

Case Report

A Primary Sarcomatoid Hepatocellular Carcinoma and a Metachronous Gastric Hepatoid Adenocarcinoma: A Rare Case Report

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Abstract

Introduction: We present a case of two metachronous rare tumors, a Sarcomatoid Hepatocellular Carcinoma (SHC) and a Gastric Hepatoid Adenocarcinoma (GHA), in a young male patient, which both metastasized after surgically and chemo-radiotherapeutically treated.

Materials and methods: A 39 year old male, was diagnosed with a mass that measured 12.5 cm in the right hepatic lobe and a second one of 4.5 cm in hepatic segment II and IV. The patient underwent an atypical hepatic resection, followed by chemotherapy. Histological examination evidenced a hepatocellular carcinoma with sarcomatoid alteration.

Six months later, an elevated Alpha-Fetoprotein (AFP) was seen and two malignancies were discovered, one in the cardias and one in the paraesophageal region. A total gastrectomy was performed, while the paraesophageal lesion was initially treated with radiotherapy. Histopathology results showed a Gastric Hepatoid Adenocarcinoma (GHA).

A year later, the paraesophageal tumor remained unaltered, while a new mass arose in the right hepatic lobe. Another atypical hepatectomy was performed, as well as a thoracotomy, so as to excise the paraesophageal lesion. The mass in the right hepatic lobe resulted secondary to the GHA and the paraesophageal lesion secondary to the primary SHC.

Results: After 3 years of chemo and radiotherapy the patient passed away, having been diagnosed with lung cancer, probably secondary to one of the primary tumors.

Conclusion: The patient had two very rare and aggressive forms of tumors that are believed to have had a common origin, due to their clinical and pathological features. The lack of increase in α -FP initially and its later elevation attributed to the GHA indicates two very aggressive and rare forms of metachronous tumors.

Keywords: Sarcomatoid hepatocellular carcinoma; Gastric hepatoid adenocarcinoma; Metachronous tumors; Alpha fetoprotein (α -FP); Metachronous tumors

Introduction

Sarcomatoid Hepatocellular Carcinoma (SHC) and gastric hepatoid adenocarcinoma are two rare forms of malignancy. Distinction between the two may be challenging, especially when the liver lesions are secondary to the extrahepatic tumor, due to similarities on a clinical and pathological level.

Alpha Fetoprotein (AFP) plays an important role on individuating and monitoring these two entities, but can also mislead. It is an

oncofetal glycoprotein, produced mostly by the fetal liver but also by the yolk sack and by some gastrointestinal cells. It decreases right after birth, and as a result of that, is used to screen and monitor hepatocellular, yolk sack and extrahepatic tumors having hepatoid differentiation [1].

In our case AFP was not as remarkably elevated as expected of a hepatocellular carcinoma. On the other hand, the elevated levels attributed to the extrahepatic tumor suggesting a very aggressive and rare form of tumor.

Case Presentation

A 42-year-old male, helicopter mechanic with clear anamnestic history, presented at the hospital complaining of an ache situated in his upper abdomen. This was mostly located in the right hypochondrium and was radiating to his chest and scapula. Pathology examination evidenced an AFP level slightly above the normal values (55,4 mg/ml, normal value <40 mg/ml) as well as an elevation of Ca 19.9 marker (19,2 μ g/ml, normal value 0-3,5 μ g/ml).

An abdominal CT scan was requested showing a mass of 8cm situated on the right hepatic lobe and one of 4 cm on hepatic segment II (Figures 1 and 2). A CT biopsy of the suspected masses was performed resulting in hepatocellular carcinoma. The patient underwent a resection of the segment of the left lobe and an atypical

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right hepatectomy. Pathology report confirmed a poorly differentiated hepatocellular carcinoma with sarcomatoid deviation, pT3 aNx Mx. Post operatively; he developed a fluid collection under the liver which was drained under CT guidance. He received chemotherapy treatment initially with sorafenib and cisplatin, but due to severe toxicity the treatment was altered to doxorubicin D2,3 and cisplatin D1.

Six months later, right after the end of his chemotherapy, he claimed dysphagia. His levels of AFP were remarkably elevated (2494 mg/ml), and for that reason a PET-CT scan was ordered, showing radiotracers at the level of cardias, a paraesophageal lymph node as well as hepatogastric and hepatic segment III lymph nodes (Figure 3). The lesion in the cardias was also confirmed by gastroscopy (Figure 4), which established the diagnosis of gastric adenocarcinoma. A new cycle of chemotherapy with DOF regimen was initiated and a restaging CT after a three months period showed a slight improvement of the lesions size.



Figure 1: Right hepatic lobe.



Figure 2: Hepatic segment II.



Figure 3: Paraesophageal lymph node.



Figure 4: Gastroscopy.

Taking all these facts into consideration, a total gastrectomy with esophago-diguno anastomosis was performed, while the paraesophageal lesion was treated with chemotherapy (capecitabine) and image guided radiation therapy associated with intensity modulated radiation therapy (IGRT - IMRT). During this time, the AFP levels were diminishing progressively. Pathology report resulted in a poorly differentiated gastric hepatoid adenocarcinoma having 12 affected lymph nodes (pT3N3a).

Upon follow-up, six months later the paraesophageal lesion did not only improve, but presented augmented (Figure 5). CT scan images confirmed also a newly formed hepatic mass in the right hepatic lobe (Figure 6), with new increment of AFP levels (from 51,7 mg/ml to 311,9 mg/ml). For this, the patient underwent a further operation, in the form of a thoracotomy to excise the paraesophageal lesion and also the newly formed hepatic lesion. The hepatic mass resulted secondary to the GHA, while the paraesophageal mass secondary to the SHC. The molecular profile of the paraesophageal lesion had the highly expressed genes ERCC1, BRCA1, TYMS, RRM1, TOPO1, TOP2A, MGMT, SPARC and TLE3, and the mutation analysis evidenced a mutation of KRAS (exon 2), with augmented expression of PDGFR α and VEGFR2.

