
CASE REPORT

Haemorrhagic Complication of Mandibular Metastasis of Hepatocellular Carcinoma Controlled by Endovascular Embolisation

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ABSTRACT

Mandibular metastasis in hepatocellular carcinoma is rarely seen. Since the first case reported in 1957, only about 70 cases have been reported. To the best of our knowledge, only two cases presenting with acute haemorrhage episodes have been reported in the literature, despite the fact that hepatocellular carcinoma is a hypervascular tumour. Moreover, only one of the cases was managed with endovascular embolisation, which did not completely control the haemorrhage. We, hereby, present a case of a 65-year-old man with known hepatocellular carcinoma with metastasis to the mandible complicated by uncontrollable haemorrhage from the tumour, which was effectively controlled by endovascular embolisation. Angiographic anatomy and endovascular treatment of this rare site of metastasis are also illustrated.

Key Words: Carcinoma, hepatocellular; Mandible; Neoplasm metastasis

中文摘要

血管內栓塞術治療肝細胞癌下頷骨轉移灶的出血併發症

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肝細胞癌轉移至下頷很罕見。自從1957年的首宗病例到現時為止，只有約70個病例報告。儘管肝細胞癌屬於富血管性腫瘤，但據我們所知，文獻中亦只有兩例有急性出血的情況。而且其中一例雖以血管內栓塞術治療，但都不能完全控制出血。本文在此報告一名65歲肝細胞癌男性病例，癌細胞轉移至下頷，轉移瘤無法控制出血，最終以血管內栓塞術有效地控制出血。本文亦討論了這種罕見部位轉移瘤的血管造影解剖和血管內介入治療。

INTRODUCTION

Mandibular metastasis in hepatocellular carcinoma (HCC) is rarely seen. The first case was described by Dick et al in 1957.¹ Since then, only about 70 cases have

been reported.² Only two cases of acute haemorrhagic complications of mandibular metastasis in HCC have been reported in the literature. Moreover, only one of the cases was managed with endovascular embolisation,

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which failed to control the haemorrhage. We, hereby, present a case of a 65-year-old man with known HCC and metastasis to the mandible who was admitted for haemorrhage from the tumour. Effective control of the haemorrhage by endovascular embolisation was achieved in our patient.

CASE REPORT

A 65-year-old man, a known hepatitis B virus carrier, initially presented with symptoms of fluid overload as evident by oedema of the lower limbs and paroxysmal nocturnal dyspnoea in July 2008. Serial ultrasonography of hepatobiliary system revealed features of liver cirrhosis and an enlarging hypoechoic nodule in segment IVa. Computed tomography (CT) verified the high possibility of HCC. Radiofrequency ablation was done but ensuing monitoring found disease recurrence. The patient was then put on transcatheter arterial chemoembolisation and was being followed up by the department of surgery.

During follow-up, the patient presented with right-sided buccal mucosal pain; a small ulcer was noted on physical examination. An orthopantomogram performed subsequently showed a radiolucent lesion in the right ramus of the mandible. Thereafter, CT showed a well-defined, lobulated, avidly enhancing soft tissue mass centred in the right mandibular ramus associated with bony destruction and involvement of the mandibular canal. Histopathological examination of the incisional biopsy of the mandibular tumour showed tumour cells with moderate amount of eosinophilic cytoplasm,

forming trabeculae with focal pseudoglandular architecture. Additional immunohistochemical study revealed that the tumour cells had moderate-to-strong cytoplasmic staining for Hep Par 1 (hepatocyte marker; Figure 1). Pathological diagnosis of metastatic HCC was then made.

Subsequently, the patient was started on palliative radiotherapy and chemotherapy to the right mandible. Despite treatment, the mandibular tumour showed progressive increase in size, along with increasing alpha fetoprotein levels on serial monitoring.

One year later (after CT diagnosis of mandibular metastatic mass), the patient presented with repeated bleeding from the oral cavity related to the mandibular tumour. Haematological examination showed significant drop of haemoglobin level from 108 to 97 g/l. In view of this finding, the patient underwent an urgent CT scan which revealed an intra-tumoural, non-enhancing hyperdensity suggestive of intra-tumoural bleeding. No definite contrast extravasation was detected (Figures 2a and 2b). The haemorrhage was not adequately controlled by surgical packing with Surgicel (Ethicon, US) and transamin. Therefore, the patient was referred to our department for endovascular management.

