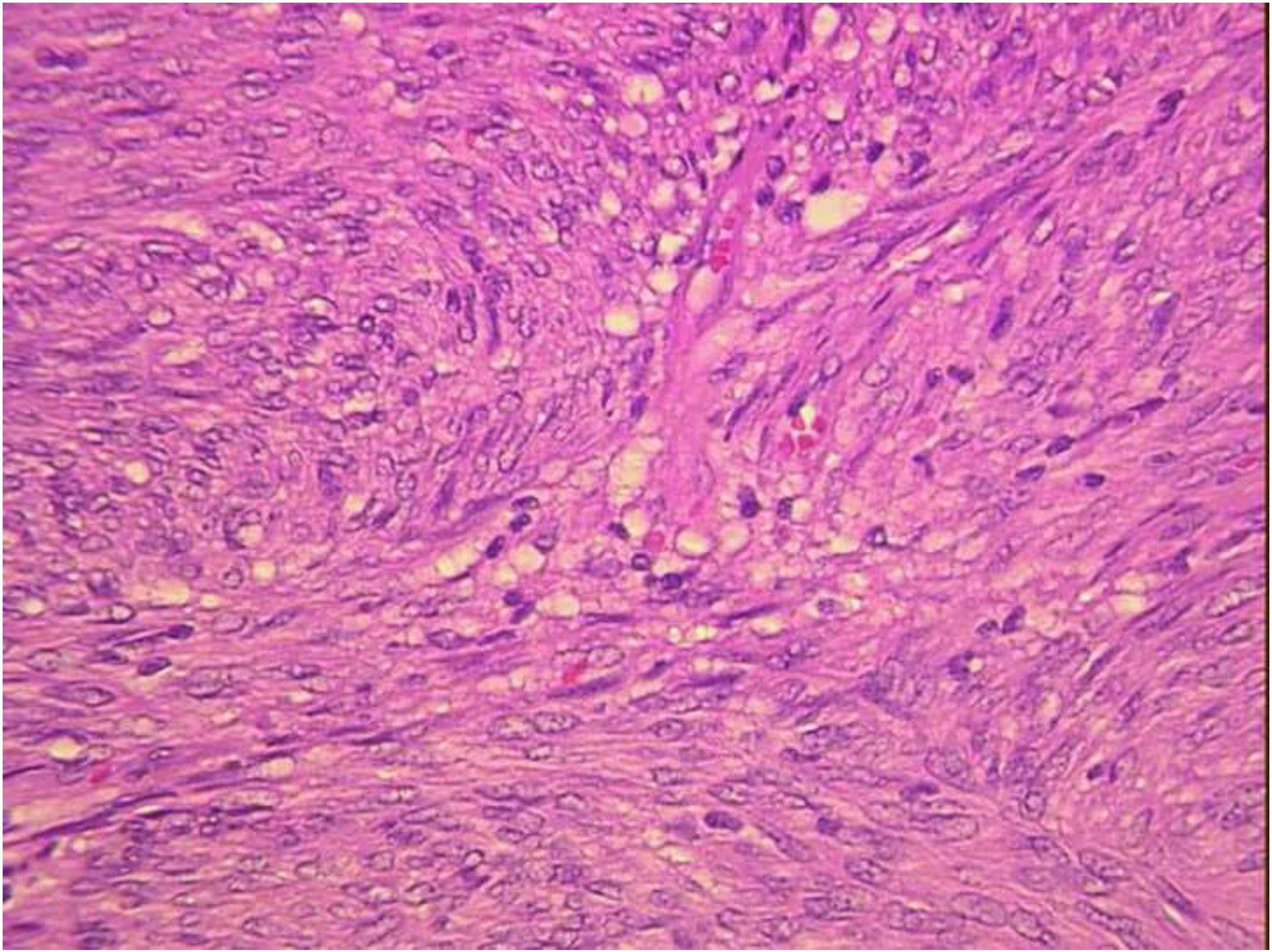


Figure 3B

Click here to download high resolution image

