Feb 25, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 7955-Lymphangioma_Case report 20140225.doc).

**Title:** Laparoscopic Segmental Colectomy for Colonic Lymphangiomas: a Definitive, Minimally Invasive Surgical Option

**Author:** Chang-Hua Zhuo, De-Bing Shi, Min-Gang Ying, Yu-Fan Cheng, Yu-Wei Wang, Wen-Ming Zhang, San-Jun Cai, Xin-Xiang Li

**Name of Journal:** *World Journal of Gastroenterology*

**ESPS Manuscript NO:** 7955

The manuscript has been improved according to the reviewer suggestions:
1. The format has been updated.

2. References and typesetting have been corrected.

3. The following revisions have been made based on the reviewers' suggestions:

-I recommend the manuscript to be revised by a person who speaks English as first language, as inappropriate use of terms may lead to clinically significant misunderstanding (e.g. uneven recovery versus uneventful recovery).

R: Associate Professor Andy Tsun, Ph.D., who is a native speaker of English and Co-PI at the Unit of Molecular Immunology, Institut Pasteur of Shanghai, Chinese Academy of Sciences, helped with editing this manuscript. We added a section of "Acknowledgements" thanking him for his work(Lines 263-266). And the manuscript also receive an extra grammar editing from AJE, a professional company of manuscript editing (EDITORIAL CERTIFICATE attached).

My content-specific comments are:

-Title: good

R: With respect to the title word limit, we have used a new title, "Laparoscopic Segmental Colectomy for Colonic Lymphangiomas: a Definitive, Minimally Invasive Surgical Option" (12 words). We can

also use the old title (16 words) if that is preferred. The editors and reviewers have the last word! We have also added a RUNNING TITLE, "Laparoscopic Resection for Colonic Cystic Lymphangiomas" (6 words) (Lines 7).

Abstract:

- it is unclear whether both cases were diagnosed with all three imaging options (please be more specific)

R: You are right. "A 36-year-old woman was admitted with one year of intermittent abdominal pain; colonoscopy, abdominopelvic computed tomography (CT) and endoscopic ultrasonography (EUS) revealed enlarged cystic masses at the ascending colon. In another 40-year-old man, colonoscopy and EUS revealed an asymptomatic lobulated cystic mass with four small sessile polyps at the sigmoid colon." has been added as shown in Lines 60-65.

- what type of cystic lymphangiomas (micro- versus macro-cystic)?

R: Pathologically, lymphangiomas may be classified as microcystic, macrocystic, and mixed subtypes, according cyst volume (with 2 $cm^3$ used as a cutoff value). Both of our cases were macrocystic lymphangioma. We have updated the manuscript with additional language (Lines 138, 170, 183-185).

- the sentences "In regards to the management for colonic lyphmangioma, it depends on the individual situation. Close surveillance or surgical resection might be consumed." are confusing to me. I would recommend to specify instead what guided the management plan (i.e. reasons for surgery, open versus MIS, surgery versus sclerosing agents, etc.).

R: The sentence has been revised (Lines 67-71). With respect to sclerotherapy (using agents such as Bleomycin, sodium tetradecyl sulphate, OK-432), most reported cases occurred at the head and neck in children and young adults. To our knowledge, no reports exist examining endoscopic sclerotherapy for colonic lesions (for unknown reasons). Maybe some complications, such as local infection, preformation, intraluminal bleeding, should be seriously considered for this intervention for colonic lesions. We did not add this point to the Abstract because of the word limit, but have included new language in the Discussion section (Lines 217-227).

Introduction:

- what is the incidence of intra-abdominal lymphangiomas? Since you say it is a rare/unusual condition, it would be helpful to understand what the actual incidence is. - the first sentence is unclear to me. Please specify of what intra-abdominal lymphangiomas are 2-5%.

R: Based on your suggestion, we have revised these sentences for clarity (Lines 96-100).

- specify what "... but resection is necessary in some specific situation." means. What kind of situation?

R: We'd like to keep this sentence as it was, if you agree. Since this "opinion" appeared right in the Introduction section. We discussed this subject in further detail in the Discussion section. Contextually, readers can understand the subject and draw appropriate conclusions. Furthermore, we have specified this in the Abstract section, based on your suggestion (Lines 67-71). Duplicate passages can be avoided if we state it in this way. Thanks!

Care Reports:

- are they micro- or macro-cystic lymphangiomas?

R: Macroscopically, both cases were macrocystic lymphangiomas with more than 2 $cm^3$ in cyst volume. We added the extra information related to the pathological diagnosis in the Case Report section (Lines 138, 170).

- do you think these lymphangiomas are congenital or acquired recently?

