



PEER-REVIEW REPORT

Name of journal: *World Journal of Clinical Cases*

Manuscript NO: 70373

Title: Treatment with sorafenib plus camrelizumab after splenectomy for primary splenic angiosarcoma with liver metastasis: A case report and literature review

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer’s code: 05200667

Position: Editorial Board

Academic degree: PhD

Professional title: Research Scientist

Reviewer’s Country/Territory: Italy

Author’s Country/Territory: China

Manuscript submission date: 2021-08-09

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-08-17 00:11

Reviewer performed review: 2021-08-20 00:59

Review time: 3 Days

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input 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 Grade E: Do not publish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 checked="" 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
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SPECIFIC COMMENTS TO AUTHORS

Specific comments: 1) Page 3, Lines 73-74: "In several cases, immunotherapy or targeted therapy is very effective in patients with angiosarcoma." This sentence is out of context, lacking citations. 2) Lines 77 - 131 should be provided with a table of the patient's demographics. 3) Fig 2 should be provided with scale bars. 4) Fig 3: "Figure 3: Digital subtraction angiography (DSA) revealed the condition of the spleen before and after artery embolization. Figure 2A: Imaging before splenic artery embolization. The black arrow indicates bleeding points. Figure 2B: Imaging after splenic artery embolization." Why did they label Fig 2A and 2B in Fig 3? In detail should be shown in the Figure legend. 5) Fig 4: "Figure 4: Plain and enhanced CT revealed multiple round shadows of low density in the spleen and liver. Figure 3A: Plain CT scan revealed the presence of circular hypo-density regions with variable densities in the left and right liver parenchyma. The spleen was enlarged, and multiple abnormal cystic solid dense shadows were observed in and around the spleen. Figure 3B: Results of the enhanced CT scan indicate slight enhancement of the solid components and no enhancement of the hypo-density regions." Why did they label Fig 3A and 3B in Fig 4? In detail should be shown in the Figure legend with arrowheads for the region of interest, plus scale bars. How did they show "multiple round shadows?" 6) Fig 5: "necrosis" - did they have any cellular and molecular assays to confirm? 7) Fig 6: "Figure 6: HE staining and IHC of the specimen. Figure 5A: HE staining showed the morphology of the tumor cells. The tumor cells were arranged in sheets, fissures, or papillae with red cytoplasm. The nuclei were fusiform, oval, or irregular. Simultaneously, mitosis was easily seen. Figure 5B: IHC revealed that the patient was positive for CD31 and Ki-67, which was the characteristic



**Baishideng
Publishing
Group**

7041 Koll Center Parkway, Suite
160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

of tumor cells. Figure 5C: The results of IHC revealed that the patient was positive for S-100 but negative for CD34. “ Why did they label Fig 5A, 5B, 5C, in Fig 6? The detail of the description should be shown in the Figure legend with scale bars in the images. How did they tell which is which for positive for CD31 and Ki-67? So did it for S-100 but negative for CD34? Could they identify those with arrowheads in the images? 8) Fig 7: “Figure 7: The level of PDL1 protein was detected using IHC by the Dako PD-L1 IHC 22c3 PharmDx kit. Figure 6A: HE staining of the specimen. Figure 6B: Negative control for the test. Figure 6C: Positive control for the test. Figure 6D: IHC revealed that this patient was positive for PD-L1 in the cytomembrane of tumor cells (TPS = 20%, CPS = 22).” Why did they label Fig 6A, 6B, 6C, 6D in Fig 7? The detail of the description should be written in the Figure legend with scale bars and arrowheads in the images. 9) Lines 133-134: “Splenectomy and liver tumor resection were performed not only to cure the disease but also to cure the disease and for the histopathological diagnosis.” This statement contradicts their reasoning of Treatment with Sorafenib plus Camrelizumab – if surgery could cure, why did they need it? 10) Lines 140-141: “The histopathological biopsy and next-generation sequencing (NGS) were then carried out” – Where did they have NGS data sets? What values of those biomarkers? 11) Lines 145: “positive for CD31, S-100, and Ki-67 (positive rate of 60%),” Where was their calculation? 12) Lines 140-146: Fig 6’s resolution could not support these statements. 13) Table 1: Review of case reports published in the last 10 years (2011 to 2021), which indicated some patients of 27 cases survived for much longer than their case report: How did they conclude “targeted therapies and immunotherapy” were advantageous? 14) Lines 150-152: “The NGS revealed somatic mutations in the PDGFRA, KIT, KDR (VEGFR2), and TP53, while IHC showed the expression of PD-L1 (Figure 7).” This statement is misleading, as no data for PDGFRA, KIT, KDR (VEGFR2), and TP53. Did they PCR to confirm? 15) Lines 179-181: “Despite the prolonged survival of some patients, the prognosis for



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7041 Koll Center Parkway, Suite
160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
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patients with liver metastases or splenic rupture after splenectomy was generally poor (Table 1).” Fig 2: “Red arrows indicate masses in the liver, while the white one indicates masses in the spleen” – simultaneous appearance? How did they verify which was the first and which was due to metastases? 16) In Discussion, Lines 244 – 246: “Therefore, we performed NGS and IHC for PD-L1, and fortunately, the patient was sensitive to sorafenib and PD-L1 inhibitor and received periodic treatment.” What was the data? 17) Lines 246 – 251: “However, After 15 months of follow-up, there is no progress or recurrence of the disease, and the prognosis is good compared to other patients without adjuvant therapy. However, there was no quantitative assessment in this patient.” What did they mean “compared to other patients without adjuvant therapy?” 18) the authors should update the literature on subclonal evolution in targeted therapies and immunotherapy. e.g., Hunting down the dominating subclone of cancer stem cells as a potential new therapeutic target in multiple myeloma: An artificial intelligence perspective. *World J Stem Cells*. 2020 Aug 26;12(8):706-720. doi: 10.4252/wjsc.v12.i8.706. Review. PubMed PMID: 32952853; PubMed Central PMCID: PMC7477658.