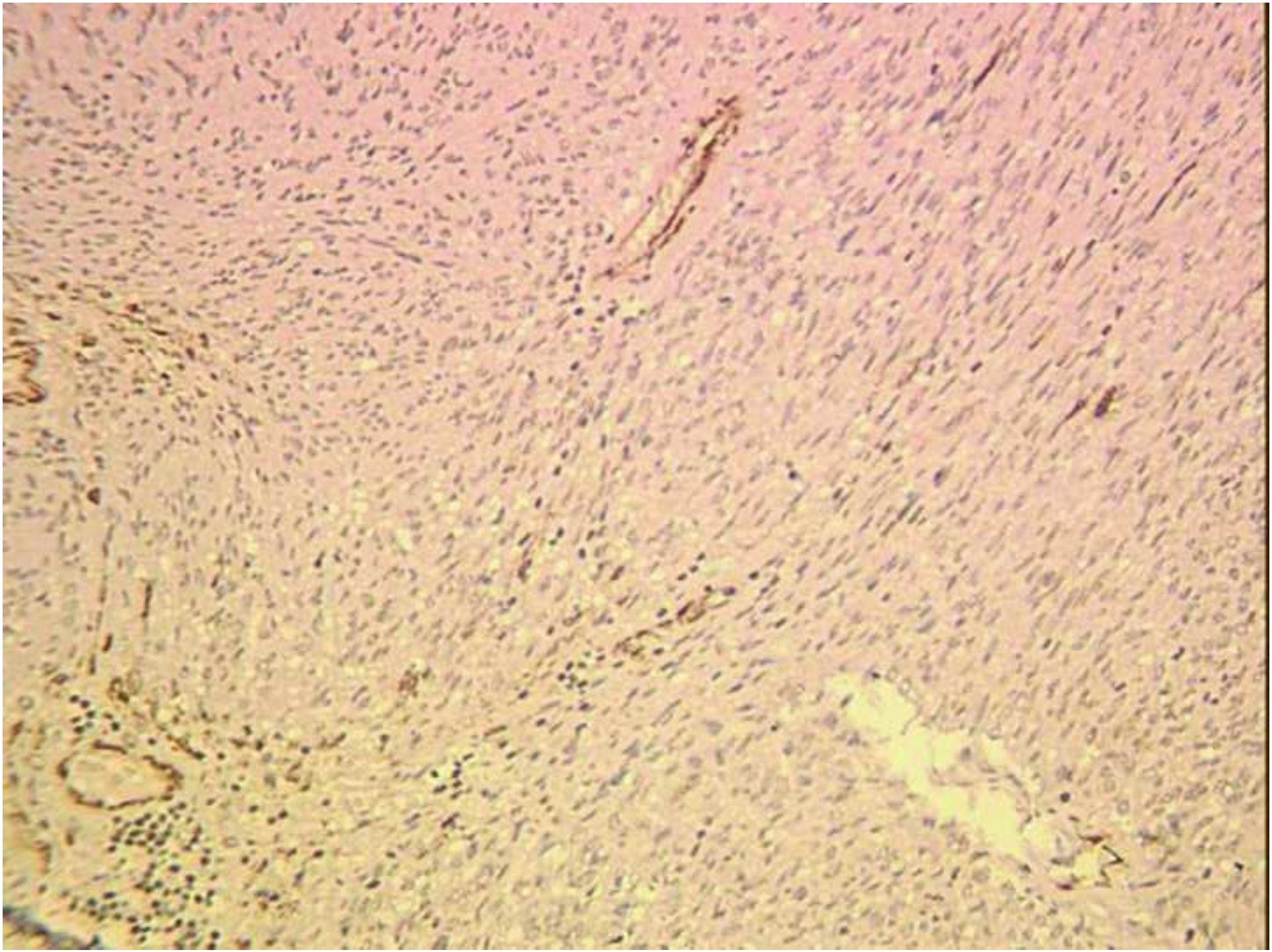


Figure 4

Click here to download high resolution image

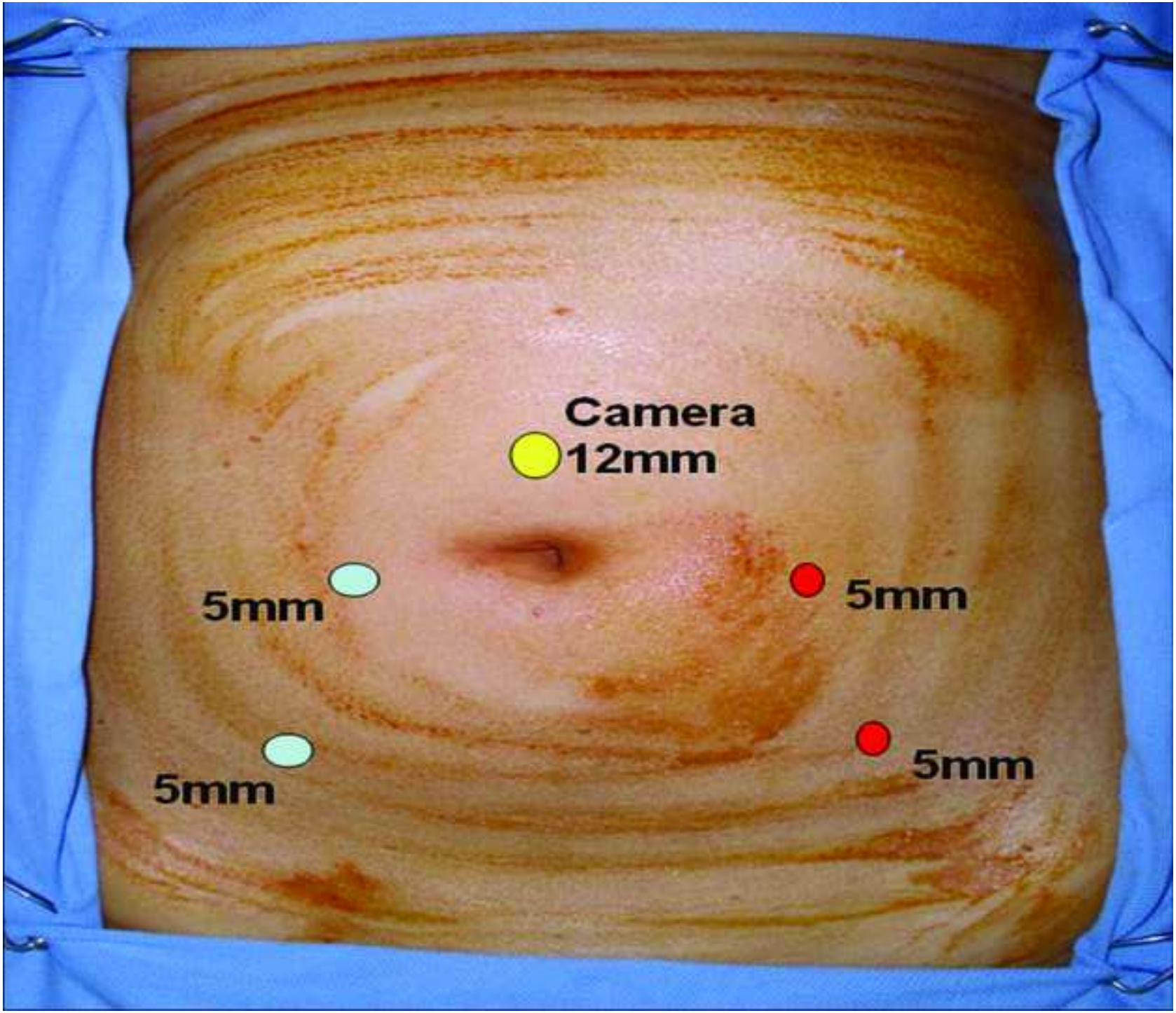


