Osteoclast-Like Giant Cell Tumor Of The Liver: A Case Report And Literature Review

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Citation

Abstract

Osteoclast-like giant cell tumor (OGCT) of the liver is a rare tumor; only eight cases have been reported in the western literature. Herein is a review of the clinical and histological presentations of nine cases of OGCT; the ninth case is derived from an autopsy at our institution. The histological findings include benign multinucleate giant cells, and malignant pleomorphic mononuclear cells, with or without the classic hepatocellular carcinoma cells. The giant cells have a reactive nature akin to the giant cells associated with giant cell tumor of the bone, and they are positive for CD-68 and are nonreactive with cytokeratin and epithelial membrane antigen (EMA). The mononuclear cells are positive for cytokeratin and EMA but are negative for CD-68. The mononuclear cells can have sarcomatoid morphology. In our case, we observed multinucleate cells in association with the primary lesion and lung metastasis but not in the lymph node metastasis.

Osteoclast-like giant cell tumors are rare tumors and have been reported in many organs, including ovary[1], pancreas[2], and urinary tract[3]. Only eight cases of osteoclast-like giant cell tumor (OGCT) of the liver have been reported in the western literature, most of which have consisted of biopsies or resection specimens with limited clinical and histologic information.

REPORT OF A CASE

A 65 year-old male presented with general weakness and right upper quadrant pain for two weeks. He had a past medical history of hepatitis C, liver cirrhosis, diabetes mellitus, and congestive heart failure. On physical examination, he had jaundice, abdominal distension and hepatomegaly. The significant laboratory findings included blood glucose 320 grams/dL, total bilirubin 2.7 mg/dL, GGT 122 U/dL, AST 97 U/dL, LDH 1156 u/dL, markedly elevated AFP 24,179 ng/dL, positive antibody for hepatitis C, and negative serology for hepatitis B. A CT scan at that time showed a large mass in the right hepatic lobe measuring 9.0 cm in greatest diameter. The diagnosis of hepatocellular carcinoma was rendered clinically; however, the patient was lost to follow-up before a tissue biopsy could be performed. One month later, due to increasing abdominal discomfort, the patient visited the emergency room, and a repeat CT showed significant enlargement of the liver mass and increasing ascites. The patient was admitted and an ultrasound guided biopsy was planned. Five days after admission, he suddenly developed hypovolemic shock and expired in spite of resuscitative measures.

PATHOLOGIC FINDINGS

A complete autopsy was performed. The patient's abdomen was tense and markedly distended; it measured 147 cm in circumference. More than five liters of bloody fluid and blood clots were found in the peritoneal cavity. A ruptured, large, necrotic hepatic mass located in the right lobe of the liver measured 13 x 12 x 12 cm. The rupture and massive bleeding were the direct cause of the sudden death. Several necrotic satellite nodules were noted around the main mass. Tumor thrombi were present in the portal and hepatic veins. Many regional lymph nodes were enlarged and grossly replaced by tumor. Bilateral lungs showed necrotic metastases. Other organs were not involved by metastatic lesions. The rest of the liver was cirrhotic, and the 370 gram enlarged spleen showed passive congestion.

Microscopic examination of the liver confirmed the macronodular cirrhosis. The majority of the sections from the hepatic mass showed extensive coagulative necrosis and tumor ghost cells and a few viable foci composed of benign osteoclast-like giant cells with abundant eosinophilic cytoplasm and a variable number of nuclei, mixed with malignant pleomorphic mononuclear cells (Figure 1. a).

Figure 1

Figure 1a: Many multinuclear giant cells mixed with pleomorphic mononuclear cells accounting for the majority of the tumor mass (200X); Nuclear number for the giant cells from several to over a hundred.
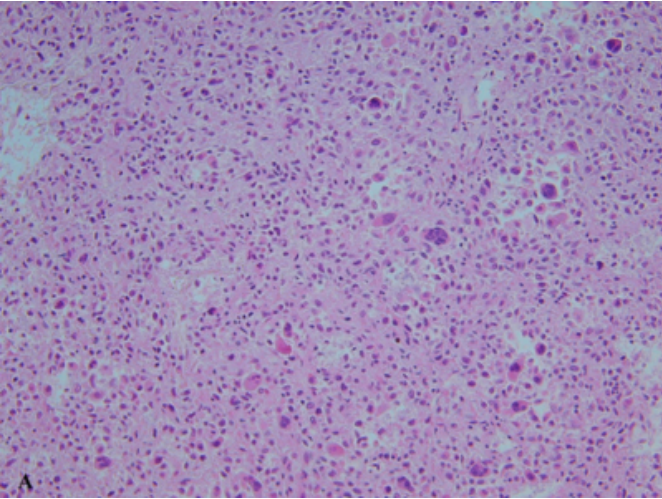
The proportion of giant cells within the tumor varied among the sections. The number of nuclei within the giant cells ranged from a few to more than 100. Mitoses were not seen among the giant cells. The mononuclear tumor cells showed cytologic features associated with malignancy, including nuclear hyperchromasia and pleomorphism and abnormal mitotic figures. In some areas, the mononuclear tumor cells displayed a sarcomatoid appearance. (Figure 1. b).

