

Solitary nasopharynx metastasis from hepatocellular carcinoma after liver transplantation

A case report

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Abstract

Rationale: Hepatocellular carcinoma (HCC) is the fifth most common cancer and third leading cause of cancer-related deaths worldwide. Nasopharyngeal metastasis of hepatocellular carcinoma is very rare. This is the first report of posttransplantation nasopharyngeal metastasis.

Patient concerns: A 45-year-old man with a history of hepatitis B related hepatocellular carcinoma (HCC) in the right segment of the liver received an orthotopic liver transplant. Two year after the transplantation, he suffered from severe headache, and head contrast enhanced CT scans did not show clues for brain or skull metastasis. Then he developed hoarseness and dysphagia.

Diagnosis: The nasopharyngeal cancer was confirmed to be metastatic tumor from liver histologically according to biopsy.

Interventions: This patient underwent radiotherapy (RT) of the metastatic nasopharyngeal tumor, and there was significant symptomatic relief.

Outcomes: The patient died 3 months after nasopharyngeal metastasis was diagnosed.

Lessons: Recurrence of hepatocellular carcinoma with metastasis of nasopharyngeal carcinoma after liver transplantation is rare, but the prognosis is very poor. Close follow-up of patients should be paid attention to prevent the occurrence of such diseases.

Abbreviations: CT = computed tomography, HCC = hepatocellular carcinoma, LT = liver transplantation, MRI = magnetic resonance imaging, RT = radiotherapy, US = ultrasound.

Keywords: hepatocellular carcinoma, liver transplantation, nasopharynx metastasis

1. Introduction

Hepatocellular carcinoma (HCC) constitutes the fifth most frequent form of cancer worldwide and is the third most common cause of malignancy-related mortality.^[1] Liver transplantation

(LT) is the best treatment option in selected patients for early HCC. When the Milan criteria are fulfilled, the long-term survival following LT for HCC is similar to that following transplantation in patients without HCC. However, both the posttransplant physiologic condition and immunosuppressive therapy affect the patient's natural immunity, resulting in accumulating and more problematic posttransplant complications such as unusual posttransplant HCC metastasis. Nasopharyngeal metastasis of posttransplant tumor recurrence is an extremely rare occurrence. Here we report a case of posttransplantation nasopharynx metastasis of HCC in an HBsAg-positive patient who had liver cirrhosis. To the best of our knowledge, this is the first such case published in the English literature.

2. Case presentation

A 45-year-old Chinese male patient with cirrhosis of the liver due to hepatitis B virus presented one focal hepatic lesions with a cytologic and histologic diagnosis of hepatocellular carcinoma (Edmondson II) in October 2015. The computed tomography (CT) showed a 4cm HCC located in the right hepatic lobe (Fig. 1). The patient was placed on a waiting list for LT. His pretransplantation serum alpha-fetoprotein level is 1210 ng/mL. The pretransplant work up for LT included a CT scan of the abdomen and chest that showed no evidence of distant metastasis. A nuclear bone scan was also negative for bone metastasis. According to Hang-Zhou Criteria of China, he received an orthotopic liver transplantation on December 17,

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L-LL and YZ These authors contributed equally to this work.

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Figure 1. Enhanced CT scan of liver structure. In the right hepatic lobe, strong degree enhancement of the mass (arrow) is shown.

2015. One day after liver transplant, the patient was given immunosuppressive therapy based on a standard rapid-taper regimen of corticosteroids and low-dose tacrolimus monotherapy (1 mg every 12 h) to the currently recommended target level. The patient had at 3-month intervals regular follow-up visits to the liver transplant clinic and had a normal alpha-fetoprotein (97 ng/mL), chest X-ray, and ultrasound (US) of the liver until March 2017.

In May 2017, he suffered from severe headache, and head contrast enhanced CT scan did not show clues for brain or skulls metastasis. Then, he developed hoarseness and dysphagia. Magnetic resonance imaging (MRI) showed that there was a mass on the posterior wall of the nasopharynx and multiple bone destruction in the basal part of the occipital bone (Fig. 2). Examination with a nasopharyngoscope was performed, which revealed a neoplasm on the posterior wall of the nasopharynx (Fig. 3). A biopsy of the neoplasm was conducted, indicating the

nasopharyngeal cancer which was proven to be the metastatic tumor from liver histologically by biopsy (Figure 3). This patient underwent radiotherapy (RT) of the metastatic nasopharyngeal tumor, and there was significant symptomatic relief. Finally, the patient died 3 months after nasopharyngeal metastasis was diagnosed.