Figure 5

Click here to download high resolution image

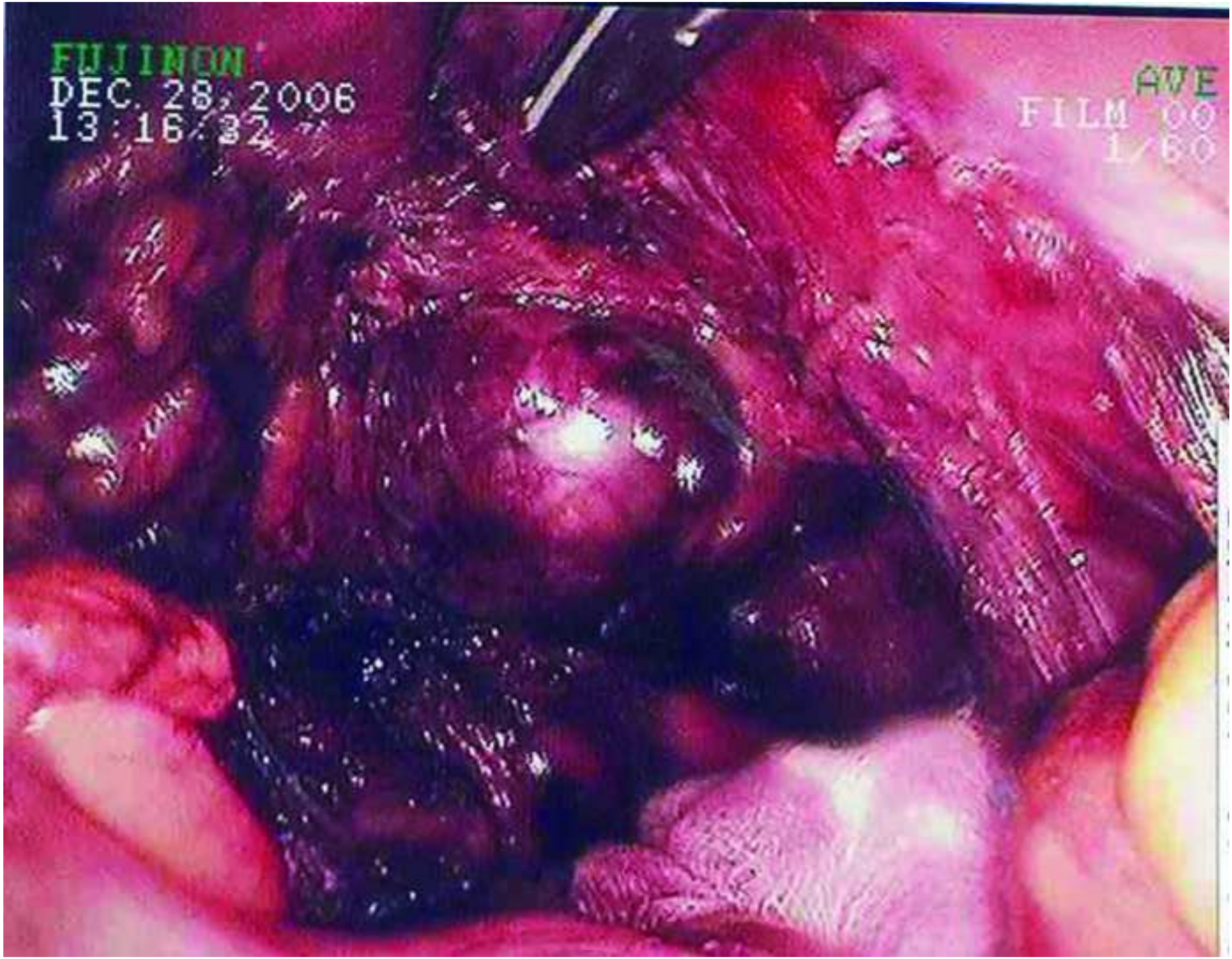


Figure 6A

