Clinico-Pathologic Conference: Case 4

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Abstract A 45 years old male patient presented with an asymptomatic right mandibular mass that extended from the angle to the premolar area. It had been present for 3 months at the time of the initial presentation. Panoramic radiograph revealed an ill-defined unilocular radiolucency. Previous dental treatment included molar extractions and antibiotic therapy. Considerable bleeding was encountered during incisional biopsy.

Keywords Hepatocellular carcinoma · Metastatic carcinoma · Differential diagnosis · Immunohistochemical studies · Carcinoembryonic antigen · Hepatocyte paraffin 1 · Alpha-feto protein · Thyroid transcription factor 1

Clinical Presentation

A 45 years old male patient presented with an asymptomatic right mandibular mass that extended from the angle

to the premolar area. It had been present for 3 months at the time of the initial presentation. Panoramic radiograph revealed an ill-defined unilocular radiolucency. Previous dental treatment included molar extractions and antibiotic therapy. The patient's personal history was significant for drug and alcohol abuse. Considerable bleeding was encountered during incisional biopsy (Figs. 1, 2).

Differential Diagnosis

Clinically, the patient revealed a large destructive mass involving the right mandible. Radiographically the lesion was an ill-defined radiolucency causing enlargement of the periodontal ligament in the adjacent molar and perforating the inferior border of the mandible. At this time and with this clinical picture, a malignant neoplasm was favored and the differential diagnosis considered was an osteosarcoma, chondrosarcoma, primary intraosseous carcinoma, malignant odontogenic tumor, central mucoepidermoid carcinoma, non-Hodgkin lymphoma and a metastatic carcinoma to the mandible.

Osteosarcoma is a malignant tumor of bone, rarely occurs in the jaws but when it does, it is commonly seen in the third and fourth decade and in males and females equally. They arise as painless or painful swelling of the facial bones and radiographically may exhibit a “sun-burst” appearance, however, on occasion this is not seen [1]. This patient showed a large mass arising from the bone but the panoramic radiograph or the CT scans did not reveal a sun-burst appearance or a calcified material in the mass.

Chondrosarcoma is a malignant tumor characterized by the formation of cartilage by the tumor cells. They rarely involve the jaws. Usually the mean age is 41.6 years and it

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Fig. 1 Panoramic radiograph showing an ill-defined unilocular radiolucency

Fig. 2 CAT revealing an expanding tumor in mandible

presents as a painless mass or swelling [2]. In this case, the patient was a little older and the lesion was on the posterior mandible. Chondrosarcoma occur most frequently in the maxilla compared to the mandible.

Primary intraosseous carcinoma is a rare tumor which can arise from ameloblastoma, some odontogenic tumors, from the lining of a cyst or de novo believed to arise from remnants of odontogenic tissue in the bone. The mean age is 57–61 years and the most common complaints are pain and swelling. Radiographically they present as ill-defined radiolucencies, but when associated with a cyst they may be well defined with some ragged borders [2, 3]. Primary intraosseous carcinoma, if left untreated, they may become very aggressive. Ameloblastic carcinoma or a clear cell

odontogenic carcinoma are, two malignant odontogenic tumors also considered in the differential. They also present as locally aggressive pathologies which radiographically present as ill-defined destructive radiolucencies. Both of these entities develop later in life around the 6th decade and the most common site is the mandible. Patients will complain of pain and swelling. This patient is in his forty's and did not present any symptoms and although he had a history of extractions in the area, they had not reported a previous pathology like a cyst or odontogenic tumor, but this does not rule out the possibility of a primary de novo intraosseous carcinoma or a malignant odontogenic tumor.

Central mucoepidermoid carcinoma is a malignant neoplasm of salivary gland origin. It accounts for about

5–10% of all salivary gland tumors, with most of them arising within the parotid gland. Central osseous origin of this tumor is exceedingly rare, representing only about 2–4% of all mucoepidermoid carcinomas. Central mucoepidermoid carcinomas (CMC) have a 2:1 predilection for the mandible, and one-half are associated with impacted teeth [4]. Radiographically, they present as well defined unilocular or multilocular radiolucencies. Root resorption and tooth displacement are not uncommon. It is believed they may arise from remnants of salivary gland tissue entrapped within the bone or from the transformation of mucous cells found in odontogenic cysts. They are usually not too aggressive [2, 4]. The patient presented with an ill-defined, aggressive radiolucent lesion, a central mucoepidermoid carcinoma is low in the differential diagnosis.

Another consideration is a lymphoma of bone. These are likely to be large cell lymphomas and most likely a diffuse large B-cell lymphoma or a plasmablastic lymphoma associated with HIV. Lymphomas of bone may cause some pain and paresthesia and radiographically they present as ill-defined or ragged radiolucencies. They can be fast growing and locally aggressive like it is seen in this case. The patient is asymptomatic and there was a lot of bleeding from the biopsy which is supportive of a lymphoma.