Digital subtraction angiogram of right common carotid artery and external carotid artery was performed, showing multiple hypertrophied vessels supplying the hypervascular right mandibular metastasis, including the right internal maxillary artery, right facial artery, right

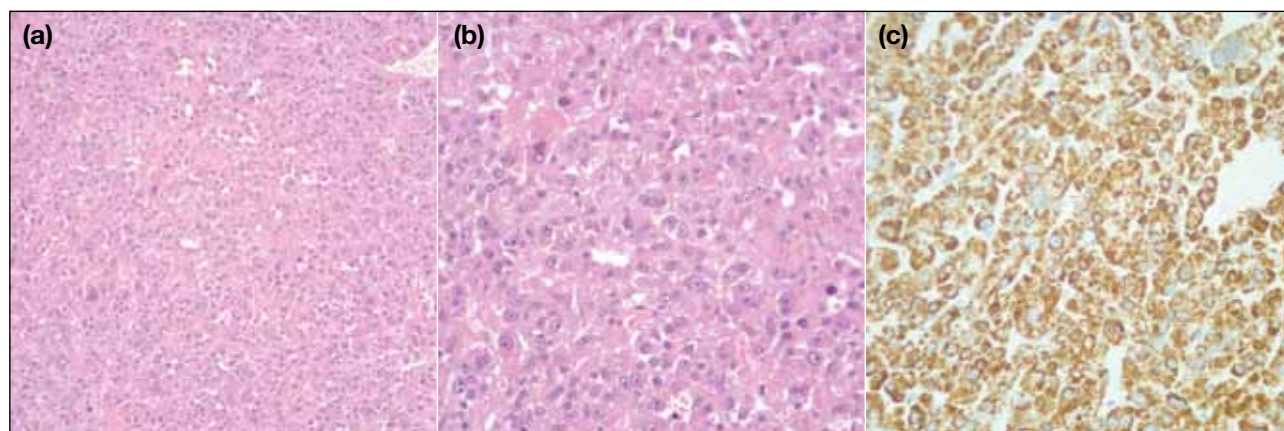


Figure 1. Histopathology of mandibular metastasis of hepatocellular carcinoma (HCC). The tumour cells form trabeculae with focal pseudoglandular architecture, with moderate amount of eosinophilic cytoplasm: (a) x 200 and (b) x 400 (H&E). The nuclei exhibit marked nuclear pleomorphism with prominent nucleoli and frequent mitoses. Scattered tumour giant cells are seen. (c) Hep Par 1 stain shows moderate-to-strong cytoplasmic staining for Hep-Par 1 of the tumour cell, which is a hepatocyte marker (x 400).