Click here to download high resolution image

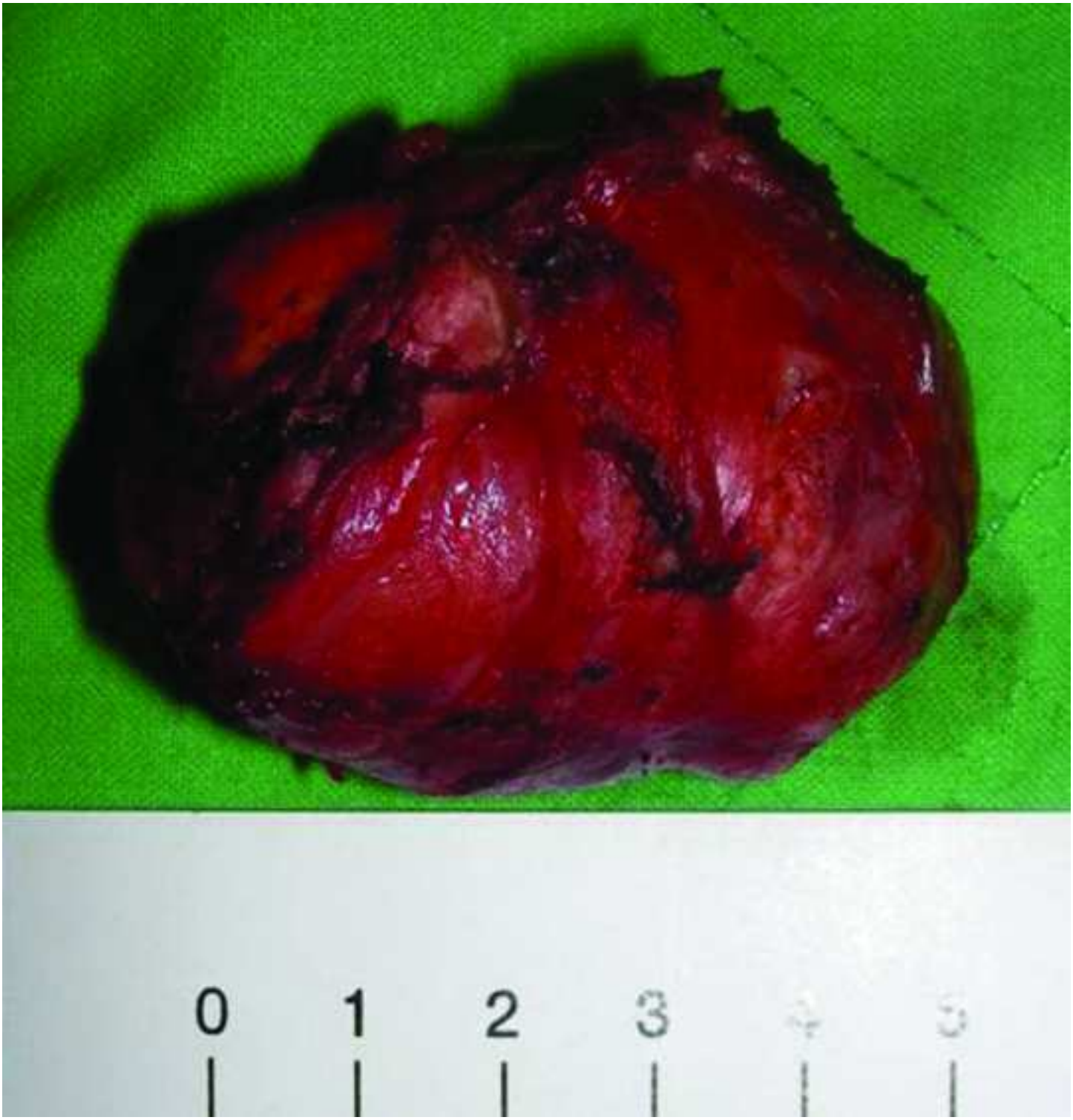
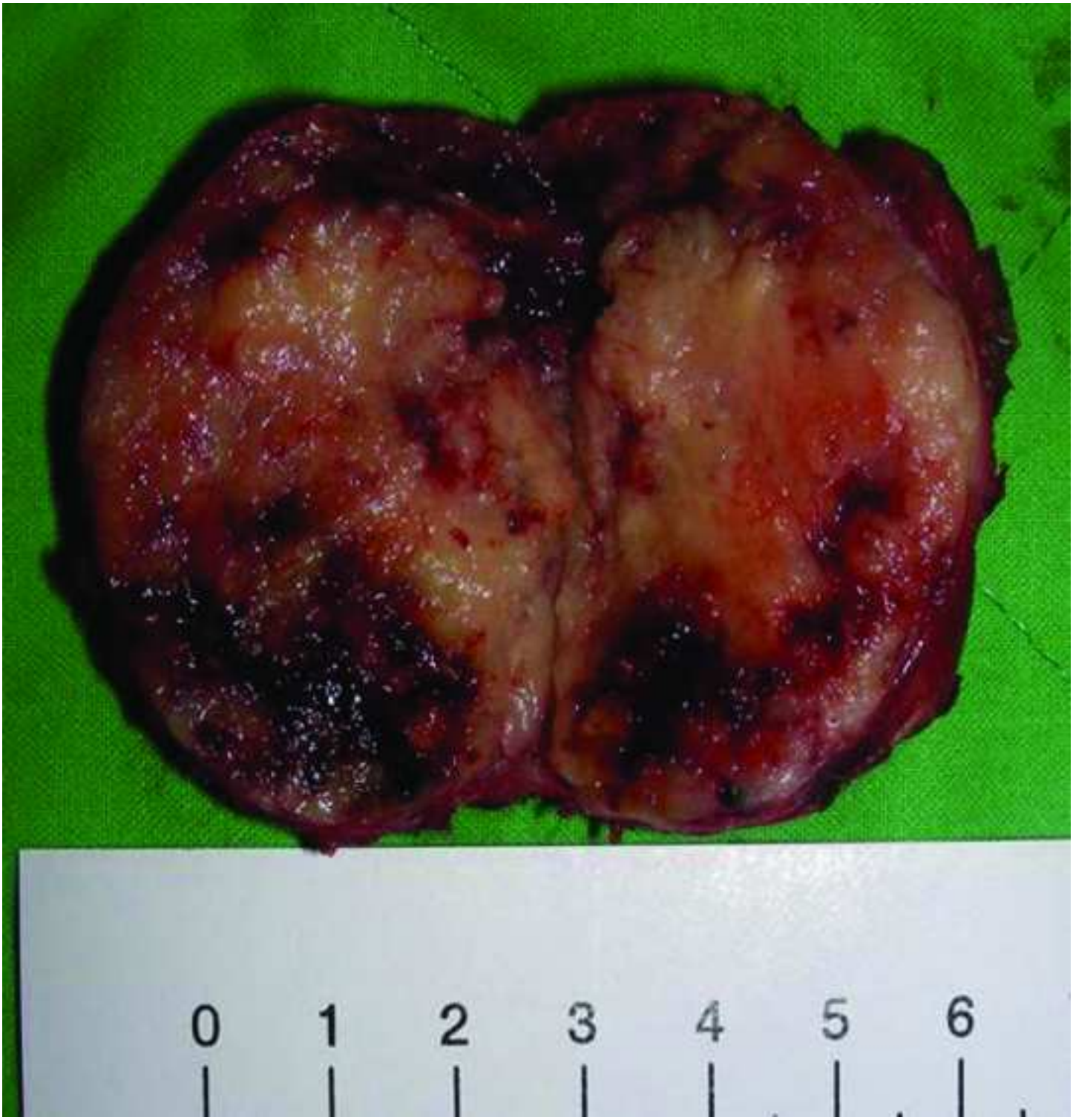