Figure 2

Figure 1b: The mononuclear cells with a sarcomatoid appearance in some areas (200X) and mixed with multinuclear giant cells.
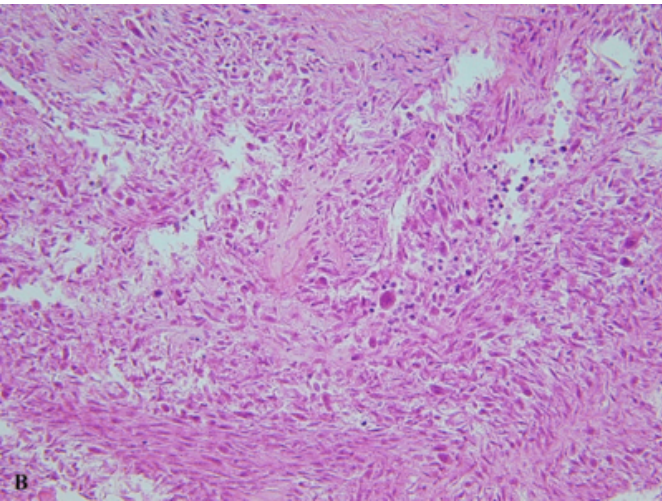
After extensive sections, the classic acinar and trabecular patterns associated with conventional hepatocellular carcinoma were identified. These were accompanied, in

some areas by signet-ring like cells, whose histocytic nature was confirmed by immunohistochemistry (CD 68 positive, pancytokeratin negative). The metastases in the lungs mirrored the morphologic features of the primary tumor in the liver, including coagulation necrosis, many benign osteoclast-like giant cells, and pleomorphic malignant mononuclear cells. Numerous tumor emboli were present in the small pulmonary arteries. However, the metastases in the regional lymph nodes demonstrated only the malignant mononuclear cells without evidence of the osteoclast-like giant cells.

Immunohistochemical studies (Ventana Medical Systems, Inc., AZ) utilizing the following antibodies: CAM 5.2, high molecular weight cytokeratin (34⬜E12), AFP, pankeratin (AE1/E3), polyclonal carcinogenic embryonic antigen (CEA), epithelial membrane antigen (EMA), vimentin, S-100, CD10, CD-68, and p53 on sections from the primary liver tumor, and the metastatic foci in the lymph nodes and in the lungs. The mononuclear sarcomatoid cells in the primary lesion, and metastatic foci in the lymph nodes and lung showed positive for CAM 5.2, focally positive for AE1/AE3, and weakly positive for AFP and EMA, negative for 34⬜E12, monoclonal CEA, vimentin, S-100, and CD-68. The osteoclast-like giant cells from the primary lesions and the metastatic lesions were strongly positive for CD-68 and vimentin, negative for CAM5.2, AE1/AE3, 34⬜E12, and S-100. A characteristic canalicular pattern of staining for CD-10 was found in the area showing conventional hepatocellular carcinoma.

DISCUSSION

All eight reported cases and the current case are reviewed and summarized in table 1.

Figure 3

Table 1: Summary of osteoclast-like gaint cell tumor(OCGC) of the liver from literatures

Source	Age	Sex	Cirrhosis or Hepatitis	Tumor size and location	Present of classic HCC	Treatment	Follow-up
Munoz et al[4]	87	M	alcoholic cirrhosis Hep B (-)	11 cm mass in right lobe with satellite nodules	none		Supportive	died at 32 days after diagnosis
Kuwano et al[5]	54	M	alcoholic cirrhosis Hep B(+)	7.5 cm mass in right lobe	HCC separated from OCOC	segmentectomy	died at 42 days after surgery
Horie et al[6]	66	M	Hep B (-)	large mass in the left lobe with invasion to right lobe and adjacent organs	none	intraarterial mitomycin C	died at 42 days after diagnosis
Hood et al[7]	37	F	Hep B (-)	large mass in the left lobe with invasion to abdominal wall	rare foci of HCC	left liver lobectomy with resection of abdominal wall chemo and radiation therapy	died at 8 months after initial presentation
McChaggage & Toner[8]	71	M	possible cirrhosis	single mass in liver	none (core needle biopsy only)	supportive	died after a few weeks
Sasaki et al[9]	42	M	cirrhosis Hep B(+)	two masses 6.0 cm 2.5 cm in the posterior and medial segments with invasion to colon and omentum	small portion of the tumor	arterial chemoembolization, surgery for rupture of the mass	died 8 months after initial presentation
Ikeda et al[10]	76	M	cirrhosis Hep C (+)	multiple masses	HCC mixed with OCGC	arterial chemoembolization, and partial hepatectomy	died 5 months after initial presentation
Rudloff et al[11]	61	F	none	10 cm mass in the right lobe	none	right hepatic lobectomy	died 3 months after surgery
Present study	65	M	cirrhosis Hep C (+)	13 cm mass in the right lobe	small portion of the tumor	supportive	died 2 months after the initial presentation