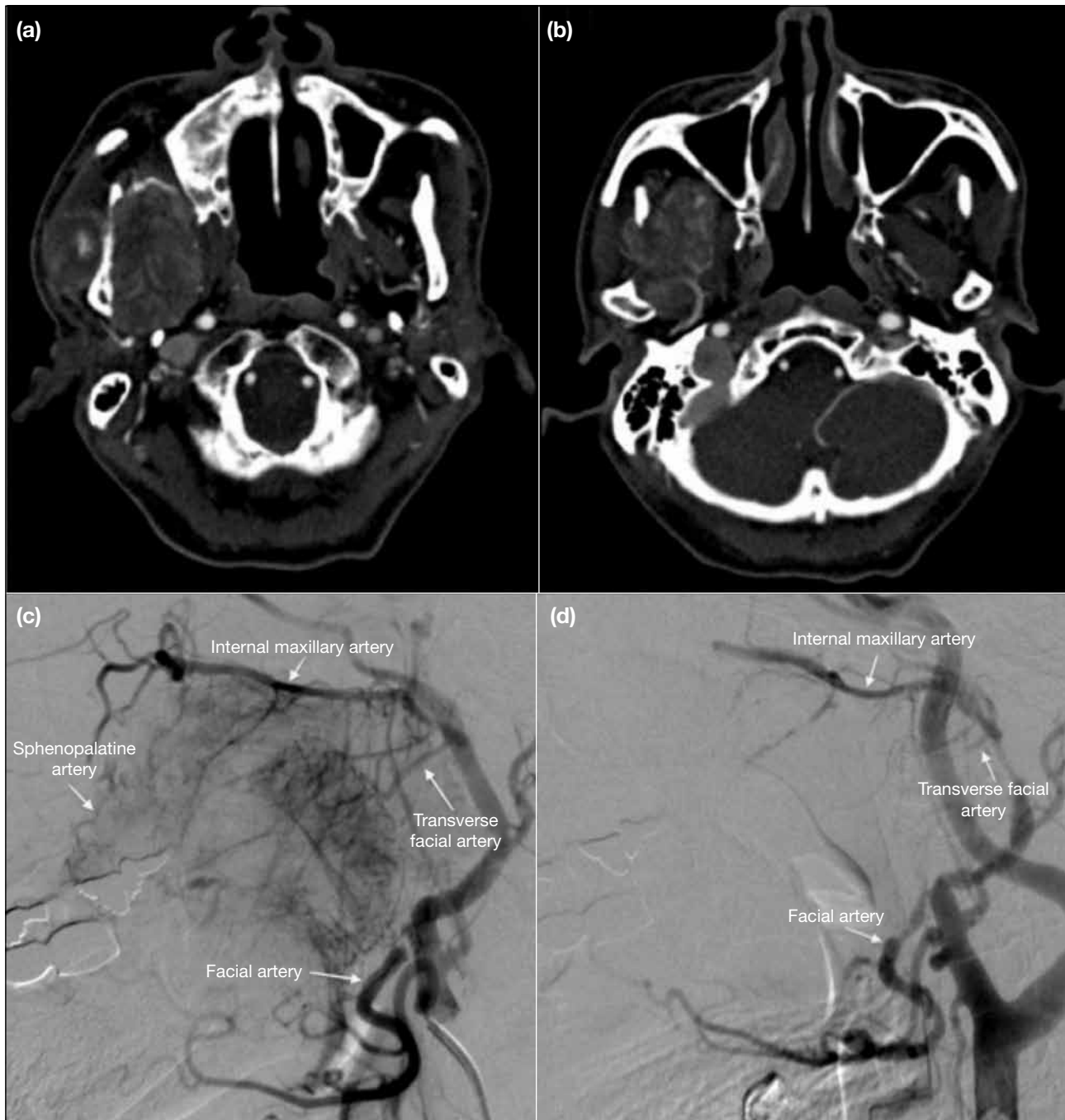


Figure 2. Contrast-enhanced axial computed tomography scans centred at the levels of (a) occipital condyle and (b) mastoid reveal a hypervascular soft tissue mass lesion representing the hepatocellular carcinoma metastasis centering in the right mandible with invasion into the right masseter muscle and right pterygoid muscles. (c) Pre-embolisation right external carotid artery digital subtraction angiogram (DSA) shows a tumour blush over the right mandibular region. Multiple prominent masseteric branches arising from right internal maxillary artery, right facial artery, right transverse facial artery, and right sphenopalatine artery were noted. No active contrast extravasation was noted in the DSA. (d) Post-embolisation right common carotid artery DSA shows marked decrease in the tumour blush.

transverse facial artery, and right sphenopalatine artery. The multiple prominent masseteric branches arising from these arteries were super-selectively catheterized by Renegade microcatheter (Boston Scientific, Ireland)

or Excelsior 1018 microcatheter (Boston Scientific, Ireland), which were subsequently embolised with 355-500 micron polyvinyl alcohol (PVA) particles till stasis. There was marked decrease in post-procedural

tumour blush of the right mandibular metastasis (Figures 2c and 2d). Bleeding was effectively stopped after embolisation. There were no immediate post-procedural complications. The patient was discharged after his condition was stabilised after a few days of stay in the hospital.

The patient, unfortunately, succumbed approximately 1 month after the procedure due to other intra-abdominal complications.

