Hepatocellular carcinoma with cutaneous metastases

Suzanne Rueben BSc, David Owen MD, Patricia Lee MD, Alan Weiss MD

S Rueben, D Owen, P Lee, A Weiss. Hepatocellular carcinoma with cutaneous metastases. Can J Gastroenterol 2009;23(1):23-25.

Two cases of cutaneous metastases from hepatocellular carcinoma (HCC) are reported. Both patients had been diagnosed with HCC at least one year before the appearance of skin lesions. The lesions presented as small reddish nodules in both patients, with a large additional vascular lesion in one of the patients. Cutaneous metastases from HCC are very rare. However, these two cases suggest that patients with HCC and presenting with skin nodules should have biopsies performed to confirm the diagnosis.

Key Words: *Granuloma pyogenicum; Hepatoma; Metastases; Neoplasm*

Carcinome hépatocellulaire avec métastases cutanées

Les auteurs signalent ici deux cas de métastases cutanées émanant d'un carcinome hépatocellulaire (CHC). Les deux patients avaient reçu leur diagnostic de CHC au moins un an avant l'apparition de leurs lésions cutanées. Chez les deux patients, les lésions ont pris la forme de petits nodules rougeâtres, accompagnés d'autres lésions vasculaires volumineuses chez l'un d'entre eux. Les métastases cutanées du CHC sont très rares. Toutefois, ces deux cas donnent à penser que la biopsie s'impose probablement pour confirmation du diagnostic chez les patients atteints de CHC qui présentent des nodules cutanés.

Cutaneous metastases from hepatocellular carcinoma (HCC) are very rare. Previous reports have described these skin lesions to be rapidly growing nodules found mostly on the face, scalp, chest and shoulders. The lesions appear singly, or in multiples as firm, painless, nonulcerative, reddish nodules that are approximately 1 cm to 2.5 cm in diameter (1,2). Others are larger, with either a pyogenic granuloma-like (1) or a hemangiomatous character (3) that bleed extremely easily and grow rapidly. Two cases of skin metastases from HCC are reported. Both patients had a lesion resembling a reddish nodule, while one patient also presented with a larger pyogenic granuloma-like lesion.

CASE PRESENTATIONS

Case 1

In 2004, A 60-year-old Middle-Eastern man initially presented with a history of mild fatigue and right upper quadrant pain. His workup revealed a large, solitary, inhomogeneous, extremely vascular lesion within the right lobe of the liver measuring approximately 13 cm × 15 cm. His carcinoembryonic antigen (CA) tumour marker level was 1.1 µg/L and his alphafetoprotein (AFP) level was 4.9 µg/L, both within the normal range. Further laboratory studies showed a total bilirubin level of 5 µmol/L (normal 0 µmol/L to 18 µmol/L), aspartate aminotransferase 95 U/L (normal 10 U/L to 38 U/L), alanine aminotransferase 32 U/L (normal 20 U/L to 65 U/L), alkaline phosphatase 237 IU/L (normal 50 IU/L to 160 IU/L), total serum protein 72 g/L (normal 62 g/L to 82 g/L), hemoglobin 111 g/L (normal 135 g/L to 175 g/L), platelet count 331×10^9/L (normal 125×10^9/L to 350×10^9/L), white blood cell count 6.9×10^9/L (normal 4×10^9/L to 10×10^9/L), lactate dehydrogenase 150 U/L (normal 90 U/L to 210 U/L) and an international normalized ratio of 1.23 (normal 0.9 to 1.2). The patient had a history of hepatitis B. His appetite was good and his weight was stable. He had no gastrointestinal-related symptoms and no significant medical history.

A needle core biopsy showed mild chronic hepatitis. The mass, however, had the characteristics of HCC and the patient was treated with chemoembolization followed by a resection of the tumour. A follow-up computed tomography (CT) scan of the abdomen showed no recurrent or residual tumour. There were no known metastases at the time.