Seven patients were male and two were female. The age ranged from 37 to 87 years with a mean 62 years, and six patients were over 60 years. The first reported case by Munoz et al[4] was in an 87 year-old male with a grade 2 papillary transitional cell carcinoma five years before the liver mass, and the case reported by Hood et al[7] was in a 37 year-old female with history of stage IC borderline ovarian cystadenocarcinoma who had undergone an abdominal hysterectomy and bilateral salpingo-oophorectomy and posteroperative chemotherapy seven years before the liver mass. No previous malignancy was reported in the remaining seven cases. There were two cases each of hepatitis B and hepatitis C. Alcohol abuse was reported in two cases. Six patients had a cirrhotic liver. The serum AFP level was significantly elevated in only two cases, a previously reported case at 206.3 ng/mL and 24,179 ng/mL in current case. The prognosis was very poor regardless of the treatment efforts, with survival ranging from weeks to 8 months. Six out of the nine patients died in less than three months, and two patients had tumor rupture and bleeding.

Grossly, the tumors could be a solitary mass, or a solitary mass with many satellite small lesions, or multiple masses. The mass was usually large, and most of the cases had a aggressive local invasion. Histology of the tumors in all cases showed two major components, the benign osteoclast-like giant cells and the malignant pleomorphic mononuclear cells, with or without a small portion of classic hepatocellular carcinoma as a third component. Four out of the nine cases did not have the third component. The giant cells were all uniformly benign with no atypia or mitoses, and the cells had no morphology differences comparing to the giant cells in the giant cell tumor of the bone with the nuclear number ranging from a few to more than 100. The mononuclear cells all showed malignant features with marked pleomorphism, high mitoses and abnormal mitoses, and formation of malignant tumor giant cells. It is clear now that the osteoclast-like giant cells have a reactive nature and the mononuclear cells are the true neoplastic component. The rapid growth of the tumors is partially due to the reactive giant cells.

The histogenesis of the giant cells and the mononuclear cells is not clear. Munoz et al[4] proposed a reticuloendothelial origin (Kupffer cell) based on ultrastructual findings. Kumano et al[5] proposed a possible histiocytic origin of giant cells as a reactive process. Hood et al[7] found that both giant cells and mononuclear cells were hepatocellular origin based on electronic microscopic findings and immunohistochemical study. Recently, by using extensive immunohistochemical staining, Ikeda et al[10] found that the mononuclear cells had hepatocytic origin showing positive stain for vimentin and albumin, and giant cells have expression of phenotypic osteoclast cells including tartrate resistant acid phosphates, CD-68, and matrix metalloprotease (MMP-9), CD51, and CD59. Further more, with in situ hybridization technique, they were able to show that receptor activation of nuclear factor kappa B (RANK), a key molecule of osteoclastgenesis, was expressed in the ostelclast-like giant cells and RANK-ligand was expressed in the hepatocytic origin mononuclear cells. They concluded that the hepatocyte-derived cells possess the potential for osteoclastogenesis. In supporting their finding, they documented that a RANK-ligand negative tumor cells did not have osteoclast-like giant cell component in this subset of tumor.

We noted that there were no osteoclast-like giant cells in the metastatic lymph nodes, but were present in the lung metastasis. Reviewing all eight previously reported cases, only two cases documented lymph node metastasis. One case did not describe the tumor morphology in the lymph nodes, and the second case did not have biopsy for the metastatic lymph nodes. The reason for this morphology difference between lung metastasis and lymph node metastasis is not clear, but two mechanisms are possible. The first is the subclonal mechanism as documented by Ikeda et al[10]. The tumor cells in the lymph nodes might not have RANK-ligands, so they could not cause

osteoclastgenesis. The second possible explanation is the microenviroment in the metastatic sites. The environment in the nodes might not support the osteoclast-like giant cell formation comparing to the micro environment in the lung. We could not perform the in situ hybridization at current to document the subclonal mechanism. However, since we could not find giant cells in many metastatic lymph nodes, we favor the micro environment theory. Obviously, more cases need to be studied to explain this phenomenon.

In summary, we report a very rare case of malignant osteoclast-like giant cell tumor in the liver and reviewed all nine cases from literatures. OGC tumor is a very aggressive malignant tumor, and many patients died shortly after diagnosis. The neoplastic component is the mononuclear cells that are positive for keratin and possible hepatic origin. The giant cells are reactive and possible histocytic origin. We also should mention a recent reported new entity at here: giant cell tumor of the extrahepatic billary tree[12]. This tumor has a very favorable prognosis in the first four reported cases. The tumor has a similar morphology as the giant cell tumor in the bone, and the mononuclear cells have histiocytic origin. A recent unreported case in our institute demonstrated the similar gross and histologic morphology as reported in the recent paper: a polypoid lesion in the common bile duct with numerous benign giant cells and mononuclear cells. Cytokeratin stain is negative and CD-68 is positive for both components. The patient is doing fine after the surgery with a follow-up over six months.

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