Figure 6B

Click here to download high resolution image



Laparoscopic Excision is an Alterative Method for Rectal Gastrointestinal Stromal Tumor

A Case Report

Sheng Chi Chang, MD, Tao-Wei Ke, MD, Hua Che Chiang, MD, Christina Wu, BS, Willian Tzu Liang Chen, MD

Division of Colorectal Surgery, Department of Surgery, China Medical University Hospital, Taichung, Taiwan

Corresponding author:
Willian Tzu-Liang Chen, MD.
Address: No.2, Yu-Der Road, Taichung 404, Taiwan
TEL:0966202253,+886-4-22052121-1638
Fax:+886-4-22029083
E-mail: tzuliang611@yahoo.com

Reprints :
Sheng chi Chang, MD.
E-mail : aaa54382000@yahoo.com.tw

Case report

Laparoscopic Excision is an Alterative Method for Rectal Gastrointestinal Stromal Tumor

A Case Report

Abstract:

Gastrointestinal stromal tumors are rarely found in the anorectum and account for less than 0.3 percent of all rectal malignancies. The major treatment of rectal GISTs is complete resection of the primary tumor with negative microscopic margin. We present an alternative method, laparoscopic-assisted local excision of rectal GIST. This was a patient with a 5 cm x 4 cm x 3 cm GIST located 4 cm above the dentate line in the right rectal wall. The tumor was mobilized by laparoscopic dissection with a clear safe margin and the specimen was removed from anus. The patient had a smooth recovery and no recurrence after 31 months following the procedure. This experience suggests that laparoscopic excision is a safe alternative for rectal GIST, offering the advantage of better visualization of structures and sparing the patient from an unnecessary abdominoperineal resections.