3. Discussion

Hepatocellular carcinoma (HCC) is the fifth most common cancer and third leading cause of cancer-related deaths worldwide. Liver transplant is now considered to be a successful treatment modality for early hepatocellular carcinoma. With the improvements in surgical methods, posttransplant care, and immunosuppressive regimens, patients with HCC who receive liver transplants have a better prognosis than patients who receive liver resection.^[2] However, as a curative modality for HCC, concerns remain regarding the possible clinical outcomes of posttransplant patients. That is, some patients may have recurrence of HCC after liver transplant, resulting in significantly lower survival rates versus patients without recurrence.^[2]

Posttransplantation tumor recurrence is related to some characteristics of the tumor. The histopathology grading and tumor diameter was significantly correlated with vascular invasion. Jonas et al have confirmed that the rates of vascular invasion in tumors larger than 5 cm were significantly lower in patients suffering from well-differentiated HCC (25%) compared with moderately and poorly differentiated HCC (100%).^[3] The pretransplantation serum alpha-fetoprotein levels also seem to be related to postoperative recurrence. A Japanese study performed on 698 HCC-LT patients found that patients who have AFP levels ≤ 200 ng/mL have a 5-year disease-free survival rate of 85%, despite being beyond the Milan criteria.^[4] Recently a meta-analysis demonstrated that immunosuppression was also a risk factor for tumor growth and HCC recurrence.^[5] Our patient had an HCC with one nodule, 4.0 cm in size. The tumor was moderately differentiated and serum alpha-fetoprotein level, at

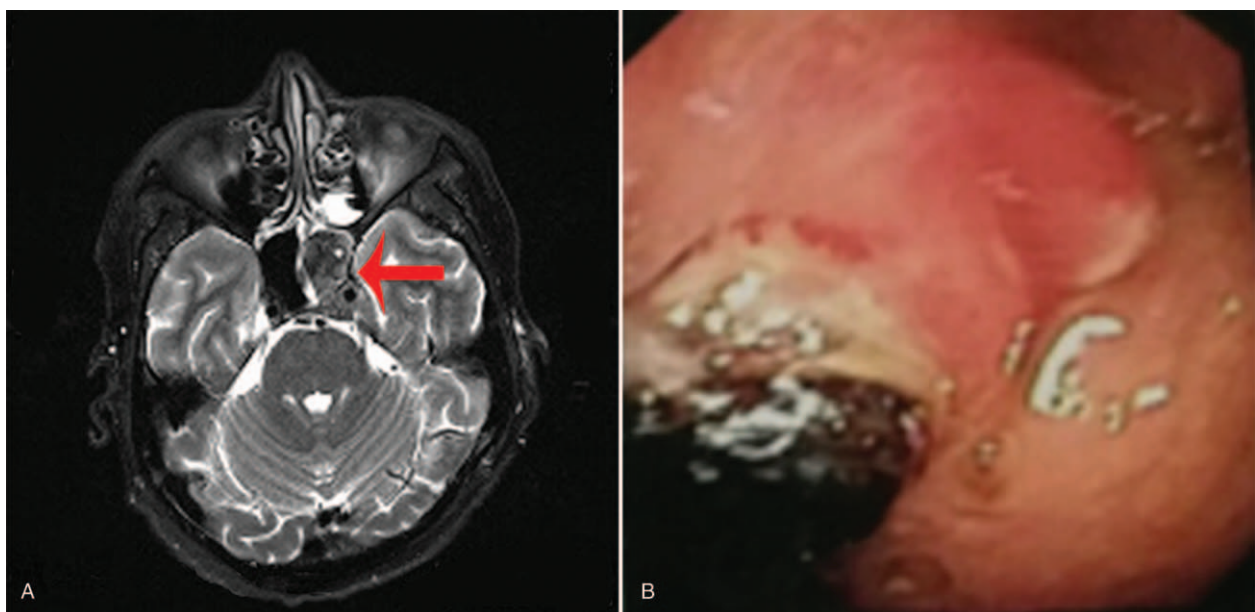


Figure 2. (A) Nasopharynx metastasis from primary. Magnetic resonance imaging showed nasopharynx metastasis (arrow). (B) Pharyngeal posterior wall tumor can be seen under nasopharyngoscopy.