The patient was asymptomatic until April 2006, when he developed several skin lesions located on his left nostril, his forehead and the right side of his neck. The lesions on his forehead and neck appeared as reddish nodules approximately 0.5 cm in size in diameter. The lesion on his left nostril however, grew rapidly with a nodular surface that was extremely vascular and bled easily. The patient initially mistook the nodules to be mosquito bites and did not seek medical attention until July 2006.

In July 2006, a biopsy performed on a left neck lesion of the patient showed features consistent with metastatic HCC. The tumour cells were positive for keratin and hepatocyte-specific antigens but negative for S100 protein.

Due to the increasing size of the left nostril lesion, which in July 2006 measured approximately 2 cm × 2 cm × 2 cm (Figure 1), a resection was performed by an otolaryngologist

Medical Oncology, British Columbia Cancer Agency, Vancouver, British Columbia
Correspondence: Dr Alan Weiss, Medical Oncology, British Columbia Cancer Agency, 600 West 10th Avenue, Vancouver, British Columbia V5Z 4E6. Telephone 604-877-6000 ext 2740, fax 604-877-0585, e-mail aweiss@bccancer.bc.ca
Received for publication December24, 2007. Accepted April 17, 2008

 ©2009 Pulsus Group Inc. All rights reserved

Figure 1) *Large nodule on the left nostril resembling a pyogenic granuloma*

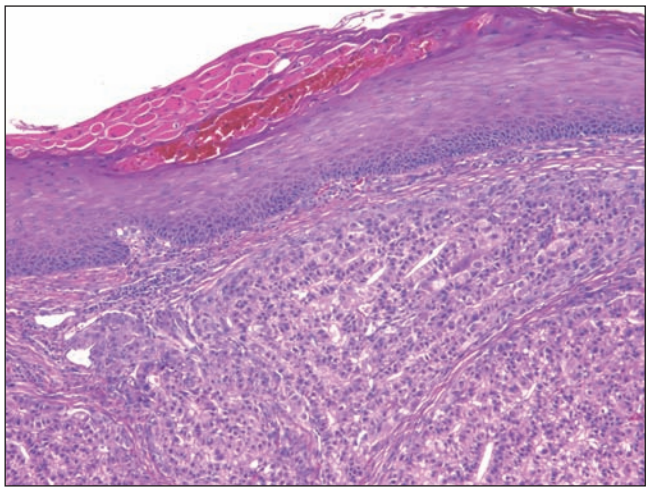


Figure 2) *Biopsy of tumour from left nostril showing a dermal deposit of hepatocellular carcinoma*

and again the pathology showed metastatic HCC (Figure 2). The tumour filled the stroma and had both trabecular and pseudoglandular patterns. Focal bile production was present.

The patient also presented with progressive weakness and numbness in both his left arm and left leg. A CT scan of his brain performed in July 2006 showed a solitary right frontal and parietal lobe mass measuring 2.5 cm × 2.8 cm. A right rolandic craniotomy and tumour resection was performed with the pathology again consistent with metastatic HCC. Further investigations showed pulmonary and bone metastases. Chemotherapy was considered, but due to the fact that the patient had developed a gluteal abscess and a weakened condition, chemotherapy was not initiated. Consequently, patient received supportive therapy and subsequently died.

