

Gingival Lesions and Nasal Obstruction in an Immunosuppressed Patient Post-Liver Transplantation

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Although rare, metastatic hepatocellular carcinoma (HCC) presenting only to the mandible, gingiva, and nasal cavity in patients subsequently found to have primary HCC has been reported. In the age of transplantation, certain HCC patients may receive treatment with an orthotopic liver transplant. Due to the proclivity of HCC for early micrometastases, immunosuppressive therapy can induce significant metastatic lesions. Nasal mass obstruction, gingival lesions, or facial growths in this population must be considered metastatic until proven otherwise.

Nasal and oral mucosal lesions in immunocompromised patients present a unique challenge to the physician. Patients receiving immunosuppressive medications to prevent organ rejection after transplantation, who present with such lesions, have a differential diagnosis consisting primarily of infection, lymphoproliferative disorders, and primary or metastatic tumors. We present the first case of nasal obstruction with concomitant gingival lesions due to metastatic hepatocellular carcinoma (HCC) after liver transplantation for HCC and discuss this tumor's rare but unique propensity to metastasize to the mandible and gingiva.

The opinions and assertions herein are the private views of the authors and are not to be construed as official or reflecting the policies of the Department of Defense or the Department of the Army.

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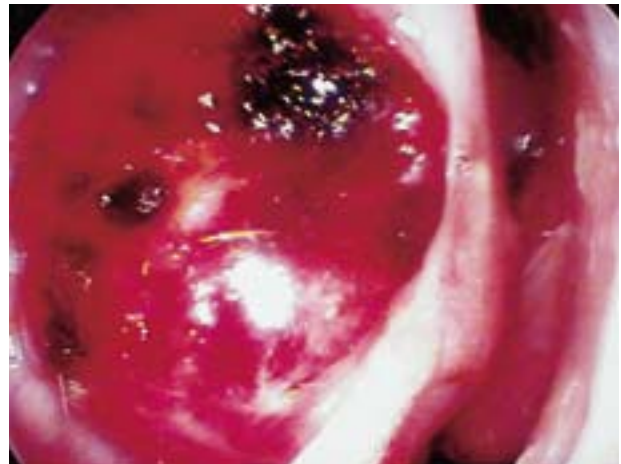


FIGURE 1. Nasal endoscopy of the right nostril reveals a large "liver"-colored mass.

Case Report

A 44-year-old Hispanic man, with a history of hepatitis C-induced liver cirrhosis complicated by HCC, was treated with an orthotopic liver transplant in 1996. He was initiated on immunosuppressive therapy with FK506/tacrolimus and completed doxorubicin hydrochloride (Adriamycin®) chemotherapy weekly for 10 weeks. In 1998, the patient complained of left facial pain, epistaxis, and decreased ability to breathe through his nostrils while receiving continued immunosuppressive therapy.

Nasal endoscopy showed a large, red mass obliterating the right nasal passage (Figure 1) and red, friable, plaque-like lesions were visible on the maxillary gingiva (Figure 2). A computed tomographic scan revealed a mass involving the right nasal passage with slight compression of the septum into the left nasal passage (Figure 3). Histopathologic evaluation



FIGURE 2. Erythematous friable plaques on the gingiva of a patient post-orthotopic liver transplantation for hepatitis C-induced liver cirrhosis complicated by hepatocellular carcinoma.



FIGURE 3. Coronal images of a facial computed tomographic scan demonstrates a mass originating in the right nasal cavity, obliterating the turbinates and encroaching upon the left nasal passage way.

revealed sheets of pleomorphic hepatocytes compatible with metastatic HCC underlying normal nasal epithelium (Figure 4).

The patient was treated with Adriamycin® and cisplatin, with concomitant reduction of the FK506 dosage. Several months later, the patient developed bony metastasis and a new liver lesion, which, on computed tomographic scan, was consistent with metastasis not present on initial evaluation. This was despite reduction in the immunosuppressive therapy without evidence of rejection.

