

Peer Review File

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Reviewer A

The authors of the manuscript entitled “Mesenteric cystic lymphangioma: case and review of the literature” report the case of a woman incidentally diagnosed with a pelvic cystic mass. Preoperative diagnostics was not conclusive, and laparoscopy was performed showing the presence of a cystic lymphatic malformation of the sigmoid mesentery. Fenestration and aspiration of the fluid content confirmed the diagnosis and at follow up the patient showed no recurrence.

Here are my comments/suggestions:

Comment 1: I suggest avoiding the term Lymphangioma. These types of malformations are well described in the ISSVA classification, and they are defined as Lymphatic Malformations. As this definition recurs more times in the text, I suggest using the abbreviation LM.

Reply 1: Thanks for your suggestions. We feel sorry for the improper wording. According to your suggestion, we have corrected the “lymphangioma” into “lymphatic malformations”, and we use the abbreviation LM. The detailed corrections are as follows.

Changes in the text: Page 1 (Line 1) Title , mesenteric cystic lymphatic malformation : a rare case report and review of the literature. Page 2 (Line 23) Background, mesenteric cystic lymphatic malformation (LM) is a rare congenital benign malformation in adults. Page 2 (Line 26) Case Description, we describe a rare case of LM of the mesentery in a 49 years old woman. Page 2 (Line 40) Conclusions, LM is a challenging and rare disease, and its diagnosis is difficult. Page 3 (Line 50) Key findings, although LM appears cystic, its imaging features are still complex and often lead to misdiagnosis. Page 3 (Line 53) It is well known that LM is extremely rare and lack specific clinical manifestations, making their accurate diagnosis challenging. Page 3 (Line 61) Introduction, LM is a rare benign congenital malformation of the lymphatic system. Page 3 (Line 64) Introduction, LM is clinically challenging to diagnose due to atypical clinical manifestations or lack of recognition of the disease, so early diagnosis is essential for treatment modalities and prognostic effects. Page 4 (Line 67) Introduction, imaging examination can assist in the diagnosis and differential diagnosis of LM. Page 4 (Lines 68-70) Introduction, this paper reports a case of LM of the sigmoid colon in an adult female, and reviews the relevant literature to provide effective clues for the diagnosis and treatment of LM of the sigmoid colon. Page 6 (Line 114) Discussion, intestinal lymphatic malformation in adults is an exceedingly rare benign neoplasm. Page 6 (Line 119) Discussion, the age distribution supports the notion that LM represents a congenital malformation often diagnosed belatedly owing to its slow growth or asymptomatic nature. Page 6 (Line 121) Discussion, 70%

of lymphatic malformations predominantly manifest in the head and neck region, often leading to dysphagia and discomfort due to potential bleeding. **Page 6 (Line 126) Discussion**, notably, studies have reported that abdominal LM is most frequently observed within the small intestine among 48 adults. **Page 6 (Line 131) Discussion**, the classification of LM is based on the microscopic evaluation of the size of the lymphatic space, resulting in three subtypes: lymphatic capillary type, cavernous type, and cystic type, as observed through clinicopathological analysis. **Pages 7-8 (Lines 153-158) Discussion**, currently, ultrasound and Computed tomography (CT) examinations have emerged as the primary modalities for initial LM screening due to their non-invasive nature and straightforward implementation. Moreover, they can be employed for precise localization diagnosis of LM. The typical ultrasound characteristics of intestinal LM include cystic or cystic-solid appearance with well-defined boundaries and multiple thin or thick septations. **Page 8 (Line 165) Discussion**, the abdominal CT examination has been widely recognized as a gold standard for diagnosing LM. **Page 10 (Line 202) Discussion**, however, Zobel et al. highlighted the limited efficacy of percutaneous injection sclerotherapy in patients with microcystic LM. **Page 10 (Lines 206-213)**, after careful consideration, it is evident that the clinical manifestations of LM lack specificity, leading to potential instances of missed diagnosis and misdiagnosis. The diverse presentation patterns observed in LM are influenced by factors such as lesion size and location. By leveraging the imaging characteristics of intestinal LM alongside endoscopic ultrasonography, clinicians can enhance the diagnostic accuracy for this disease while formulating comprehensive and effective treatment strategies, ultimately improving patient prognosis.

