

Peer Review File

Article information: <https://dx.doi.org/10.21037/acr-23-188>

Reviewer A

Comment 1: A very interesting and timely case report discussing a key point in this setting. Some changes are needed.

Reply 1: We gratefully thank the reviewer for the time spent making your constructive remarks and useful suggestions, which has significantly raised the quality of our manuscript.

Comment 2: The introduction should be expanded and the evolving treatment scenario for GBC should be further discussed and some recently published papers added, only for a matter of consistency (PMID: 33756174; PMID: 33592561; PMID: 35031442 ; PMID: 37535194).

Reply 2: We gratefully appreciate for the reviewer's valuable feedback. We read more related references and revised our manuscript.

Changes in the text: "Biliary tract cancers (BTCs) ... Vater cancer (AVC) ² (Please check out Page 4 , Line 8) .", "The ABC-02 and BT22... for advanced disease (Page 4 , Line 17) , " The modest survival benefit ... of metastatic BTC ²² (Page 5 , Line 3) ", "Over the past decade... are underway. (Page 8 , Line 17) "

1. [Rizzo, A. & Brandi, G. Neoadjuvant therapy for cholangiocarcinoma: A comprehensive literature review. Cancer Treat Res Commun 27, 100354, doi:10.1016/j.ctarc.2021.100354 \(2021\).](#)

19. [Rizzo, A. & Brandi, G. First-line Chemotherapy in Advanced Biliary Tract Cancer Ten Years After the ABC-02 Trial: "And Yet It Moves!". Cancer Treat Res Commun 27, 100335, doi:10.1016/j.ctarc.2021.100335 \(2021\).](#)

20. [Rizzo, A. et al. Second-line Treatment in Advanced Biliary Tract Cancer: Today and Tomorrow. Anticancer Res 40, 3013-3030, doi:10.21873/anticancer.14282 \(2020\).](#)

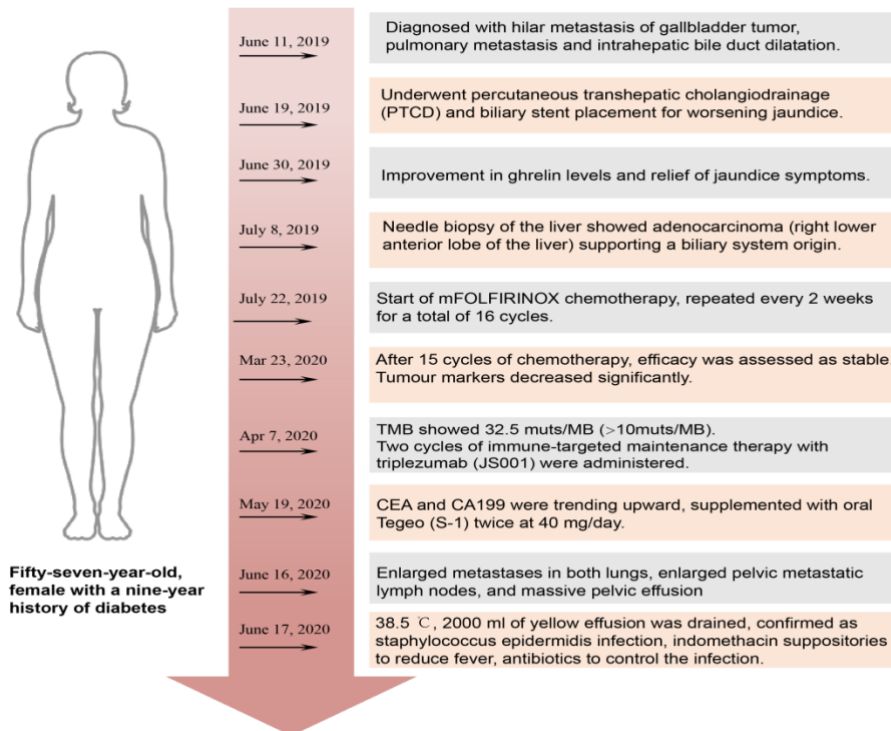
27. [Santoni, M. et al. The impact of gender on The efficacy of immune checkpoint inhibitors in cancer patients: The MOUSEION-01 study. Crit Rev Oncol Hematol 170, 103596, doi:10.1016/j.critrevonc.2022.103596 \(2022\).](#)

28. [Mollica, V. et al. The impact of ECOG performance status on efficacy of immunotherapy and immune-based combinations in cancer patients: the MOUSEION-06 study. Clin Exp Med 23, 5039-5049, doi:10.1007/s10238-023-01159-1 \(2023\).](#)

Comment 3: A timeline summarizing the main events of this case report should be included.

