A Rare Case of Mistaken Identity: Metastatic Hepatocellular Carcinoma to the Nose

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ABSTRACT
Hepatocellular carcinoma most often metastasizes to the lungs, abdominal lymph nodes, or bone. The identification of extrahepatic metastases of hepatocellular carcinoma to the sinonasal region has rarely been reported. We report a case of a 49 year-old man with a history of stage IV hepatocellular carcinoma presenting with two adjacent pigmented lesions on the tip of his nose. Initial pathological staining identified the lesion as a primary melanoma. However, upon further examination with the chemical markers CEA, CAM 5.2, and Keratin, it was determined that the lesions were consistent with hepatocellular carcinoma. This case highlights a potentially rare situation of mistaking a liver metastasis for a malignant melanoma.

INTRODUCTION
Hepatocellular carcinoma (HCC) is the most prevalent of the liver cancers. It is predominantly found in men 50-60 years of age, and is most commonly due to cirrhosis secondary to alcoholism, viral Hepatitis B or C, haemochromatosis, or autoimmune diseases. Hepatocellular carcinoma metastasizes via blood, direct spread, or lymphatic dissemination. Extrahepatic metastasis of HCC has been reported in advanced disease, such as stage III and IV. In such cases, distant metastases occur from the primary site in the liver through the portal vein to the lungs most predominantly (55%), followed by abdominal lymph nodes (41%) and bones (28%) (1). Less frequently, there have even been reports of hepatocellular carcinoma metastasizing to the sinonasal regions of the nasal septum, nasal sinuses, and nasal cavity (2). We report the case of a patient with stage IV hepatocellular carcinoma secondary to liver cirrhosis from alcoholism and hepatitis C with distant metastasis to the nasal tip. In our review of the literature, this is the first reported case of hepatocellular carcinoma to the skin of the nasal tip.

CASE REPORT
The patient is a 49 year-old Hispanic male who underwent orthotopic liver transplantation for what was originally believed to be cirrhosis secondary to alcoholism and Hepatitis C. However, pathologic examination of the hepatectomy specimen revealed the presence of multi-focal, moderately differentiated hepatocellular carcinoma, trabecular and pseudoacinar type, with involvement of the portal vein. Two regional lymph nodes showed no evidence of tumor. The patient was subsequently staged as T4N0M0, Stage IV hepatocellular carcinoma. The
remainder of the liver parenchyma showed cirrhotic changes. The patient was maintained on a stable immunosuppressive regimen of cyclosporine, and anti-viral amantadine therapy.

He did well for 7 years postoperatively until the patient noted a small dark spot on the tip of his nose. On examination the patient actually had two lesions on the right lateral tip of the nose, each measuring approximately 2mm. The lesions continued to increase in size and the patient underwent a biopsy at an outside facility in his homeland of Mexico. Histological examination with haemotoxylin and eosin staining was interpreted by the pathologist to be consistent with a 6 mm deep, Clark’s level 5 melanoma. There was no lymphadenopathy found in the head and neck region. The patient was given the diagnosis of melanoma and referred to our clinic for wide local excision and reconstruction (see Figures 1 and 2, which illustrate the presenting lesions following initial biopsy). The patient underwent excision of these lesions with wide 2 cm margins. The area of resection extended down to but not through the cartilage. The patient underwent two stage nasal reconstruction using a traditional left paramedian forehead flap that went on to heal uneventfully.

Immunoperoxidase staining was performed at our facility to confirm the diagnosis. Results of initial immunostaining with the common melanoma markers, S100, HMB45, and MELAN-A, were not expressed as would have been expected for a primary melanoma. Given the patient’s prior history of hepatocellular carcinoma, additional staining with CEA, CAM 5.2, and Keratin were performed and found to be positive; this is consistent with metastatic hepatocellular carcinoma. Subsequent work-up with computerized tomography scanning showed multiple small lesions in the lung parenchyma bilaterally, as well as mediastinal lymphadenopathy. Biopsy of several of these lung lesions similarly confirmed the diagnosis of metastatic hepatocellular carcinoma. The patient went on to receive adjuvant chemotherapy.
DISCUSSION

In a review of the literature, this is the first report of HCC metastasizing to the skin of the nose. In a recently published review by Magana and Gomez, cutaneous metastases of HCC have been reported in men older than 50 years of age, presenting as a single lesion on the head, specifically the face (2). While there have been several reports of HCC metastasizing to the nasal sinuses, there has not been a report of metastasis to the skin of the nasal tip. In all of these reports, metastases of HCC to the nasal region have diverse presentations. Just as in our case, the rarity of this type of metastasis can initially indicate histology that is consistent with primary melanoma, which only upon further histological testing results in the final diagnosis of hepatocellular carcinoma metastasis. These findings suggest that in evaluating pigmented lesions of the nasal region in patients with a history of HCC, one should consider the testing for specific chemical markers in addition to examination with haemotoxylin and eosin staining to differentiate a primary melanoma from the rare presentation of metastases. The key histological hepatic chemical markers include GGT (3), but may also consist of CEA, CAM 5.2, and Keratin such as in our case.

The reason for a predominance of metastases of HCC to the skin of the face in men over the age of 50 years is uncertain at this time. One theory may involve prolonged damage by ultraviolet radiation in sun exposed areas such as the face. Such UV radiation could alter local protein structure, thereby enhancing the capacity for HCC cells to adhere to receptors in this region. Additionally, the predominance in men may be linked to testosterone’s ability to enhance transforming growth factor alpha-related hepatocyte proliferation (4). The rare presentation of HCC metastasis to the nasal region specifically is rather curious as well, and has not been elucidated. One possible explanation is adhesion proteins or chemical receptors in nasal tissue, which attract hepatocellular carcinoma cells to this region of the body. A recent study by Jan et al has shown a correlation between over-expression of focal adhesion kinase and extrahepatic metastatic sites in patients with HCC (5). Future studies could investigate the presence of this and other protein receptors in the nasal region of patients with HCC, which could serve as potential beacons for HCC cells to migrate and adhere. While these theories have not yet been fully explored, they serve as a preliminary basis explaining the rare presentation of metastatic HCC to the nasal region.

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