Metastatic carcinoma is the most common form of cancer involving bone. The most common carcinomas to involve the gnathic bones are breast, prostate, lung, thyroid and kidney. Clinically, the patients may develop pain, swelling, loosening of the teeth, a large soft tissue mass, enlargement of the periodontal ligament of the teeth involved or paresthesia. Radiographically, they present as ill-defined radiolucencies with a “moth eaten” appearance, as seen on the panoramic radiograph close to the angle of the mandible in this case. The patient’s history of alcoholism and drug abuse plus his clinical findings of right abdominal asymptomatic distention may contribute to a diagnosis of a systemic involvement.

Diagnosis and Discussion

This 45 years old male had a personal history only significant for drug and alcohol abuse. He developed trismus caused by the tumor. Following antibiotic treatment there was no clinical resolution. The patient’s local dental service referred him to an oral maxillofacial surgeon at General Hospital, where an unexplained extraoral insufficient incisional biopsy was performed. After that, the patient then went to the dental school seeking a definitive diagnosis. Because of the original size of the obtained tissue, our team performed an intraoral biopsy. A significant bleeding was noted at the time of the surgery but was easily handled. At clinical examination, slight right

Fig. 3 Pleomorphic epithelial cells exhibiting lobular organization of solid sheets intermixed with sinusoids resembling hepatic lobules

Fig. 4 Hyperchromatic and binucleated nuclei, prominent nucleoli and abnormal mitotic figures. These tumor cells resembled hepatocytes with moderate nuclear atypia

abdominal asymptomatic distention was palpated. The tissue was processed for H&E stain.

The microscopic features noted revealed a malignant neoplasm characterized by pleomorphic epithelial cells exhibiting lobular organization of solid sheets intermixed with sinusoids resembling hepatic lobules. The cells had hyperchromatic nuclei, some of them binucleated, and prominent nucleoli. Duct like structures were also observed. Lack of epithelial adhesion existed in some tumor areas. An increased number of mitotic figures were noted, some of them were abnormal. These tumor cells resembled hepatocytes with moderate nuclear atypia (Figs. 3, 4).

A diagnosis of epithelial malignancy consistent with *hepatic carcinoma metastatic to mandible* was made.

Fig. 5 Epithelial duct-like structures showing positivity to CEA

Fig. 6 Hepatocytes positive to Hep Par 1

Ultrasound demonstrated neoplastic activity in the liver. By this time, the patient decided to travel to another health center located in another Mexican state looking for treatment. Meanwhile the paraffin block tissue was sent to the Pediatric National Institute in Mexico City to determine the immunohistochemical profile.

Panels of antibodies were performed such as the endothelial marker CD34 showing positivity; the sinusoids in the normal liver do not stain for CD34, but the sinusoid-like vasculature in HCC often shows strong expression of this antibody. Cytokeratins AE1/AE3 (Dako, 1:200 dilution), 7 (Dako, 1:50 dilution) and 8 (Dako, 1:100 dilution) run positive but with lower expression. Like AE1/AE3, CK7 tends to be stronger in poorly differentiated HCC. Hepatocyte paraffin (Hep Par 1 Dako, 1:80 dilution) antibody was positive. The carcinoembryonic antigen (CEA Dako 1:150 dilution), alpha-feto protein (AFP Dako, 1:100 dilution) and thyroid transcription factor (TTF-1 Dako 1:80 dilution) were also performed showing positivity (Figs. 5, 6). These panel of antibodies helps to distinguish HCC from metastatic adenocarcinoma, neuroendocrine tumors, renal cell carcinoma, adrenocortical carcinoma, melanoma and epithelioid angiomyolipoma.

The immunohistochemical studies confirmed the histopathological diagnosis of hepatocellular carcinoma metastatic to the mandible without confirmed hepatic disease diagnosed at the time of the mandibular presentation. The follow up was hard to achieve because of the distance. We were unable to determine at that time if there were metastatic lesions to other organs, however, upon further follow-up we became aware that the patient died in February 2009.

Hepatocellular carcinoma (HCC) has an annual incidence of more than 6,00,000 newly diagnosed patients. Thus, HCC constitutes the sixth most frequent form of cancer worldwide, and it holds third place concerning

malignancy-related mortality. Incidence rates of this neoplasm are steadily rising both in Europe and the US. Chronic hepatitis B is the major risk factor for developing HCC in Africa and Asia, while in the US, Europe and Japan chronic hepatitis C is the leading cause of HCC. Eighty percent of liver cancers are found in cirrhotic livers, which in themselves carry a high risk for HCC. It metastasizes mainly to lung, lymph nodes, adrenal glands and bone [5–8]. Inversely, oral cavity metastases are very uncommon [9]; these have been previously reported in 73 cases [10–12]. Most of them (59 cases) has been presented in men with a median age of 62 years. They occur mostly at the posterior mandible and gingiva. In 42 cases [13], and as in this particular case, oral tumor was found before the primary. A diagnosis of hepatocellular carcinoma turns to a very poor prognosis with patients died within 2 years after the diagnosis was made. Immunohistochemical studies might include Hep Par 1, CEA, AFP and TTF-1 to confirm the diagnosis [10, 13].

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