

A case report of metastatic hepatocellular carcinoma in the mandible and coracoid process

A rare presentation

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Abstract

Rationale: We report a rare case of hepatocellular carcinoma (HCC) with metastases to the mandible and coracoid process of scapula without evidence of lung involvement.

Patients concerns: The patient was diagnosed with HCC, presented 5 months later with right lower tooth pain, swelling over the right mandible area and right shoulder pain.

Diagnoses: Histopathological examination of mandible showed findings suggestive of metastatic HCC. Magnetic resonance imaging (MRI) of the right shoulder revealed findings of irregular enhancing lesion at the right coracoid process causing erosion of the coracoid process.

Interventions: Patient was subsequently referred for palliative medicine care.

Outcomes: He received adequate analgesia.

Lessons: Oral cavity and scapula metastases from HCC are very rare. Most oral metastases are associated with lung metastases, and they possibly occur by hematogenous route. In our case, the possible pathway of metastasis is an anastomotic network of paravertebral veins that bypasses the pulmonary, inferior caval, and portal venous circulations.

Abbreviations: AFP = alpha-fetoprotein, ALP = alkaline phosphatase, anti-HB core total = hepatitis B core total antibody, anti-HCV = hepatitis C antibody, AST = aspartate transaminase, CK = cyokeratin, CT = computed tomography, EMA = epithelial membrane antigen, ESR = erythrocyte sedimentation rate, GGT = gamma-glutamyl transferase, H&E = hematoxylin and eosin, HBsAg = hepatitis B surface antigen, HCC = hepatocellular carcinoma, HepPar-1 = hepatocyte paraffin antigen-1, INR = international normalized ratio, MRI = magnetic resonance imaging, TTF-1 = thyroid transcription factor 1.

Keywords: bone metastasis, coracoid process, hepatocellular carcinoma, mandible

1. Introduction

Hepatocellular carcinoma (HCC) is the fifth and ninth most common neoplasm among men and women worldwide, respectively.^[1] Identifying the presence of extrahepatic metastases is essential in establishing the appropriate treatment plan for patients with HCC. Lungs, intraabdominal lymph nodes, adrenals, and bones (vertebrae, ribs, and long bones) are usual sites of extrahepatic metastases.^[2,3] We reported a rare case of

HCC with metastases to the mandible and coracoid process of right scapula without lung involvement.

2. Case report

A 61-year-old Malay male who was first diagnosed with HCC in July 2013 from another hospital with the presentation of progressive jaundice with abdominal pain and distension for 5 months duration. There was associated loss of weight of 6 kg. His computed tomography (CT) abdomen showed evidence of liver cirrhosis with multiple heterogeneous enhancing lesions with necrotic centre seen in the liver, the largest at the segment VIII of the liver measuring 8.0 cm × 6.9 cm × 6.7 cm that has a feeding artery within it which shows washout on portal phase. Alpha-fetoprotein (AFP) is elevated with level of >1507 µg/L. The cause of liver cirrhosis is unknown with negative for hepatitis B surface antigen (HBsAg), hepatitis B core total antibody (anti-HB core total) and hepatitis C antibody (anti-HCV). The patient has a background history of diabetes and hypertension for more than 10 years. He does not consume alcohol. There was no evidence of lung metastasis on CT thorax. He was then referred to another hepatobiliary center for further management but unfortunately he defaulted the clinic appointment. The patient works as a security guard.

The patient presented to our center in December 2013 with 1 month history of right lower tooth pain and swelling over the right mandible area associated with intermittent fever. He also complained right shoulder pain for the past 2 weeks with no associated trauma. On physical examination, the patient was

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Informed consent: Written informed consent was obtained from the patient for publication of this case report and its accompanying images.

The authors have no conflicts of interest to disclose.

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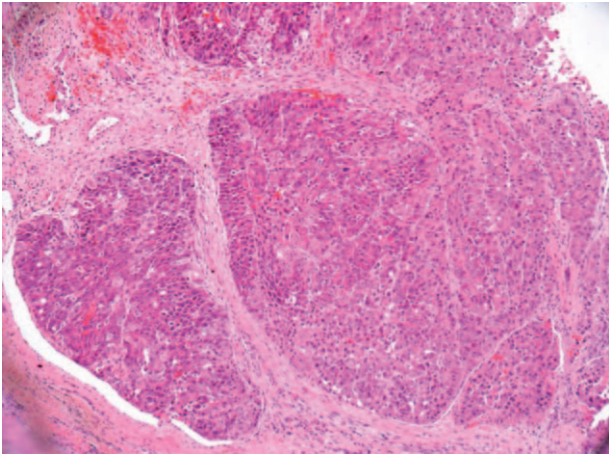