Key Wards: GIST, rectal, laparoscopy, excision

Laparoscopic Excision is an Alterative Method for Rectal Gastrointestinal Stromal Tumor

A Case Report

Introduction

The gastrointestinal stromal tumor (GIST) constitutes the largest group of gastrointestinal mesenchymal tumor that is most commonly found in the stomach and small bowel. Anorectal GISTs account for less than 0.3% of all rectal malignancies and comprise approximately 5% of all GISTs. [1] These tumors have a characteristic mutation in the KIT proto-oncogene that results in overexpression of the KIT protein from the interstitial cell of Cajal (ICC).[1]

While the majority of rectal GIST cases are treated with a complete resection of the primary tumor, the best surgical method for rectal GISTs remains controversial. Local excision is suggested in patients with "benign" rectal GISTs (<5 cm in size and <5 mitoses/50 HPF) for the advantage of minimal morbidity and sphincter preservation.[2] Various techniques of local excision have been established, such as the transrectal approach, the transsacral approach and the transvaginal approach. Taking into consideration the magnifying capabilities of laparoscopy when used for visualization of the pelvis cavity, laparoscopic surgery for the rectal tumor can offer adequate surgical margin, less tissue trauma, and thus an alternative method for management of rectal GISTs. In this present case, we performed a laparoscopic-assisted wide excision of rectal GIST on an old woman, resulting in a favorable course of recovery as described in this article.

Case Report

Clinical Course

The patient was a 67-year-old female with history of hypertension and cerebrovascular disease. She visited to our gynecologic clinic for a regular Pap smear examination in November 2006. On the initial examination, a hen-egg sized mass with smooth surface was palpated in the right lateral wall of the rectum about 4 cm above the dentate line. The rectal mass was firm, immobile, and painless. Tracing back to her symptoms, the patient mentioned heavy sensation in the lower abdomen along with nocturia and frequent urination for six months. Peripheral blood tests, blood biochemistry tests, and routine urinalysis at the time of the initial examination did not reveal any abnormal findings. Tumor marker tests showed normal levels of carcinoembryonic antigen and carbohydrate antigen 19-9. A urodynamic test reported normal bladder function. Further colonoscopic examination revealed a 5 cm bulging mass with an intact mucosal surface, located at the lower rectal valve (Fig. 1). Pelvic magnetic resonance imaging (MRI) revealed a 5 cm x 4 cm round, smooth mass protruding from the right rectal wall with no invasion of surrounding tissue and no pelvis lymph node enlargement (Fig. 2). A mesenchymal tumor composed of spindle cells with infrequent mitosis was identified during a transrectal needle biopsy (Fig. 3). An immunohistological examination showed strong positive staining for c-kit and CD34 while there was negative staining for smooth muscle actin, desmin, and S-100. Preoperative diagnosis was a 5 cm low-grade malignant GIST originating from the low rectum without lymph node enlargement. Based on these findings, local resection of the tumor via laparoscopy was considered as a viable approach.

Surgical Procedure

A mechanical bowel preparation, achieved by using 90 ml of sodium phosphate (NaP) diluted with a cold clear liquid or water, was given at 6:00-7:00PM before the day of surgery. Broad-spectrum intravenous antibiotics were given preoperatively. The patient was placed in a standard lithotomy position and received general endotracheal anesthesia. A supraumbilical 12 mm trocar was inserted and pneumoperitoneum was maintained at 10-14 mmHg. In addition, four 5 mm trocars were placed in the left lower quadrant, left iliac fossa, right lower quadrant, and right iliac fossa, respectively, under laparoscopic guidance. A Fujinon flexible laparoscope was used. The surgery began with maneuvering the uterus and suspending it in the abdominal cavity to provide adequate exposure of the pelvis. The whole sigmoid colon was mobilized after dividing the left lateral avascular attachments. The retrorectal space was entered after division of the posterior peritoneal reflection. The bilateral pararectal fascia was then separated along the rectum to develop the retrorectal space between the rectal fascia propria and the presacral fascia. During the presacral dissection, the hypogastric nerve branches should be identified and preserved carefully, also avoiding injury to the presacral venous plexus. Mobilization of the upper and mid-rectum was accomplished after dissecting the anterior wall of rectum via Denonvillier's fascia. Then, the smooth-surfaced tumor was gradually exposed and identified near the right side of the posterior rectal wall (Fig.4). The mass, located at right posterior aspect of the rectal wall, was carefully dissected free from the surrounding areolar tissue with a clear safe margin under direct laparoscopic vision. The tumor was properly mobilized, completely excised with partial rectal mucosa, then removed via the low rectal wound. Finally, the low rectal wound was repaired with transanal interrupted suturing. The operative procedure was completed in 170 minutes and blood loss volume was 50 ml. No incision

wound was visible over the abdominal wall aside from the site of trocar insertion.

