

Dear Prof. Ma and Reviewers:

Thank you for your letter and for the reviewers' comments concerning our manuscript entitled "Achievement of complete response to nivolumab in a patient with advanced sarcomatoid hepatocellular carcinoma: A case report" (ID: 55301). Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made correction which we hope meet with approval. Revised portion are marked in red in the paper. The main corrections in the paper and the responds to the reviewer's comments are as flowing:

Responds to the reviewer's comments:

Reviewer #1:

Special thanks to you for your good comments to this report.

Reviewer #2:

1. Response to comment: (The patient had chronic hepatitis B with cirrhosis and portal hypertension and has had entecavir therapy for 5 years at the time of Diagnosis of SHC. At the time of diagnosis, he was HBsAg (-). There is no information of HBV DNA, HBeAg status, anti-HBc, anti-HBs. Even though he may have lost to HBsAg (-), HBV is the etiology for this case and is not eliminated by nucleoside analogue. And one wonders if the patient has continued on anti-HBV therapy.)

Response:

As you know, the patient has taken nucleotide analogues orally for five years. And he has continued on anti-HBV therapy using nucleotide analogues orally named entecavir. At the time of diagnosis, he was HBsAg (-), and the HBV DNA<100, HBeAg (-), anti-HBc (-), anti-HBs (-); and because of the previous clear diagnosis of hepatitis B, physicians do not recommend discontinuation.

2. Response to comment: (Just curious why authors used the terminology, SGPT and SGOT in place of ALT and AST.)

Response:

SGPT and SGOT are abbreviations of full names, since ALT and AST are more commonly used in clinic, we agree to use ALT and AST in place of SGPT and SGOT.

Special thanks to you for your good comments.

Reviewer #3:

1. Response to comment: (I have major comments regarding their pathological diagnosis. I know differential diagnosis among SHC, SCC, and SCHC is very difficult in some cases. And consideration for rationale of SHC based on pathological findings must be documented.)

Response:

We actually agree with you it's very difficult to differentiate diagnosis among SHC, SCC, and SCHC in some cases. About our case, we invite the pathologist

(Jianning Chen) to examine the pathological slice again. On macroscopy examination, the cut surface of the tumor was fleshy and reddish. The boundary was irregular. On microscopy examination, the tumor showed an invasive pattern, and the tumor cells were spindle or epithelioid, with abundant cytoplasm. In some areas, the tumor arranged in a trabecular pattern, resembling that of HCC. In addition, the bile duct cells embedded in the tumor showed no or minimal atypia. On immunohistochemical staining, the tumor cells were intensely positive for CK8 and CK18, and weak or partial positive for CK7 and CK19. The other immunohistochemical results showed: CK (+), Vimt (+), Hep (-), Arginase-1 (-), Glypican-3 (-), CD34 (vascular +), HBsAg (-), PCEA (-), GS (partial +), Ki-67 (30%).

Based on these pathological findings, the final diagnosis was sarcomatoid hepatocellular carcinoma (HCC) with satellite nodule formation and neurologic invasion, and without definite intravascular thrombus formation (Fig.1).

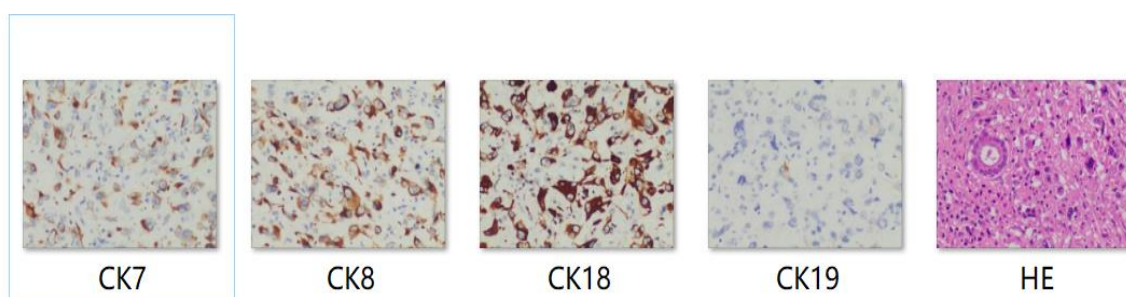


Fig.1 HE and immunohistochemical staining results(200X), including CK7、CK8、CK18、CK19; HE staining showed the bile duct structure is normal.

In addition, the documents about the rationale of SHC based on pathological findings have been illustrated in the discussion part, and the documents are in the reference No.4 and 6. And abbreviations used in immunohistochemistry (such as CK, Hep, PCEA, and GS) have been spelled out in the text.

Special thanks to you for your good comments.

thanks to the help of pathology expert Jianning Chen. His e-mail is chjning@mail.sysu.edu.cn, and from the Pathology Department, The Third Affiliated Hospital of Sun Yat-Sen University.

With best regards,

Yours sincerely,

Guoying Wang and affiliations