Figure 1. Histology from the right mandible showing neoplastic cells arranged in sheets, small islands, and as individual tumor cells, H&E, 10 \times .

orientated to time, place, and person with presence of jaundice. There was swelling over right mandible region measuring 4 \times 3 cm which was firm in consistency, warm, and tender on palpation. Right submandibular lymphadenopathy measuring 2 \times 2 cm was present. Oral cavity examination revealed swelling at right retromolar area involving lingual region measuring 2.0 \times 2.5 cm in size with presence of blood clot and pus at the lingual region. This swelling pushes the tongue medially. Abdominal examination revealed distended abdomen with positive shifting dullness. There was no hepatosplenomegaly or spider naevi. There was presence of bilateral pitting leg edema up to the knee level. Cardiovascular and respiratory examination was unremarkable. His right shoulder was swollen and tender with associated limited active range of movement in all directions.

Laboratory data revealed leucocytosis $27 \times 10^9/L$ with predominant lymphocyte cells (92%), raised erythrocyte sedimentation rate (ESR) of 90 mm/h, calcium 1.95 mmol/L, international normalized ratio (INR) 2.0, gamma-glutamyl transferase (GGT) 142 IU/L, mixed picture of obstructive and hepatitis jaundice; bilirubin 130 $\mu\text{mol/L}$, alkaline phosphatase (ALP) 438 g/L, alanine transaminase (ALT) 53 g/L, aspartate transaminase

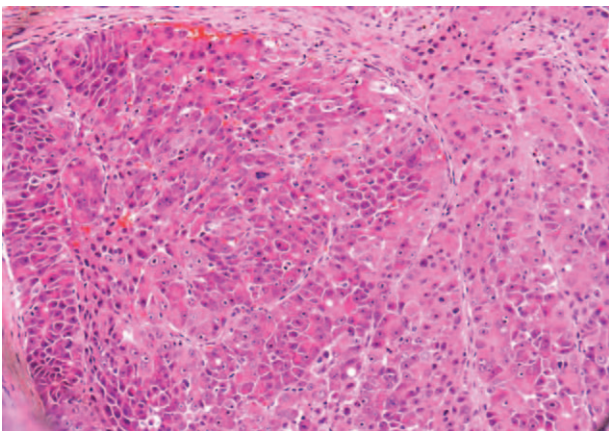


Figure 2. Histology from the right mandible showing neoplastic cells exhibit cellular and nuclear pleomorphism irregular nuclear chromatin, multiple, and prominent nucleoli with vascular infiltrations, H&E, 20 \times .

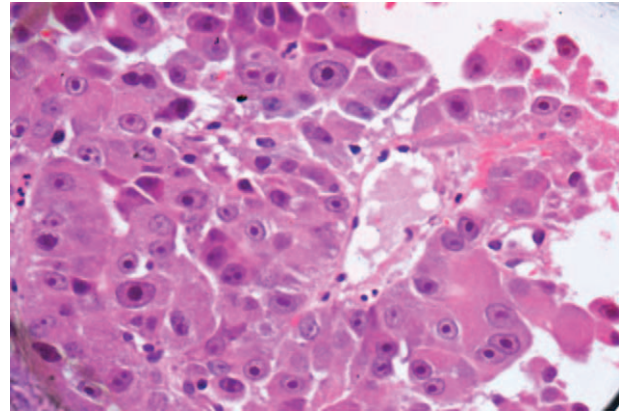


Figure 3. Histology from the right mandible showing tumor cells exhibit eosinophilic granular cytoplasm, H&E, 60 \times .

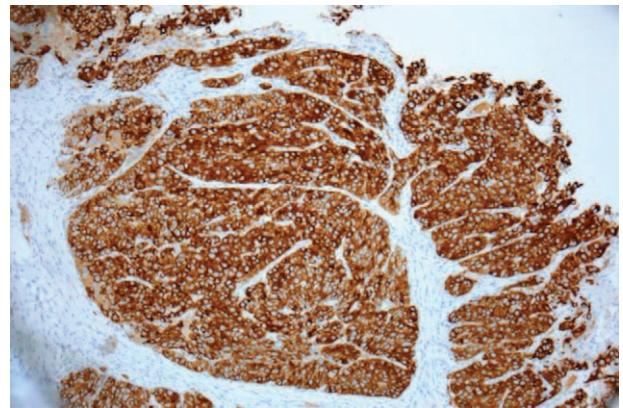


Figure 4. Immunocytochemistry from the right mandible biopsy showing the tumor cells are strongly positive for pancytokeratin, 10 \times .