Case 2

The second patient was a 76-year-old woman known to be hepatitis B-positive and routinely monitored by abdominal ultrasound. In February 2005, an ultrasound revealed three solid lesions that were consistent with hepatoma. A blood test showed an elevated tumour marker AFP level of 16 µg/L (normal less than 11 µg/L). Her laboratory findings showed a white blood cell count of 11.6×10^9/L (normal 4×10^9/L to 10×10^9/L), hemoglobin of 107 g/L (normal 135 g/L to 175 g/L), platelet count of 434×10^9/L (normal 125×10^9/L to 350×10^9/L), a direct bilirubin of 60 µmol/L (normal 0 µmol/L to 5 µmol/L), aspartate aminotransferase 82 U/L (normal 10 U/L to 38 U/L), alanine aminotransferase 90 U/L (normal 20 U/L to 65 U/L), gamma-glutamyl transpeptidase 161 U/L (normal 10 U/L to 55 U/L), alkaline phosphatase 173 IU/L (normal 50 IU/L to 200 IU/L), lactate dehydrogenase 226 U/L (normal 90 U/L to 210 U/L) and an international normalized ratio of 1.27 (normal 0.9 to 1.2). A subsequent CT scan confirmed these findings showing two lesions within segments II/III (diameter, 5 cm) and V/VIII (diameter 2 cm), as well as changes consistent with cirrhosis. The patient was treated with alcohol ablation of the left lesion because resection was thought to be associated with a high risk of liver decompensation due to the cirrhotic appearance of the liver and the large volume of liver that would need to be resected. The lesion on the patient's right side was to be treated once the patient had recovered from the procedure. During the procedure, however, a biopsy was taken of the surrounding tissue and revealed cirrhosis. At the time, the patient was asymptomatic with no significant medical history. She did, however, have a positive family history of liver cancer.

A follow-up CT scan showed several new hypervascular nodules scattered throughout the liver as well as an elevated AFP level of 14 µg/L. Subsequently, a chemoembolization of the right hepatic artery was performed in December 2005. There was also evidence of portal vein thrombosis and cholelithiasis. Subsequent imaging showed successful chemoembolization of the right lesion.

At the end of May 2006, the patient noticed a lump on her right upper and lower eyelid that was causing significant tearing (Figure 3). She was seen by an ophthalmologist. The lesion was initially thought to be a stye. However, because local treatments did not help, a biopsy was performed in July 2006. The pathology revealed metastatic adenocarcinoma consistent with metastatic HCC (Figure 4).

The patient's condition had deteriorated. She had visible lumpiness of both the upper and lower eyelid. She reported a loss of appetite as well as severe dyspnea and orthopnea. She presented with fever, ascites, pedal edema and crackles in her right thorax. A CT scan of her thorax showed diffuse pulmonary nodules consistent with metastases. The patient's condition continued to deteriorate; she received supportive care and subsequently died.

DISCUSSION

Metastases to the skin from internal malignancies are very uncommon (4). The most common cancers that metastasize to the skin are of pulmonary or breast origin. The most common site of HCC metastases are the lungs, followed by the periportal lymph nodes and the bones (5). Skin metastases from HCC, however, are very rare. In one study by Peters (6), skin metastases were shown to account for only 2.7% of cirrhotic HCCs and no cases in noncirrhotic HCC. Otherwise, only a few case reports exist. Of these case reports, some describe cutaneous metastases due to direct implantation from a procedure such as a biopsy or ablation treatment of HCC. One report (7) described a nodule presenting at the injection site of a percutaneous ethanol injection therapy performed three months previously. These direct deposits are, of course, different in etiology than distant metastatic disease, which occured in the present two cases.

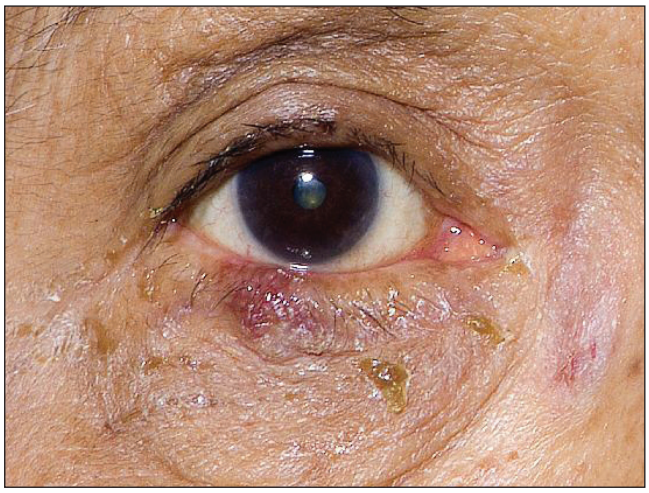


Figure 3) *Eyelid lesion representing a dermal deposit of hepatocellular carcinoma (case 2)*