Comment 2: As LM in the sigmoid mesentery are exceedingly rare, I suggest reporting it in the title.

Reply 2: Thanks for your suggestions. We have changed the title of the article to Mesenteric cystic lymphatic malformation : a rare case report and review of the literature.

Changes in the text: Page 1 (Line 1) Title: Mesenteric cystic lymphatic malformation : a rare case report and review of the literature.

Comment 3: Page 3 (lines 57-58): I do not really understand this sentence. What do you mean with “more comprehensive treatment plan”?

Reply 3: We feel sorry that we did not explaining the meaning of this sentence clearly. We feel sorry for our carelessness. We have corrected it and we also feel great thanks for your pointour. The detailed corrections are as follows.

Changes in the text: Page 3 (lines 57-58): Through the above examination methods, the size and location of LM can be obtained and classified according to the size of the cystic part, so as to develop a treatment strategies for distinct types of LM.

Comment 4: Page 4 (Line 76) I suggest avoiding this art of timeline in reporting the case. You write “One month ago?”. Above in the text (Page 5, line 98) you report a date. Please change it.

Reply 4: Thank you for your reminding. And we have corrected it according to your suggestion.

Changes in the text: Page 5 (lines 93-95): Following the exclusion of surgical contraindications, laparoscopic sigmoid mesocolic cyst fenestration and intestinal adhesiolysis were performed under general anesthesia.

Comment 5: Page 5 (lines 91-93). Is This information important for the understanding of the case?

Reply 5: Thank you for your reminding. And we have corrected it according to your suggestion.

Changes in the text: We have removed that paragraph.

Comment 6: Case presentation: To correctly define the diagnosis, immunohistology should be reported.

Reply 6: Thanks for your correction. And we have corrected it according to your suggestion.

Changes in the text: Page 5 (lines 101-103): Postoperative immunohistochemical pathological (Figure 3) analysis further confirmed the diagnosis of sigmoid lymphangioma.

Comment 7: Case presentation: Recurrence in case of simply fenestration of a LM is well known. Did you perform follow-up examinations like ultrasound? How long do you plan to continue the follow up?

Reply 7: Thank you for your reminding. The patient was examined by ultrasound 3 months after surgery and did not observe any signs of recurrence. We plan to follow the patient continuously for one year.

Changes in the text: Page 5 (lines 103-105): The patient was examined by ultrasound 3 months after surgery and did not observe any signs of recurrence. We plan to follow the patient continuously for one year.

Comment 8: Page 6 (line 115): Lymphatic malformations are not neoplasms. They are malformations! Please change the word neoplasm.

Reply 8: Thanks for your correction. We feel sorry for our carelessness. And we have corrected it according to your suggestion.

Changes in the text: Page 6 (line 114): Intestinal lymphatic malformation in adults is an exceedingly rare benign disease.

Comment 9: Page 6 (Lines 118-120): In the reported prevalence, pediatric population is not considered.

Reply 9: Thank you for your reminding. We have taken pediatric population into account, but may not have expressed them precisely enough. We mean that the disease has a wide age distribution, with epidemic trends mainly occurring between the ages of 20 and 50 years.

Changes in the text: Page 6 (Lines 117-119): The disease mainly occurs in people between the ages of 20 and 50 years, without any apparent gender predilection.

Comment 10: Pages 6-7 (Lines 131-137). You report two different classifications according to the microscopic appearance. I suggest using the ISSVA, that classifies LM as micro-, macrocystic and mixed according to the size of the cysts, as you report above in the text. This is the worldwide accepted classification for LM and vascular anomalies.

Reply 10: Thanks for your correction. And we have corrected it according to your suggestion.

Changes in the text: We have deleted the paragraph.

Comment 11: Page 8 (line 166): The classification according to the size was not demonstrated by Dr Hoang. It was previously described. Please refer to ISSVA classification.