Comments

Orthotopic liver transplantation has been indicated in certain patients with HCC, but is often complicated by recurrent or metastatic disease.¹ Hepatocellular carcinoma has a tendency for early vascular penetration of the portal vein and inferior vena cava, which promotes the possible seeding of other tissues with micrometastases before liver transplant.^{1,2} Therefore, the subsequent immunosuppressive agents, by decreasing host immunity, can accelerate the growth of micrometastases to clinically significant lesions.³ The most common sites of HCC metastasis are the lung, bone, and brain.⁴ The head and neck are rare locations. However, multiple reports of mandibular metastases with or without gingival involvement have been reported in the literature.⁵⁻¹⁰ In 1998, Patankar *et al.*² published, to their knowledge, the first reported case of metastatic HCC of the nasal cavity in an immunocompetent patient. Gingival metastases have been the initial presentations of primary HCCs, but have not been reported in the post-liver transplant population to date.⁵⁻¹⁰ The pathway of metastasis limited to the oral cavity is unknown, but

is postulated to occur through hematogenous spread through the vertebral venous plexus.⁶

Malignant and metastatic tumors of the nasal cavity cause obstructive symptoms early in the clinical course and can also cause epistaxis, hyposmia, anosmia, hypesthesia, facial or buccal edema, or otalgia.^{11,12} Gingival metastases, however, are usually asymptomatic.⁶ The most common tumors to metastasize to the nasal chamber include renal, lung, breast, and prostate cancers.¹² The differential diagnosis in immunosuppressed patients with nasal space growths also includes lymphoma, Kaposi's sarcoma, and infiltrative fungal sinusitis.¹³ Similarly, metastatic gingival lesions can be confused with Kaposi's sarcoma, leukemia, or lymphoproliferative disorders, and often are misdiagnosed as pyogenic granulomas, hemangiomas, or peripheral fibromas.¹⁴

The medical history and physical examination of immunocompromised patients with clinical symptoms suggestive of nasal obstruction are enhanced with nasal endoscopy, computed tomography, and magnetic resonance imaging.^{12,15} Biopsy of the lesions can easily identify the primary tumor type. Hepatocellular carcinoma has the tendency to be hypervascular, and a case of significant post-biopsy bleeding of a mandibular lesion has been reported.⁷ Ashar *et al.*⁷ attributed the hemorrhage to the inherent hypervascularity of HCC and not to coagulation abnormalities.

In conclusion, the status of post-liver transplant patients with HCC who present with any nasal complaints of obstruction, or swelling with or without friable gingival lesions, must be assumed to have metastatic HCC until proven otherwise. These patients should have routine oropharynx examinations during follow-

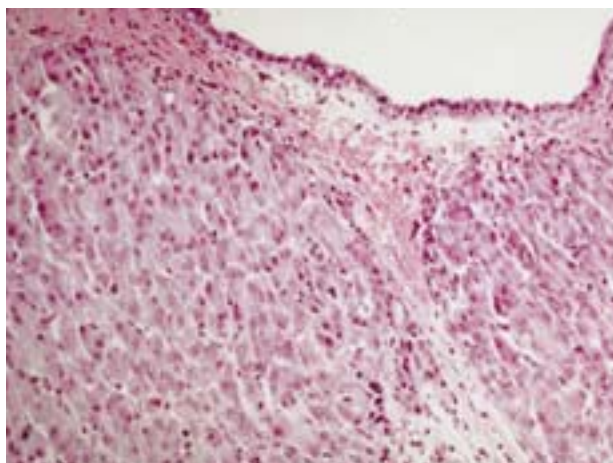


FIGURE 4. Histopathology of the nasal mass reveals sheets of malignant hepatocytes consistent with metastatic hepatocellular carcinoma (H&E; original magnification, X 40).

up, regardless of the presence of symptoms. This is because the initial presentation of metastatic spread may not be to the lung, bone, or brain, but rather to the gingiva, oropharynx, or both. Unfortunately, patients with metastatic HCC have a poor prognosis.⁴

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