DISCUSSION

Bone metastasis occurs in about 1.6% to 16% of HCCs, most commonly in the vertebrae, pelvis, and ribs.³ Although it is not uncommon to see HCCs metastasising to the bone, mandibular metastasis is exceedingly rare. Only about 70 cases have been reported since the first reported case by Dick et al in 1957.^{1,2} In 1998 Chin et al⁴ reviewed the reported cases of metastatic HCCs in the oral cavity; they found that these cases were much more common in males (male:female = 46:4) and in patients older than 50 years (90% of patients aged >50 years old; range, 15-88 years). In 66% of these patients, metastatic oral tumours were discovered even before the primary hepatic lesions.²

The most frequent site of involvement is the posterior angle of the mandible, which may be attributed to the abundance of haematopoietic tissue enabling tumour emboli to implant and grow.⁵ In addition, the mandibular angle and body have a rich vasculature. Blood flow slows down in this area, allowing metastatic deposits.⁶

There are two postulated pathways of spread from liver to the maxillofacial area. One involves the communication between the hepatic artery and portal vein, in which the lungs are reached first. Accordingly, most of the reported mandibular metastases of HCCs are associated with lung metastasis.² However, no definite pulmonary metastasis was noted in our patient. The other hypothesis is through a possible connection between the azygos or hemiazygos vein and the vertebral venous plexus (Batson's plexus).³ The vertebral venous plexus is valveless and communicates with intracranial veins, thus, permitting blood flow in either direction and allowing tumour cells to be transported from the abdomen to the oral cavity. The presence of mandibular metastasis without definite pulmonary foci in our patient may further consolidate the second hypothesis.

Radiographic features of documented HCC metastasis to the jaw are variable, but universally osteolytic.⁷ These typically present with an osteolytic lesion with ill-defined borders, which are typical for aggressive lesions,¹ or expansile soft tissue masses with bone destruction.⁵ Lesions with an appearance mimicking a radicular cyst have also been reported.⁶ In our patient, the mandibular HCC metastasis presented as a well-defined lobulated soft tissue mass with bone destruction.

The reported symptoms in these case reports include swelling, paraesthesia, or excessive tissue growth.¹ Haemorrhage from the tumour may occur, which may be caused by the high vascularity of these lesions, and concomitant coagulopathy associated with primary liver disease.² Haemorrhage may occur spontaneously or after biopsy of the mass.³

To the best of our knowledge, only two cases with complications of acute haemorrhage from metastasis of HCC to the mandibular have been reported.^{3,8} Of these, only one study by Huang et al³ mentioned endovascular management of haemorrhage from mandibular metastasis of HCC, which failed to completely stop the haemorrhage by endovascular embolisation. In this case, the left maxillary artery and the main feeding artery of the left mandibular tumour were occluded by injection of PVA particles, which obliterated 90% of tumour stain. Persistent oozing from the left buccal wound led to the decision of treatment by radiotherapy. In the report by Junquera et al,⁸ the haemorrhage was treated by bone wax and Surgicel. We found that the tumoural arterial supply came from the right transverse facial artery, right facial artery, and right internal maxillary artery; bleeding from these sites was effectively controlled by endovascular embolisation.

Other reported methods of controlling haemorrhage from HCC metastatic lesions include haemostatic agents, compression, and wide sutures in mild cases. Reported treatment methods for more severe cases include Surgicel, bone wax packing, electrocauterization, tissue glue, endovascular embolisation, palliative radiotherapy, external carotid artery ligation, and radical excision of the tumour.^{2,3}

The prognosis of patients with metastatic HCC in the oral cavity is poor, with reported mean survival rate of 21 weeks,¹ and 2-year survival of around 4%.⁶ Our patient expired about 1 year after the diagnosis of mandibular metastasis. Palliative treatment is

often indicated, but occasionally radical excisions are performed for cosmetic or functional betterment in patients with relatively preserved liver function.

In conclusion, we report a case of metastasis of HCC to the mandible, with a rare manifestation of haemorrhage, and illustration of the angiographic anatomy and endovascular treatment of this rare site of metastasis.

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