(AST) 167 g/L. Histopathological examination of the incisional biopsy of the right mandible revealed neoplastic cells with immunocytochemistry shows the tumor cells are strongly positive for pancytokeratin, focally positive for hepatocyte paraffin antigen-1 (HepPar-1), cytokeratin 20 (CK20), and thyroid transcription factor 1 (TTF-1) and negative for CK7, CK5/6, and epithelial

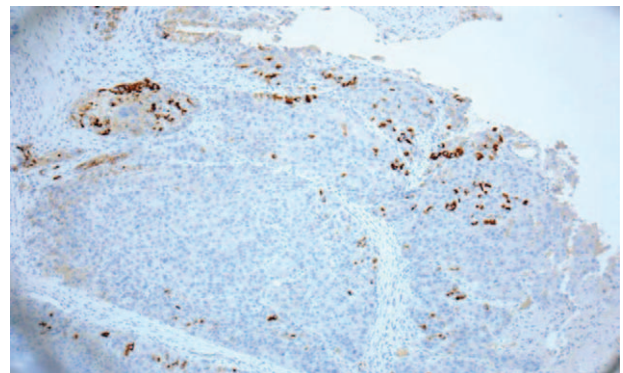


Figure 5. Immunocytochemistry from the right mandible biopsy is positive for hepatocyte paraffin antigen-1 (HepPar-1), 10 \times .

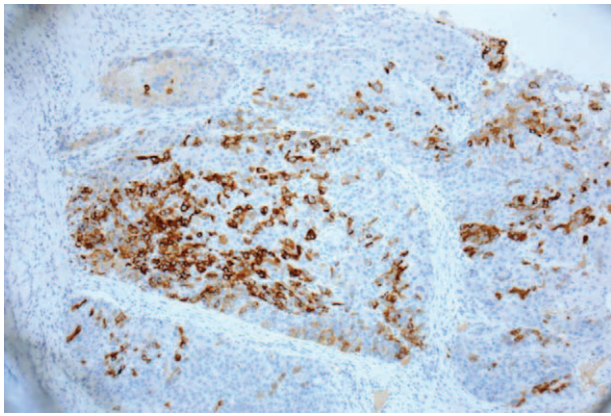


Figure 6. Immunohistochemistry from the right mandible biopsy is positive for cytokeratin 20 (CK-20), 10 \times .

membrane antigen (EMA) (Figs. 1–6). These findings were consistent with metastatic hepatobiliary carcinoma. CT head and neck showed heterogenous enhancing destructive soft tissue lesion in the angle of the right mandible measuring 4.6 \times 4.7 \times 5.1 cm. This lesion causes destruction of the angle and ramus of the right mandible as well as the lateral aspect of the inferior alveolar process (Fig. 7). There was a rim enhancing lesion noted at the right floor of the mouth measuring 2.7 \times 1.3 \times 2.1 cm displacing the mylohyoid muscle medially. Magnetic resonance imaging (MRI) of shoulder showed an irregular enhancing lesion at the right coracoid process measuring 2.1 \times 2.6 cm, causing erosion of the coracoid process. It extends intraarticularly into the anterior aspect of the right glenohumeral joint (Fig. 8). Intravenous antibiotic was administered. Patient was referred to the palliative medicine team and was given breakthrough and regular analgesics. Patient was able to be discharged after 2 weeks of hospitalization and was under Hospice palliative care.

3. Discussion

Oral cavity metastasis are uncommon, accounting only 1% to 4% of all oral carcinoma and can occur in the jaw bones, the oral

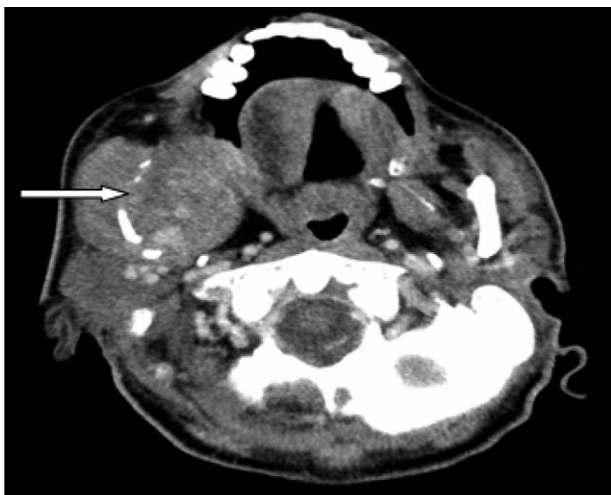


Figure 7. CT head and neck showed heterogenous enhancing destructive soft tissue lesion in the angle of the right mandible (indicated by arrow).