The tumor was macroscopically encapsulated and measured to be 5 cm x 4 cm x 3 cm in size (Fig.5A). The cut surface was whitish and solid with a homogenous consistency, scattered with blood clots (Fig.5B). The tumor was growing mainly from the tunica muscularis propria toward the lateral tunica serosa. There was no tumor infiltration on the mucosal surface. The histopathological report revealed tumor growth mainly in the subserosal layer and a composition of spindle cells. There were zero mitoses per 50 high-power fields (HPF), and the findings corresponded to those of a low-grade malignant GIST. The immunochemical study revealed positive results for CD 117 and CD 34, and negative results for smooth muscle actin, desmin, and S-100 protein.

The patient experienced a fast postoperational recovery without any complication and was discharged on the fourth day after sugery. No adjuvant chemotherapy was given and the patient was regularly followed-up at our clinics. To date, at 31 months after surgery, there has been no reported recurrence.

Discussion

Gastrointestinal stromal tumors are a kind of mesenchymal tumor derived from the interstitial cells of Cajal. GISTs are most commonly found in the stomach (60%-70%), followed by the small intestine (20%-25%), and only about 5% of all GISTs originate in the rectum.[3] The typical rectal GIST is often located in the submucosa, regardless of its extension into the muscularis propria. and few (10-15%) will spread to the mucosa.[4] In 2001, the National Institutes of Health (NIH) workshop defined the role of KIT immunopositivity in the diagnosis of GISTs and assessing the risk of malignant behavior ranging from very low to high based on tumor size and mitotic count. A rate of ≤ 5 mitoses per 50 HPF is commonly used as a limit for a tumor with expected benign behavior, and has been proven to be a way of distinguishing benign tumors from malignant ones, especially in gastric GISTs.[5]

The key to adequate control of rectal GISTs is complete surgical resection of the primary tumor with negative microscopic margin (R0 resection). Neither radiotherapy nor conventional chemotherapy has any proven efficacy as adjuvant therapy. Unlike adenocarcinoma, GISTs rarely metastasize to local regional lymph nodes and lymphadenectomy is considered only for evident nodal involvement. Although surgical resection of GISTs was widely known as the best choice, the rarity of rectal GISTs makes it difficult to ascertain the extent of surgical resection in such situations. Local excision offers the advantages of minimal morbidity and sphincter preservation while radical surgery, including low anterior resection and abdominoperineal resection, may offer complete removal of the rectal tumor. However, there is no evidence that procedures more extensive than removal of all gross neoplasm prolong survival or delay recurrences.[6] Miettinen et al[2] collected 144 cases of anorectal GISTs and described the tumors in very low-risk group (< 2 cm of size and < 5 mitoses/HPF) have an indolent behavior and low rates of recurrence, making them suitable candidates for

local excision. In the study, the majority of anorectal GISTs with malignant behavior (> 5 cm of size or > 5 mitoses/50 HPF) that had high rates of recurrence or developed metastasis (55-85%) revealed no significant differences in survival rates when comparing types of surgery performed. Currently, en bloc resection of the tumor (R0 resection) and surrounding normal tissue is still the conventional treatment of rectal GISTs, followed by surveillance for metastasis and recurrence.[7] Radical surgery involves anterior or abdominoperineal resection with sacrifice of sphincter function, making it an anatomical resection of the rectum that may provide a better oncologic outcome. Despite the promising results, radical surgery may also result in morbid complications such as anastomotic leakage, sepsis, or incontinence. It is also important to note that the use of a stoma after abdominoperineal resection may not always be tolerated by patients. Therefore, laparoscopic tumor excision may be an alternative method of surgery, considering its advantages. First, laparoscopic surgery offers better visualization of the structure, especially in narrow anatomic spaces, and allows ease in excising the rectal GIST with an adequate safety margin under laparoscopy. Second, laparoscopic tumor excision results in minimal trauma to the rectum and preserves the sphincter, which reduces the rate of morbidity and mortality. In the present case, R0 resection of the rectal GIST was achieved laparoscopically with no postoperative complications. Neither local recurrence nor distal metastasis was noted even after the 31 month follow-up.

Several minimally invasive treatment options had been published for favorable lesions in the rectum. The transrectal approach is most frequently performed for local excision of anorectal tumors, including those within 3 cm from the dentate line.[8] However, this approach is limited by size and position of the tumor and will not ensure an adequate tumor-free margin if the tumor is too large or too high in the rectum.

