Author's response to reviews

Title: Acute Hepatic Failure and Multi-System Organ Failure Secondary to Replacement of the Liver with Metastatic Melanoma

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Author's response to reviews:

Reviewer #1:
1. Please clarify if the lesion was excised under local anesthesia considering it as mole or was it diagnosed as melanoma earlier? Mention clearly that the lesion was excised (considering it as mole which was later reported as melanoma and that the work up of metastasis was underway when the patient presented with pre-terminal event. If the diagnosis was melanoma earlier, the metastatic work-up is inadequate as evaluation of liver is part of work up of melanoma of any location. At least an ultrasound study of liver is desirable.

RESPONSE: The case report has been revised to indicate that the lesion resected was initially considered a mole and then later reported as a melanoma. The metastatic work up was under way when he presented to hospital.

Reviewer 2:
Report acceptable for publication.

Reviewer 3:
The main corrections have been done. The paper is much improved. I think, the following points should be mentioned in the Discussion.
1. The clinical suspicion of the syndrome of acute hepatic failure secondary to replacement of the liver with carcinoma is essential for preventing inappropriate referral of the patient to transplantation center.
2. The underlying pathogenetic mechanism of ALF due to malignancy is the widespread hypoxic hepatocellular necrosis as the result of massive sinusoidal infiltration and obliterative invasion of the hepatic vessels by the tumor cells. Hepatic hypoxia may also be attributed to cytokine release by the tumor cells (particularly in hematological malignancies). The latter is inducing damage to the bile ducts and activation of leucocytes and sinusoidal cells impeding sinusoidal microcirculation. In favor to hepatic hypoxia is the observed predominance of AST elevation and the high LDH values.

RESPONSE: We agree that the reviewer raises important points that should be included in the discussion. These points have been added accordingly (paragraphs 3 and 4 in the discussion).

Reviewer 4:
The paper has been revised to suggest that either acute liver failure or tumor lysis syndrome could be the mechanism underlying the patient's clinical deterioration. Yet, the paper remains just a case report without a good discussion. The authors have not provided any theories or speculations of why acute liver failure, or tumor lysis syndrome for that matter, had developed in this case. Such a discussion would add to the depth and meaning of the paper.

RESPONSE: We have expanded the discussion to consider the mechanisms of acute liver failure in our patient. Please see paragraph 3 of the discussion.