Reply 11: Thanks for your correction. We feel sorry for our carelessness. We have found an error in the cited reference, so we have replaced it with the correct one. The detailed corrections are as follows.

Changes in the text: Page 8 (Lines 162-165): Li, J et al. classified according to the size of the cyst diameter, the macrocystic (cysts >1cm in diameter), microcystic (individual cysts <1 cm in diameter), and mixed types were classified according to the cyst diameter.

Comment 12: Page 9 (Lines 193-196): Due to the risk of major complications like volvulus and bleeding, I'm not sure that the follow-up alone is a good option. The reference you report (No 20, PMID 36822939) do not suggest a conservative approach and the cutoff of 12.5 cm define the necessity of performing the resection of the underlying bowel loop.

Reply 12: We feel sorry that we did not explaining the meaning of this sentence clearly. The point we want to make is as follows. In terms of treatment, reference (NO 20) states that surgical resection is recommended when the LM mass exceeds 12.5 cm in diameter and is accompanied by major complications such as volvulus or bleeding, whereas simple follow-up is not recommended. reference (NO 12) also mentions a similar view that surgical resection should also be chosen when LM masses involve surrounding tissues or organs.

Changes in the text: Page 9 (Lines 187-190): Based on the findings from Chen et al. , surgical resection is advised when the median size of LM exceeds 12.5cm and there are clinical symptoms and/or complications present, whereas simple follow-up is not recommended.

Comment 13: Page 10 (line 205): The use of the word "demonstrated" is imprecise.

Reply 13: Thanks for your correction. We feel sorry for our carelessness. The detailed corrections are as follows.

Changes in the text: Page 10 (lines 199-201): Thiam et al. proposed that in the management of complex or unresectable masses, cysts can be punctured using a fine needle for content evacuation, with or without concurrent administration of sclerosing agents.

Reviewer B

Comment 1: 1- line 75: "underwent a physical examination..." whether this was a routine exam or the patient was symptomatic- and if so what were her symptoms?

Reply 1: Thank you for your reminding. The physical examination was a routine exam and the patient did not develop any symptoms. In order to avoid confusion reviewers, we have removed this paragraph.

Changes in the text: We have removed that paragraph.

Comment 2: in relation to this specific medical entity, it is postulated that trauma, intraoperative injury, fibrosis and... are hypothesized as a trigger factors for such benign tumors- whether the patient had any of these triggers?

Reply 2: We thank the reviewers for their thorough consideration of this article. The patient does not have any of these triggers.

Comment 3: why the authors decided to do fenestration and not complete surgical excision, as the latter is the best therapeutic option?

Reply 3: Thank you for your question. After careful consideration, our clinicians made a deliberate decision to perform fenestration and drainage in this patient described here due to the small size of the mass, measuring only 6 cm in diameter, and the absence of any clinical symptoms or complications.

Comment 4: 3 months of follow up is such a short time to rule out recurrence for such type of tumor- I would suggest to follow the patient up to 1 year at least.

Reply 4: Thank you for your reminding. The patient was examined by ultrasound 3 months after surgery and did not observe any signs of recurrence. We plan to follow the patient continuously for one year.

Changes in the text: Page 5 (lines 103-105): The patient was examined by ultrasound 3 months after surgery and did not observe any signs of recurrence. We plan to follow the patient continuously for one year.

Comment 5: digital rectal examination was done during physical exam- if so what were the findings- is the tumor palpable?

Reply 5: Thank you for your reminding. Unfortunately, we are unable to provide information because the patient did not undergo a digital rectal examination program.

Comment 6: I was wondering if a multidisciplinary team approach was done- nowadays, one therapeutic option is interventional radiology with/without ablation therapy- was this option discussed?

Reply 6: Thank you for your reminding. We had a preoperative multidisciplinary team discussion that involved the fields of surgery, radiology, and ultrasonography but was not included in the consideration of ablation therapy.

Comment 7: did the patient underwent colonoscopy- the primary diagnosis was for stromal tumor of the sigmoid colon...

Reply 7: Thank you for your reminding. We recommended a colonoscopy, but the patient was not accepted.