Transsacral (transcoccygeal) excision was described by Kraske[9] as a way to resolve higher lesions in the posterior wall of the rectum. Unfortunately, this technique will damage surrounding tissue and is associated with an increased risk of complications such as fecal fistula, anal dysfunction, and poor perineal wound healing.[10] A transsphincteric approach, as originally described by Mason[11], is the usual approach for lower rectal tumors that are too large for a transanal resection, but long-term continence still remains as a main concern after the procedure. Minia et al[12] published a safe alternative method for larger tumors in the rectal wall using the transvaginal approach which resulted in extremely low morbidity rates. This approach still had its limitations of gender and location of the tumor contributing to an unclear margin. As presented in our case, laparoscopic tumor excision can provide both, good visualization to attain an acceptable tumor free margin and no limitations on the lesion site in the rectum. Furthermore, removal of the specimen via the rectum can offer better cosmetic results and decrease postoperative wound pain. Several published case reports[13-15] have discussed the laparoscopic resection of presacral tumors, including sacrococcygeal teratomas, Schwannomas and ganglioneurofibroma. The conclusions of these reports agreed with our results: laparoscopy is a safe and efficient approach for pelvic tumors, providing better visualization of the abdomen and pelvis, especially in narrow anatomic spaces.

In conclusion, the surgical technique and outcomes discussed above indicate the possibility of laparoscopic tumor excision becoming an alternative treatment for such rectal GISTs. As demonstrated in this case, it is a safe and minimally invasive surgical modality that holds promising results. This evidence leads us to believe that the laparoscopic approach of rectal GISTs provides a reasonable alterative and should be consider more often.

Reference

1. Changchien CR, Wu MC, Tasi WS, Tang R, Chiang JM, Chen JS, Huang SF, Wang JY, Yeh CY. Evaluation of prognosis for malignant rectal gastrointestinal stromal tumor by clinical parameters and immunohistochemical staining. Dis Colon Rectum 2004;47:1922-9.
2. Miettinen M, Furlong M, Sarlomo-Rikla M, Burke A, Larsota J. Gastrointestinal stromal tumors, intramural leiomyomas and leiomyosarcomas in the rectum and anus. Am J Surg Pathol 2001;25:1124-33.
3. Tran T, Davila JA, El-Serag HB. The epidemiology of malignant gastrointestinal stromal tumors: an analysis of 1,458 cases from 1992 to 2000. Am J Gastroenterol 2005;100:162-8.
4. Tworek JA, Goldblum JR, Weiss SW. Stromal tumors of the anorectum: a clinicopathologic study of 22 cases. Am J Surg Pathol 1999;23:946-54.
5. Miettinen M, Sarlomo-Rikala M, Lasota J. Gastrointestinal stromal tumors: recent advances in understanding of their biology. Hum Pathol 1999;30:1213-20.
6. Matsushima K, Kayo M. Transsacral Approach for Rectal GIST. Surg Today 2007;37:698–701.
7. Lo SS, Papachristou GI, Finkelstein SD, Conroy WP, Schraut WH, Ramanathan RK. Neoadjuvant Imatinib in gastrointestinal stromal tumor of the rectum: report of a case. Dis Colon Rectum 2005;48:1316–9.
8. Koscinski T, Malinger S, Drews M. Local excision of rectal carcinoma not exceeding the muscularis layer. Colorectal Dis 2003;5:159-63
9. Kraske PZ. Zur Extirpation hechsitzender Mastdarm Krebse. Verh Dtsch Gs Chir 1885;14:465-74.
10. Terkivatan T, Hoed PT, Lange JFM Jr, Koot VCM, Goch JJ, Veen HF. The place of

the posterior surgical approach for the lesions of the rectum. Dig Surg 2005;22:86–90.

11. Mason AY. Surgical access to the rectum—a transsphincteric exposure. Proc R Soc Med 1970;63:91-4.
12. Hellan M, Maker VK. Transvaginal excision of a large rectal stromal tumor: an alternative. Am J Surg 2006;161:121-3.
13. Konstantinidis K, Theodoropoulos GE, Sambalis G, Georgiou M, Vorias M, Anastassakou K, Mpontozoglou N. Laparoscopic resection of presacral Schwannomas. Surg Laparosc Endosc Percutan 2005;15:302-4.
14. Bax NMA, van der Zee DC. The laparoscopic approach to sacrococcygeal teratoma. Surg Endosc 2003;18:128-30.
15. Kohler C, Kuhne-Jeid R, Klemm P, Tozzi R, Schneider A. Resection of presacral ganglioneurofibroma by laparoscopy. Surg Endosc 2003;17:1494-500.

FIGURE 1. Colonoscopic image of the 5 cm bulging mass with an intact mucosal surface. The mass was located at the lower rectal valve.

FIGURE 2. The pelvic magnetic resonance imaging (MRI) showed a rectal mass and its anatomic relationship to adjacent structures. A: Axial view B: Sagittal view

FIGURE 3.**A** The tumor was composed of spindle cells arranged in an interlacing pattern (H&E stain). **B** The tumor cells were immunoreactive for CD 117 (immunoperoxidase)

FIGURE 4.Exposure of the rectal gastrointestinal stromal tumor at right side of the posterior rectal wall via laparoscopy

FIGURE 5.A.Grossly, the tumor was encapsulated and measured 5 x 4 x 3 cm in size. B. The cut surface was whitish and solid, with a homogenous consistency and scattered blood clots