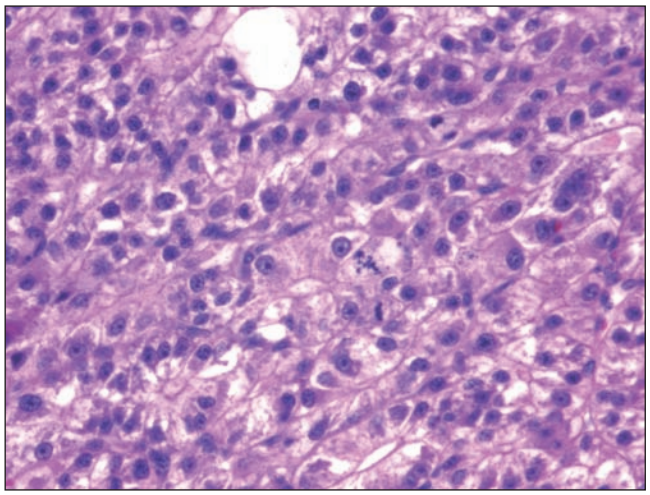


Figure 4) *High-power view of hepatocelluar carcinoma showing a predominately solid pattern with compressed sinusoids and ill-formed psueudoacini*

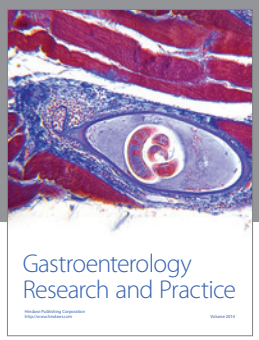
Previous reports (1,2) have described these skin lesions to be rapidly growing nodules found mostly on the face, scalp, chest and shoulders. The lesions appear singly or in multiples as firm, painless, nonulcerative, reddish nodules which are approximately 1 cm to 2.5 cm in diameter. Other lesions are larger and have been described morphologically to resemble either a pyogenic granuloma (1) or a hemangioma (3), both of which bleed easily and grow rapidly. Recently, a skin lesion was even described as being 'abscess-like' (8). While both patients reported and presented with lesions resembling reddish nodules, one patient presented with a larger vascular lesion that resembled a pyogenic granuloma. Biopsies from both patients diagnosed metastatic HCC.

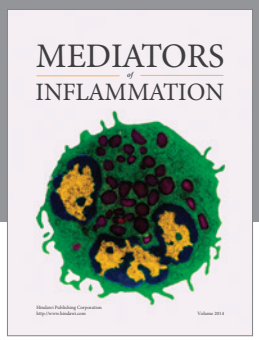
Cutaneous metastasis can present as the first clinical sign of HCC (8-10). Both of our patients, however, presented with cutaneous metastases approximately one year following diagnosis of HCC. In both patients, the skin lesions were the first sign of metastatic disease, although further follow-up revealed other metastatic sites.

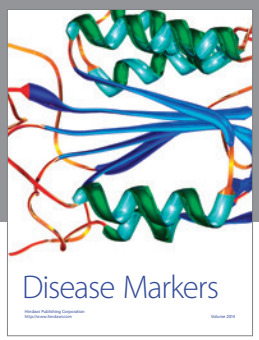
Because cutaneous metastases are a very uncommon manifestation of HCC, the present two cases should increase awareness of their existence. The possibility of skin metastasis should be considered in HCC patients who present with skin nodules, and the diagnosis should be confirmed by biopsy.