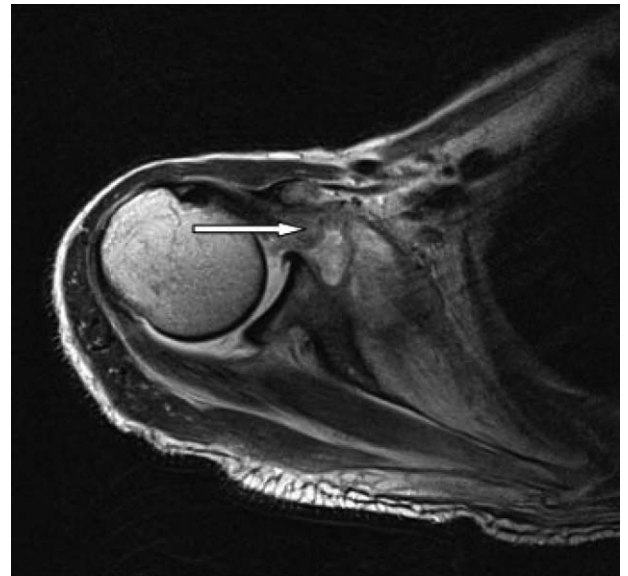


Figure 8. MRI of right shoulder showed an irregular enhancing lesion at the right coracoid process causing erosion of the coracoid process (indicated by arrow).

soft tissues, or even both.^[4] Mandible metastasis from HCC is rare with only about 70 such cases have been reported in the literature.^[5–7] HCC metastasizes to the oral area through several mechanisms. The tumor reaches the circulation through hematogenous route by invasion of hepatic arterial or portal venous branches.^[8] Most oral metastases are associated with lung metastases, and they possibly occur by this hematogenous route.^[9] Another possible pathway of metastasis is an anastomotic network of paravertebral veins that bypasses the pulmonary, inferior caval, and portal venous circulations.^[10,11] This pathway may be responsible for metastasis to the vertebral bodies, which are the preferred site of bony HCC metastasis. This could be the most likely pathway from HCC without pulmonary metastasis,^[12] as observed in our patient. The mandibular angle and body have a rich blood supply, and blood flow slows down in this area, allowing deposition of metastatic cells in the case of mandibular metastasis.^[13]

Metastasis to the scapula bone is even rarer with only few cases were reported in the literatures.^[14,15] A similar case has been reported in a patient with HCC secondary to chronic hepatitis B virus infection with metastasis of to the tip of the coracoid process of left scapula.^[16] In our case, it involved metastasis to the coracoid process of right scapula based on the MRI findings of irregular enhancing lesion at the right coracoid process causing erosion of the coracoid process. However, biopsy from the coracoid process was not taken due to patient's refusal. Pain, impaired function, and pathological fractures of the affected limb are associated with metastasis of HCC. Breast, renal, and lung carcinomas, or multiple myeloma commonly metastasis to the shoulder girdle bone. It usually affects the middle third and proximal third of the humerus.^[17]

Histopathological examination of metastatic HCC lesion may comprise strands or duct-like patterns composed of cells resembling hepatocytes, in a highly vascular stroma. Immunohistochemical markers such as glypican-3, HepPar1, CD34 are used to assist in confirming the microscopic diagnosis of HCC.^[18,19] HCC patient who had undergone surgical treatment

have a relatively good survival rate, with a 5-year cumulative survival rate of more than 50%.^[20] However, the survival rate decreases sharply when there is bone metastasis; 1-year survival is 15% and 2-year survival is 4%.^[21,22]

Patients with HCC who have extrahepatic metastases generally has poor prognosis due to the poor controllability of intrahepatic lesions and the liver performance status. Early diagnosis and treatment of patient with primary HCC resulted in the higher incidence of bone metastases. Multiple osteolytic appearance are characteristic of bone metastases from HCC which usually involve the vertebrae, pelvis, ribs, and skull.^[23] Using a whole-body bone scan to detect bone lesions gives rise to a high rate of false-negative results as a rapid osteolytic process without obvious new bone formation is seen in HCC with bone metastases.^[24]

It is important to control the symptoms that are associated with bone metastases in preventing skeletal events as indicated in a few studies in which some HCC patient with bone metastases have been reported to survive longer than those without bone metastases.^[25] Palliative care, including radiotherapy and adequate analgesics improves the prognosis and survival time of HCC patients with metastatic bone tumors by improving their general conditions.^[26]

In conclusion, we report a rare case of HCC with metastases to mandible and coracoid process of scapula without lung involvement.

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