

The following peer-review report and comments from the Editorial Office (*World Journal of Clinical Cases*) (Science Editor, Editorial Office Director, and Company Editor-in-Chief) are provided for your reference.

1 Peer-review report

Reviewer #1:

Scientific Quality: Grade E (Do not publish)

Language Quality: Grade B (Minor language polishing)

Conclusion: Rejection

Specific Comments to Authors: Thank you for the opportunity to review this case report. In this case, the authors reported multidisciplinary therapy for colorectal cancer with liver metastasis such as mFOLFOX6+Endostar, FOLFIRI+Endostar, TACE, and γ -knife. It is true that mFOLFOX6+Endostar and TACE, may achieve a pathologically complete response (pCR), but in fact, the liver metastases recurred 2 months after surgery, and FOLFIRI+Endostar was administered. This is not mentioned in the Abstract or Core Tip. While I appreciate the effort of the work, I think this case report does not reach the level of the *World Journal of Clinical Cases*.

Response: In the abstract of the previous version of this manuscript, we have clearly stated that liver metastases recurred 2 months after surgery, and FOLFIRI+Endostar was administered. We have also added this part to the Core Tip of our revised manuscript as follows:

After the recurrence of liver metastasis, the patient received TACE comprising irinotecan/leucovorin/fluorouracil therapy plus Endostar® and was treated with γ -knife.

CASE SUMMARY¹

A 42-year-old man was diagnosed with ascending colon cancer and liver metastases.

Due to the huge lesion size and compression of the right portal vein, the liver metastases were initially diagnosed as unresectable lesions. The patient was treated with preoperative transcatheter arterial chemoembolization (TACE) consisting of 5-fluorouracil/leucovorin/oxaliplatin/Endostar®. After four courses, radical right-sided colectomy and ileum transverse colon anastomosis were performed. Postoperatively, pathological analysis revealed moderately differentiated adenocarcinoma with necrosis and negative margins. Thereafter, S7/S8 partial hepatectomy was performed after two courses of neoadjuvant chemotherapy. Pathological examination of the resected specimen revealed a pathologically complete response. Intrahepatic recurrence was detected more than two months after the operation, and the patient was then treated with TACE consisting of irinotecan/leucovorin/fluorouracil therapy plus Endostar®. Subsequently, the patient was treated with a γ -knife to enhance local control. Notably, a pathologically complete response was reached, and the patient's overall survival time was >9 years.²

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: #1 In the discussion, the authors mentioned mFOLFOX6 and Endostar®, but I think it would be easier for readers to understand if the authors specifically describe how it works compared to other treatments.

Response: In 1971 [1], researchers proposed that the formation of new tumor blood vessels led to the growth and metastasis of cancer cells; thus, angiogenesis inhibitors, like bevacizumab and Endostar®, were developed for cancer treatment [2, 3]. Endostar® and bevacizumab show competitive anti-tumor efficacy. Bevacizumab is a recombinant human monoclonal antibody that blocks angiogenesis by inhibiting vascular endothelial growth factor A (VEGF-A) [4]. Endostar®, developed in China, is a recombinant human vascular endothelial inhibitor and a multi-targeted tumor cell inhibitor. Endostar® directly inhibits the proliferation of vascular endothelial cells and exerts its anti-angiogenic effects through several targets, including VEGF, VEGF receptor-2 (VEGFR-2), and the platelet-derived growth factor receptor [5]. It can also normalize tumor blood vessels and exert anti-tumor effects [6]. We have added this part to our revised manuscript.

#2 Some of the CT photos, especially those of the colon, are difficult to understand. Please add a little cropping to make them easier to understand. I don't think it is necessary to use the same overall image.

Response: The CT photos of colon cancer are images at different time points, and not the same time. For the CT image of colon cancer as shown in Figure 1, we have clearly stated the different treatment time points, disease progression and recent follow-up time. Simultaneously, we have added some arrows in the images and text for clarity. However, we still made some changes in our revised manuscript for facilitating better understanding. We have included the enlarged images of the anastomosis in the colon cancer surgery area on the upper right panels of Figures 1E, G, and I. We marked the position of the anastomotic stoma with a red arrow.

#3 I think the diagrams of pathology are also important, but I don't know which part of the pathology is shown in the illustrations. The authors should add arrows or a schema or something to make it easier to understand the illustration.

Response: We have added content below Figure 2 in our revised manuscript to illustrate the source of the pathological tissue.

Minor point #1 P9.L16-17. "in this study" should be corrected to "in the present case" or something like that.

Response: We have made changes in our revised manuscript accordingly.

Reviewer #3:

Scientific Quality: Grade A (Excellent)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (High priority)

Specific Comments to Authors: The title correctly reflects the main subject of the manuscript. The manuscript adequately describes the background, present status and significance of the study and describes the methods used in adequate detail. I conclude that the research objectives are achieved by the experiments in this study. The manuscript interprets the finding adequately and appropriately, highlighting the key points concisely, clearly and logically and the findings are stated in a clear and definite manner. The discussions are accurate and clear. The figures, diagrams and tables are sufficient and of good quality and appropriately illustrative of the paper contents. The manuscript is well, concisely and coherently organized and presented. The style, language and grammar is accurate and appropriate. The authors prepared the manuscript according to the appropriate research methods and reporting. My assessment is that the overall quality of this article is excellent and should be accepted for publishing with high priority.

Response: Thank you for the constructive comments on our manuscript.

REFERENCES

1. **Folkman J.** Tumor angiogenesis: therapeutic implications. *N Engl J Med.* PMID 1971; 285: 1182-1186
2. **Liao WJ,** Shen P, Wu Wy, Shi M, Luo RC. Short-term therapeutic effect and safety of endostar combined with XELIRI regimen in the treatment of advanced colorectal cancer. *Nan Fang Yi Ke Da Xue Xue Bao.* PMID 2010; 30: 813-814
3. **Emmanouilides C,** Sfakiotaki G, Androulakis N, Kalbakis K, Christophylakis C, Kalykaki A, Vamvakas L, Kotsakis A, Agelaki S, Diamandidou E, Touroutoglou N, Chatzidakis A, Georgoulas V, Mavroudis D, Souglakos J. Front-line bevacizumab in combination with oxaliplatin, leucovorin and 5-fluorouracil (FOLFOX) in patients with metastatic colorectal cancer: a multicenter phase II study. *BMC Cancer.* PMID 2007; 7: 91
4. **Jin Y,** Wei L, Jiang Q, Song X, Teng C, Fan C, Lv Y, Liu Y, Shen W, Li L, Huang D, Xin T. Comparison of efficacy and toxicity of bevacizumab, endostar and apatinib in transgenic and human lung cancer xenograftzebrafish model. *Sci Rep.* PMID 2018; 8: 15837

5. **Ling Y**, Yang Y, Lu N, You Q, Wang S, Gao Y, Chen Y, Guo Q. Endostar, a novel recombinant human endostatin, exerts antiangiogenic effect via blocking VEGF-induced tyrosine phosphorylation of KDR/Flk-1 of endothelial cells. *Biochem Biophys Res Commun*. PMID 2007; 361: 79-84
6. **Guan Y**, Li A, Xiao W, Liu S, Chen B, Lu T, Zhao C, Han F. The efficacy and safety of Endostar combined with chemoradiotherapy for patients with advanced, locally recurrent nasopharyngeal carcinoma. *Oncotarget*. PMID 2015; 6: 33926-34