Reply 3: We gratefully thank you for pointing out this issue. We indeed should make it more clearly. Figure 1 has been updated. (Please check out Page 5 , Line11 and Figure 1)

Changes in the text:



Comment 4: A linguistic revision is needed.

Reply 4: We apologize for the poor language of our manuscript. We worked on the manuscript for a long time and the repeated addition and removal of sentences and sections obviously led to poor readability. We have carefully examined the paper, and

the presentation of English language and the ambiguous statements have been accordingly improved and updated.

Reviewer B

1. Highlight Box: please introduce all abbreviations in their first appearance in the highlight box.

Key findings

- A patient with advanced GBC and high TMB benefited from first-line treatment with mFOLFIRINOX.
- The patient underwent sequential chemotherapy with immunotherapy, but unfortunately experienced tumor recurrence and metastasis.

Reply 4: We have added it in the Highlight Box. (Please check out Page 3 , Line 5)

2. Highlight box: please reply the second question ‘What is known and what is new?’

What is known and what is new?

- Report here about what is known.
- Report here about what does this manuscript adds.

Reply 5: We have revised and updated it. (Please check out Page 3 , Highlight Box)

3. Line 90, please revise the typo, it should be ‘she’ not ‘he’.

89 | pelvic cavity (Fig. 6). The patient received a percutaneous peritoneal fluid puncture for drainage
90 | and approximately 2000 ml of yellow fluid was drained. During the drainage procedure he
91 | developed a fever with a body temperature of 38.5 °C. The fever was reduced with an

Reply 6: We gratefully thank you for pointing out this issue. This sentence has been revised and updated. (Please check out Page 7, Line 17)

4. Figures and table

- 1) Figure 3, please provide the staining method in the figure legend.

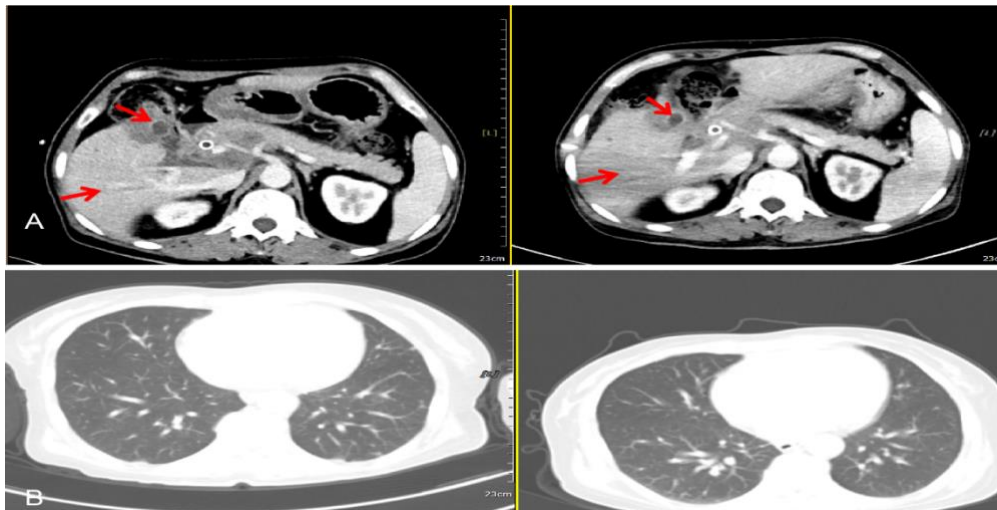
Reply 1): We have added it. Figure 3 shows the results of HE staining. (Please check out Page 20 , Line10)

2) Figures 4-6, please explain the meaning of red arrows in the figure legends.

Reply 2): We agree with the comment and add some details. (Please check out Page 20 , Line 12, Page 21, Line 6,11)

3) Figure 5, to protect the patient's privacy, it is suggested that the detailed time be removed from the image.

Reply 3): As suggested by the editor,we have made the requested changes, please contact us if you have any questions. (Please check out Page 19, Fig. 5)



4) Table 1, please add a main heading in the top left cell.

Reply 4): Thank you for this suggestion. We have revised it. (Please check out Page 17, Table.1)

Important mutations variation	Mutation rate of abundance/copy
TP53: NM_000546: exon8: c.886delC: p.H296fs	25.20%
ERBB2: NM_004448: Copy number	2.83%
IDH1: NM_005896: exon4: c.C395T: p.R132H	1.00%
TMB (mut/Mb)	32.50

Objective response rate (ORR, 100%)	36.90
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5) Any abbreviations used in figures and tables or their description should be defined in a footnote beneath each corresponding table/figure. Even if they were explained in the main text, full terms must be presented again in the corresponding figures and tables, so that figures and tables can be read on their own.

Reply 5): Thank you so much for your careful check. As suggested by the editor, accordingly, we revised the whole manuscript.