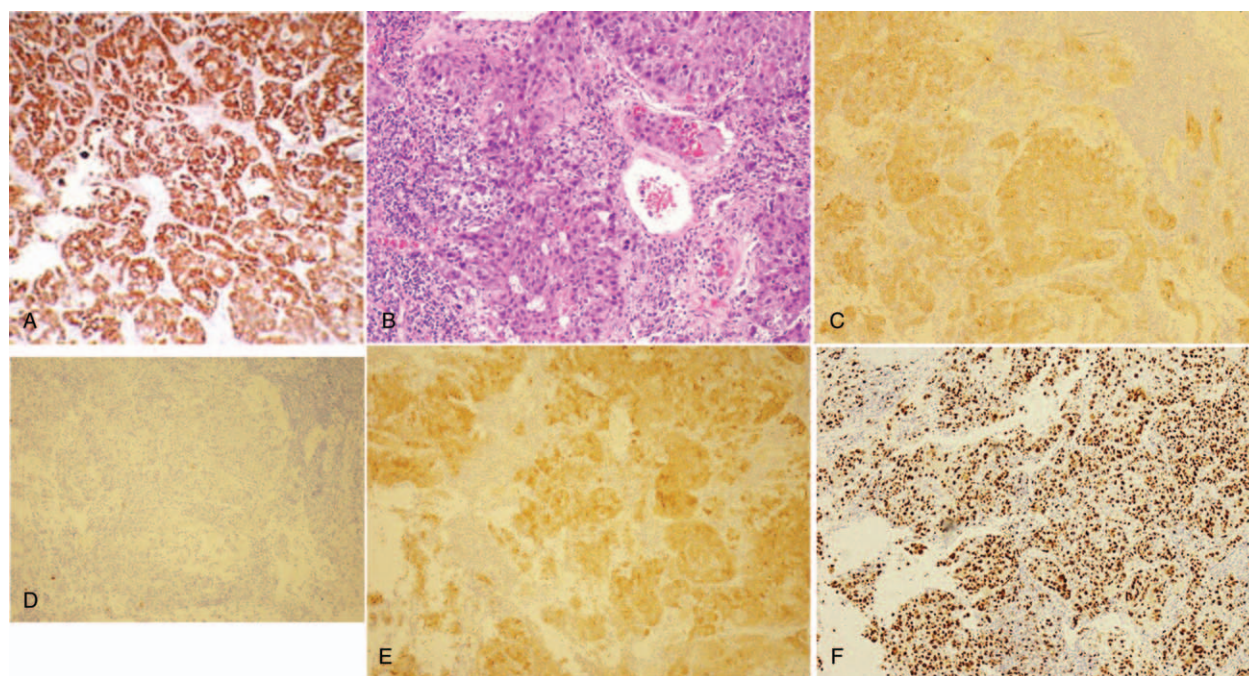


Figure 3. Pathological findings of the biopsy specimen from nasopharynx mass. (A) Hematoxylin and eosin staining of nasopharynx adenocarcinoma with coagulative necrosis. Immunoreactivity for GPC3 (B), CK20 (C), Ki67 (D), Vilin (E), and HEPA (F). Magnification $\times 100$ for (A–F).

the time of LT, was 1210 ng/mL. Long-term use of immunosuppression after transplantation also increased tumoral growth rate. All of these factors are considered to represent a risk for tumor recurrence before and during the postoperative period.

Hepatocellular carcinoma metastasises is mainly to the lungs, bones, and the adrenal glands.^[6] Carcinoma metastatic to the nasopharynx from the primary liver cancer is rare, and there are only two reports in the literature concerning this condition. Wang et al reported a case of nasopharynx metastasis from liver in a 50-year-old male patient who was diagnosed with primary hepatocellular carcinoma (nodular and diffuse-type) in 2014 and underwent interventional therapy for two times.^[7] A similar case reported by Abhay et al presented a case of a 70-year-old male who was referred to hospitalization with history of nasal obstruction and nasal bleeding which on further evaluation was diagnosed to have an isolated metastasis to nasopharynx from liver primary.^[8] In this article, we present a case of solitary nasopharyngeal metastasis from recurrent HCC after living-donor liver transplant.

Why did hepatic cancer cells invade the nasopharynx? In our present case, the cirrhosis was attributable to HBV infection. After infection, scar tissue replaces normal liver tissue. We suggest that pathophysiologic changes associated with the long-term inflammation caused by HBV infection initiated tumorigenesis. In response to transforming growth factor, cancer cells might undergo a reversible phenotypic change involving loss of intercellular adhesion, epithelial polarization, and increased invasiveness, which promoted cell entry into the vasculature. Both the abdominal and cranial vein lack venous valves, allowing bidirectional blood flow. We assumed that cancer cells invaded a vein, and that an increase in intra-abdominal pressure caused metastasis to the cavernous sinus, allowing retrograde venous flow to the nasopharynx hematogenously.

HCC recurrence after liver transplant has a significant effect on the patient's prognosis, and treatment outcome data are limited.

In the few published studies, the median time to recurrence was 7.9 to 12.9 months and the median survival time after HCC recurrence was 8.7 to 12 months.^[9] Most cases of extrahepatic metastases from HCC have been prescribed symptomatic treatment. In a report from Japan, no patient who underwent only symptomatic treatment for extrahepatic metastasis from HCC survived for more than 2 years, whereas the 1- and 3-year survival rates after development of extrahepatic metastasis in patients who received some treatment—surgery, chemotherapy, radiotherapy, or immunotherapy—were 42.3% and 17.8%, respectively.^[10] With all other cancers, treatment for HCC recurrence after liver transplant should be decided in a multidisciplinary fashion, taking into account patient comorbidities, tumor stage, and available resources.

4. Conclusion

In conclusion, recurrence of HCC after liver transplant as nasopharyngeal metastasis, although rare, may indicate an extremely poor prognosis and therefore should be considered as a possible site of recurrence. Patients with high risk factors related to posttransplant recurrence should especially be followed up with imaging (CT or MRI) as a cautionary measure.

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Author contributions

Supervision: Xiao-Lin Guo.

Validation: Xiao-Lin Guo.

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