

PEER-REVIEW REPORT

Name of journal: *World Journal of Clinical Cases*

Manuscript NO: 69881

Title: Pneumatosis intestinalis after systemic chemotherapy for colon cancer: A case report

Reviewer's code: 06097293

Position: Peer Reviewer

Academic degree: MD

Professional title: Associate Professor

Reviewer's Country/Territory: China

Author's Country/Territory: Taiwan

Manuscript submission date: 2021-07-17

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-07-17 10:32

Reviewer performed review: 2021-07-17 10:57

Review time: 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input checked="" type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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SPECIFIC COMMENTS TO AUTHORS

This is an interesting and educational case report. The authors had shown a high degree of decisiveness in dealing with problems. However, several similar papers had been published and the issue had been discussed already. Such as in: 1. Pneumatosis intestinalis after cetuximab-containing chemotherapy for colorectal cancer. Yoon S, Hong YS, Park SH, Lee JL, Kim TW. *Jpn J Clin Oncol*. 2011 Oct;41(10):1225-8. doi: 10.1093/jjco/hyr114. Epub 2011 Aug 10. PMID: 21835823; 2. Pneumatosis cystoides intestinalis during palliative chemotherapy for colorectal cancer]. Mais L, Galoo E. *Rev Med Brux*. 2012 Jan-Feb;33(1):48-50. PMID: 22512149; 3. Pneumatosis intestinalis after cetuximab-containing chemotherapy for colorectal cancer. Yoon S, Hong YS, Park SH, Lee JL, Kim TW. *Jpn J Clin Oncol*. 2011 Oct;41(10):1225-8. doi: 10.1093/jjco/hyr114. Epub 2011 Aug 10. PMID: 21835823. I would expect more novelty or deep thinking/comparison.

Answer: Thank you for the comments. Although fewer cases report about this complication have been reported in the literatures, our case may also represent the typical features of this rare complication and add the important clues for clinical physicians to manage the oncologic patients with PI following chemotherapy.

PEER-REVIEW REPORT

Name of journal: *World Journal of Clinical Cases*

Manuscript NO: 69881

Title: Pneumatosis intestinalis after systemic chemotherapy for colon cancer: A case report

Reviewer's code: 05904643

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Academic degree: MD, PhD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: Taiwan

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Reviewer performed review: 2021-07-23 08:18

Review time: 2 Days and 17 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

1. The discussion part of the article states that cetuximab may be an important cause of Pneumatosis intestinalis., please explain the possible reasons and whether there are similar reports in other documents . 2. This article emphasizes that Pneumatosis intestinalis needs to be differentiated from chemotherapy-induced fulminant complications (such as ischemia, infarction, and perforation of the gastrointestinal tract system), but there is no discussion about differential diagnosis in the article, please add.

Answer:

1. Based on the literatures reviews [4,11,13–16], four chemoagents (fluorouracil, leucovorin, irinotecan, and cetuximab) might have contributed to the development of PI in our patient. However, no recurrence of PI was observed after subsequent FOLFIRI treatment without cetuximab. Therefore, this suggests that cetuximab played an essential role in the development of PI. For the ethical problem, we could not apply Cetuximab for this patient to confirm this diagnosis. These discussions were summarized in the page 8 as” Many cytotoxic chemotherapeutic agents have been reported to be associated with PI; they include cyclophosphamide, cytarabine, vincristine, doxorubicin, daunorubicin, etoposide, docetaxel, irinotecan, cisplatin, methotrexate, fluorouracil, paclitaxel, tyrosine kinase inhibitors (imatinib, sunitinib, sorafenib, and erlotinib), bevacizumab (a monoclonal body to vascular endothelial growth factor), and cetuximab (a monoclonal antibody to epidermal growth factor receptor)[4,11,13–16]. This may contribute to cytotoxic damage, loss of mucosal integrity, mucosal ischemia, and the development of PI[4]. Although four chemoagents (fluorouracil,

leucovorin, irinotecan, and cetuximab) might have contributed to the development of PI in our patient, no recurrence of PI was observed after subsequent FOLFIRI treatment without cetuximab. This suggests that cetuximab played an essential role in the development of PI.”

2. PI is a radiologic diagnosis which may induced from benign (primary form, 15%) or fulminant complications (Secondary form, 85%). CT is the gold standard technique in detection of both primary and secondary forms of IP . When PI is found, the cause should be investigated. We add the discussion in the page 9 as “The CT scan is the most sensitive imaging tool for differentiating intraluminal air from the submucosal layer and identifying additional causes of PI, which include portal air, colonic tissue stranding, and dilated bowel[1]. In a review of 37426 abdominal and pelvic CT scans, Hawn et al detected PI in 108 (0.3%) patients[18]. In another review involving 28326 abdominal CT scans, Morris et al discovered that out of 104 (0.37%) patients who were diagnosed as having pneumatosis, only 23% had observable PI on their plain radiographs [17]. Cyst-like gas collection is usually benign, whereas linear collection tends to be associated with bowel infarction[10,18]. However, the recognition of these patterns should not be the sole basis for differentiating benign and fulminant conditions. “

PEER-REVIEW REPORT

Name of journal: *World Journal of Clinical Cases*

Manuscript NO: 69881

Title: Pneumatosis intestinalis after systemic chemotherapy for colon cancer: A case report

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
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SPECIFIC COMMENTS TO AUTHORS

Chemotherapy-induced PI is relatively rare, Only a small number of cases have been reported so far. PI is a radiologic sign and not a diagnosis, which is a key message for radiologist.

Answer: Thank you for the kindly response.