We are sorry that we could not confirm this based on the patient history we collected. Both masses were initially found by colonoscopy with a limited duration. According to the literature, most lymphangiomas occur in young children. The early (acquired) or even congenital appearance in life and the lesion architecture suggest lymphangiomas are the result of developmental malformations (Ref. 11) (Lines 344-346).

- what is the follow-up plan and time?

R: We have updated this information in the Case Report section for both cases (Lines 139-140, 170-171).

Case 1:

- the operative procedure is not described in sufficient detail: -- did you exclude any additional lesions laparoscopically? -- how much colon was resected? -- what suture and ports were used?

R: You are correct. We have included additional information related to the surgical procedure (Lines 129-136).

Case 2:

- What was the indication for surgery in this patient, since he described to be asymptomatic?

R: We noticed that this patient had a lesion larger than 2.5 cm in diameter along with four small sessile polyps in the adjoining location at the sigmoid colon. In this situation, we thought that he had an indication for surgical intervention, even though he was asymptomatic. We provided the patient with several options, including open or laparoscopic segmental resection of the affected colon, endoscopic snare of the polyps while treating the cystic lesions, or no treatment along with endoscopic follow-ups. He made the final decision to undergo laparoscopic surgery. This subject is covered in the Discussion section as "In the current cases, they were implicated to surgical intervention for the reason of relatively large and fast growing lesion or lesion with concurrent polyps." (Lines 233-235).

- do not use abbreviations at the beginning of a sentence (e.g. EUS)

R: Thanks. We have made revisions accordingly.

- what was the reason for puncturing the cyst in situ? what if the lesion turned out to be malignant?

R: Actually, endoscopic puncture was attempted as a minimally invasive therapy, as were pre-surgical pathological and cytological exams. The patient was found to have a recurrent cystic lesion and decided to undergo surgical intervention. Unlike the trans-abdominal fine needle aspiration, the risk of tumour metastasis through the needle track when performing endoscopic aspiration is no higher than for endoscopic biopsy. For colonic cystic lesions, however, routine endoscopic cytology or biopsy is not a common practice. So in order to avoid confusing and misleading, we preferred to delete those sentences about puncture and aspiration. We also updated in Discussion section about this point as "Endoscopic aspiration for cytology evaluation or biopsy has often no diagnostic value and may result in an efflux of lymphatic fluid or even local infection"(Lines 206-208).

- please describe the surgical procedure in more detail

R: We have included additional details related to the surgical procedure (Lines 158-167).

**Discussion:**

- did you consider the utilization of sclerosing agents (i.e. OK-432)? If not, why not?

R: No, we did not. Most reports on the use of sclerotherapy for lymphangiomas are cases occurring at the head and neck of children. To our knowledge, endoscopic sclerotherapy for colonic lesions had not been reported in the literature. Perhaps potential complications, such as local infection, preformation, or intraluminal bleeding, should be considered when discussing endoscopic sclerotherapy intervention for colonic lesions. We have added relevant information to the Discussion section (Lines 217-225).

- discuss the decision-making process in more detail (why resection, why MIS, why puncturing the cyst in patient #2)

R: R: We outline the process in the Discussion section (Lines 228-233, 239-241). We have also updated the Discussion section with information regarding the cyst puncture (Lines 206-208, 239-241).

- specify what type of literature review was performed (i.e. date of literature search, how many relevant articles were found, resource, what surgical approach was searched for, etc.). It doesn't have to be a systematic literature review, but some more details on the literature review would help understand the scope of the review.

R: A systematic review on the topic of “laparoscopic surgery for colonic lymphangiomas” was not possible since these are extremely rare cases. We searched PubMed and Embase.com using the terms of "lymphangioma", or "lymphatic malformation", with "colon" or “colorectal” in a period between Jan 1st, 1950 and Dec 31, 2013, there were about 167 articles after duplicates were deleted. We looked into the articles individually, but most were cases discussing mesentery or other intraabdominal sites. For those “qualified” cases, all were case reports or case series, which we could not review systematically. With respect to laparoscopic surgery, all the reported cases were discussed the mesentery, so we had to perform a common literature review based on our own cases. We discussed etiology, pathology, diagnostic modality and management. We paid more attention to the laparoscopic approach for colonic

lymphangiomas.

- do not finish a sentence with etc. (e.g. "Other diagnostic modalities include Barium enema[15] and CT colonography[17], etc."

R: We have revised the manuscript accordingly.

- unclear meaning of "... less physiological intervention..."

R: We have revised the manuscript to clarify the sentence (Lines 259-261).

Figure 3A: - add asterisk to mark the lesion

R: We have made updates to Fig 3A and to the Legends section (Lines 467-470).

**Others:**

We have also added the **COMMENTS** pertaining to the "WRITING REQUIREMENTS OF CASE REPORT" by BSP Group, as stated in Lines 268-312.

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

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