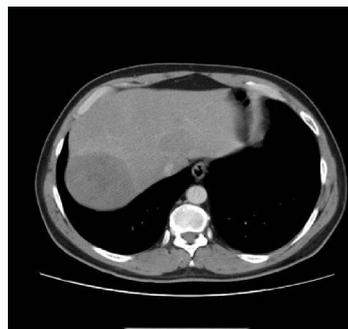


Figure 5: Paraesophageal lesion.

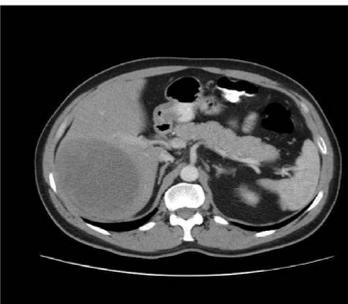


Figure 6: Right hepatic lobe.

He received chemo and radiotherapy for 3 more years, until the time he passed away following a further finding of a new mass in his right lower pulmonary lobe (with elevated levels of AFP).

Discussion

Sarcomatoid hepatocellular carcinoma

Hepatocellular Carcinoma (HCC) is the commonest type of primary liver tumor. However several variants do exist with different pathological, clinical and prognostic features. Some of these are the Clear Cell Carcinoma (CCC), Giant Cell Carcinoma (GCC), Sarcomatoid Carcinoma (SC) and the Combined Hepatocellular Cholangiocarcinoma (CHC). These can be identified mainly postoperatively with pathology and immunohistochemical staining [2].

SC is a rare type of hepatic tumor (incidence 1,8% to 3,9% of HCCs), featuring histological changes of both hepatic sarcoma and HCC. Symptoms are vague, but patients with SC are more susceptible to recurrences and distant metastasis after surgery. Male gender predominates and tumor size tends to be bigger in respect to other subgroups. SC has the worst outcome among the HCC types, with median overall survival after 3 years around 8,7 months with no cases of survival after 3 years. AFP serum levels, bilirubin, liver enzymes and FIB-4 score are lower than the ones expected for non-sarcomatous types, having also higher incidence of extrahepatic metastasis.

SC is characterized by the presence of spindle-cell proliferation with predominant sarcomatous features that present both epithelial and mesenchymal differentiation in the same lesion. Mixed elements of differentiation (Rhabdoid, astroid, chondroid) can also be presented [3].

Although pathogenesis is unclear, it is said that SC originates from sarcomatous alteration of mesenchymal metaplasia of HCC, rather than a combined effect of HCC and sarcoma. There is no specific background (Hep B+C, cirrhosis, liver reserve systemic diseases) that favors the transformation into the sarcomatoid group and only anticancer treatments are said to promote sarcomatous transformation. CK 8 is a good marker, differentiating sarcomatoid cancers from primary sarcomas and metastatic ones. SALL 4 is also a newly introduced marker useful in distinguishing hepatocellular carcinomas from hepatoid gastric carcinomas.

CT scan findings evidence central necrosis of the tumor. Hence the reason why there is never enhancement of the central part of the tumor during the portal venous phase, contrary to CT findings on the cholangio-cellular carcinoma or metastatic liver lesions [2].

Surgical treatment is currently the treatment of choice, followed by chemo and radiotherapy.

Gastric hepatoid adenocarcinoma (GHA)

Hepatoid adenocarcinoma is an extrahepatic tumor, with incidence around 0.1% - 1%, that may affect lungs, gallbladder, esophagus, uterus, but more frequently the stomach. It shares some similarities with the hepatocellular carcinoma [4].

Initially Kodama et al described two different histological types of gastric carcinoma producing AFP, the medullary and the papillary one that could also coexist sometimes in the single same tumor. Later on, Ishikura imported the term "gastric hepatoid adenocarcinoma" to describe a primary gastric tumor with hepatoid differentiation, producing AFP.

Pathogenesis is still unclear, although some hypothesis suggests the activation of repressed liver genes, expressing cells with the hepatic phenotype. It is a high angioinvasive tumor, like HCC, with poor prognosis due to its extensive metastasis to the liver and regional lymph nodes [5].

There is predominance in males, around 64 years (44-85 years), without typical symptoms. Patients present mostly with upper abdominal pain, occasionally associated with melaena. In most cases, the tumor is in an advance state at the time of the diagnosis, with elevated serum AFP (up to 700.000 ng/ml). CT scan may reveal eccentric gastric wall thickening.

Diagnosis is mainly based upon Hematoxylin-Eosin (H-E) and immunohistochemical staining. While H-E stain evidence similar features to the hepatocellular carcinoma, immunohistochemistry confirms the expression of AFP in 100% of the cases [4]. Treatment today remains surgical followed by adjuvant chemo e radiotherapy.

Conclusion

The patient was diagnosed with two very rare forms of tumors. What is even more uncommon is the presence of these two forms in a metachronous situation. There is only one more case described in international bibliography with a SHC and a metachronous GHA. GHA can be easily misdiagnosed as a hepatocellular carcinoma, because of the frequency that the tumor metastasises to the liver. The presence of HAS in patients with cirrhosis or Hep B, complicates the diagnosis further.

He had two very rare forms of tumors, that is believed to have had a common origin. The lack of increase in AFP initially and it's later elevation attribute to the GHA and indicates two very aggressive and rare forms of two metachronous tumors. Having conducted a thorough bibliographic research, this is the second case of a sarcomatoid hepatocellular carcinoma and a metachronous gastric hepatoid adenocarcinoma.

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