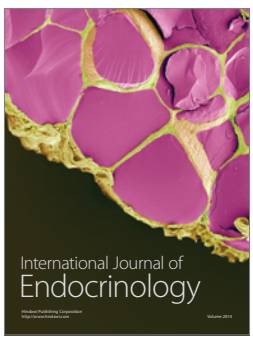
REFERENCES

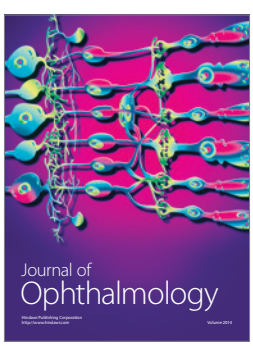
1. Kubota Y, Koga T, Nakayama J. Cutaneous metastasis from hepatocellular carcinoma resembling pyogenic granuloma. Clin Exp Dermatol 1999;24:78-80.
2. Reingold IM, Smith BR. Cutaneous metastases from hepatomas. Arch Dermatol 1978;114:1045-6.
3. Ackerman D, Barr RJ, Elias AN. Cutaneous metastases from hepatocellular carcinoma. Int J Dermatol 2001;40:782-4.
4. Donald P, Lookingbill MD, Spangler N, Sexton FM. Skin involvement as the presenting sign of internal carcinoma. J Am Acad Dermatol 1990;22:19-26
5. Brownstein MH, Helwig EB. Spread of tumours to the skin. Arch Dermatol 1973;107:80-6.
6. Peters RL. Metastatic patterns of HCC. In: Okuda K, Peters RL eds. Hepatocellular Carcinoma. New York: John Wiley & Sons Inc, 1976:156-64.
7. Nagaoka Y, Nakayama R, Iwata M. Cutaneous seeding following percutaneous injection therapy for hepatocellular carcinoma. Intern Med 2004;43:268-9.
8. Amador A, Monforte NG, Bejarano N, et al. Cutaneous metastasis from hepatocellular carcinoma as the first clinical sign. J Hepatobiliary Pancreat Surg 2007;14:328-30.
9. De Augustin P, Conde E, Alberti N, et al. Cutaneous metastasis of occult hepatocellular carcinoma: A case report. Acta Cytol 2007;52:214-6.
10. Hodkinson HJ, Kew MC. Sister Joseph's nodule in hepatocellular carcinoma. Eur J Gastroenterol Hepatol 2001;13:865-7.

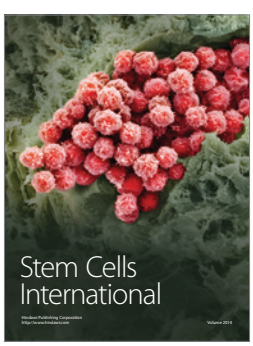


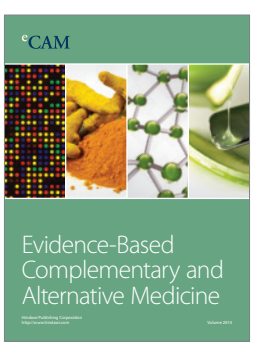


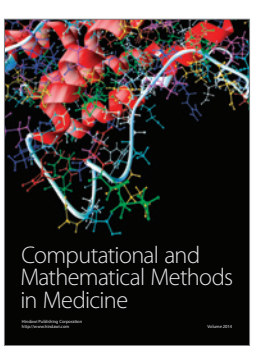


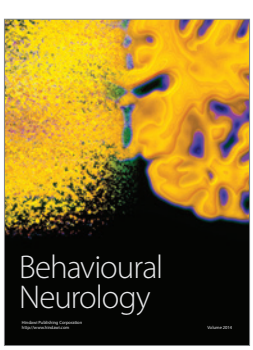


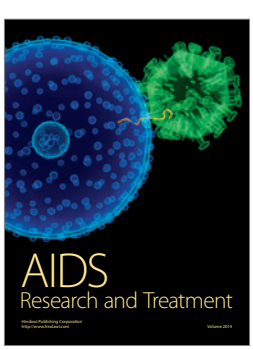


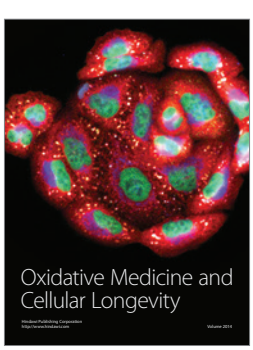












Hindawi

Submit your manuscripts at
http://www.hindawi.com