Hepatoid carcinoma of the pancreas

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Abstract

The authors describe a case of a 23-years-old male presenting weight loss, abdominal pain, fever and at a later stage, diarrhoea and vomiting. The patient was admitted to clarify the aetiology. On admission, a painful and distended abdomen with an epigastric mass and hepatomegaly were observed. The diagnosis was reached after several tests, including abdominal mass biopsy with a histological exam revealing a Hepatoid Carcinoma of the Pancreas. After a literature review we just find 8 cases described of this entity. We present the case and make a literature review about it.

Key words: Hepatoid carcinoma, pancreas.

CLINICAL CASE

The clinical case is presented of a 23-year-old Caucasian male patient, a cleaning operative, apparently healthy until March 2004, at which point he started to suffer from intermittent aching abdominal pain of moderate intensity in the right hypochondrium, progressive unquantified weight loss, fever in the evenings and nocturnal sudoresis. In May of the same year, the patient's situation worsened, with persistent abdominal pain, vomiting food, and diarrhea. The patient denied any symptoms in other organs or systems.

On objective examination, he presented accentuated mucocutaneous pallor, fever (38.5ºC axillary), distended and tympanic abdomen, painful in the right hypochondrium and epigastrium, where a hard, homogenous mass, adherent to the deep planes and hepatomegaly (3 cm below the costal margin, with rhombus edge and smooth surface) was felt on palpation. The rest of the objective examination did not present any abnormalities. In view of the clinical symptoms, the investigation focused on the most likely diagnostic hypotheses: neoplastic disease or infectious disease.

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Laboratory evaluation showed normochromic normocytic anemia (Hg - 5.1 g/dL), leukocytosis (30,900/mm3) with neutrophilia (75.5%), thrombocytosis (platelets – 504,000/µl); lactate dehydrogenase (496 U/L), alkaline phosphatase (306 U/L), elevated VS (127 mm) and CPR (22.3 mg/dL). Both α -fetoprotein and β2 microglobulin presented normal values and the viral serologies and hemocultures were negative.

The patient underwent Upper Digestive Endoscopy which revealed edematous gastric folds, histologically compatible with focal edema of the gastric mucosa.

Abdominal Echography showed the presence of heterogeneous hepatomegaly of bosselated edges, with the left lobe greatly enlarged by multiple dispersed, hypoechogenic nodule formations, related to probable secondary nodules; pancreas difficult to visualize, especially at the tail, of homogeneous appearance; small tab of perisplenic ascitic fluid; and in the left hypochondrium, a solid mass with a diameter of approximately 10 x7.5 cm that appeared to merge with the edges of the kidney, though its exact location is difficult to pinpoint.

The thoracoabdominal CT scan highlighted: voluminous hepatomegaly, with hypodense nodule formation in segment IV, measuring about 4 cm, and other nodule formations of smaller dimensions in segments II and III related to lesions occupying the hypovascular space; voluminous splenomegaly and adjacent to splenic hilum and to the pancreatic tail a voluminous solid formation with craniocaudal extension (11x9cm) compatible with exophytic neoformative lesion of the tail of the pancreas (*Fig. 1*).

The biopsy of the lesion revealed a carcinoma whose morphology and immunohistochemical profile (positivity for the cytokeratin types 7, AE1/AE3, MNF

116, α1 antitrypsin and CEA) were compatible with hepatoid differentiation. Taking size and absence of cleavage plane of the neoformation with the pancreatic structures into account, we reached the conclusion of Hepatoid Carcinoma of the Pancreas. The patient was sent to the Portuguese Oncology Institute of Lisbon for potential therapeutic approach, having started a chemotherapy program with carboplatin, paclitaxel and etoposide. The patient died five months after the diagnosis.

DISCUSSION

Hepatoid carcinomas are considered for new category of tumors defined as primary extrahepatic tumors with morphological and immunohistochemical characteristics, as well as a behavior similar to that of hepatocellular carcinoma.[1,2] The first case was described by Ishikuma et al, in 1985, in a primary gastric tumor.[1]

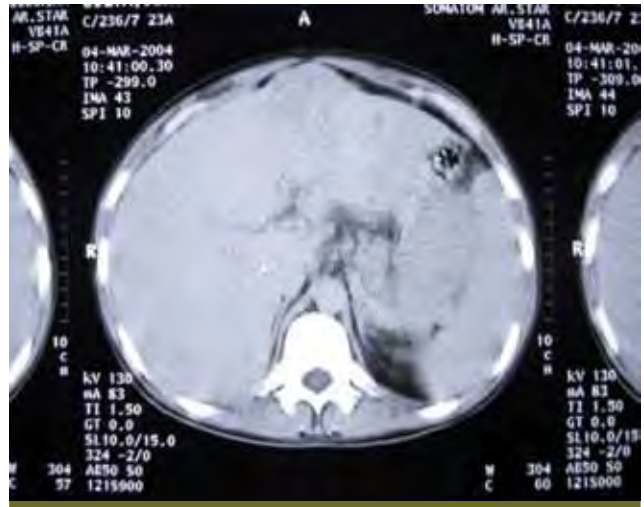
Hepatoid carcinomas have also been described at other sites, specifically in the stomach (63%), esophagus, ampulla of Vater, colon, lung, gallbladder, suprarenal gland, kidney, bladder, ovary, uterus, vagina and testicle.[3,4]

The case described here was located in the pancreas. Following a literature review, we found only eight reported cases of hepatoid carcinoma of the pancreas, which makes this entity very rare.

The diagnosis is essentially morphologic and immunohistochemical.[2] The production of α-fetoprotein (AFP), of proteins synthesized by the liver, the PAS (periodic acid-Schiff) positivity, the production of bile and the detection of albumin mRNA allows us to establish a link with the hepatic strain. However, if all these products do not need to be present for diagnosis.[5] In the case described, we verified the absence of AFP production yet the immunohistochemical profile and the morphologic structure of the carcinoma were compatible with its hepatoid differentiation.

In AFP-producing tumors, the serum levels of this substance are useful for diagnosis and serve as markers of disease evolution and of the response to therapy.[6]

The prognosis of hepatoid carcinoma of the pancreas is reserved. This behavior was seen in our patient, who only survived for five months after the diagnosis. However, there are not enough cases to establish the prognosis with greater accuracy. The aggressiveness of this neoplasia is demonstrated by the lymphatic and venous invasion, mimicking the



Abdominal CT scan, showing the absence of cleavage plane between the mass and the pancreas.

FIG. 1

behavior of the hepatocarcinoma.[3] This aggressiveness may be related to the fact that they produce alpha-1--antitrypsin (AAT) and/or alpha-1-antichymotrypsin (ACT) that have immunosuppressive and protease inhibiting properties.[7]

Hepatic differentiation can occur in any one of the main pancreatic cells (acinar, ductal and islet cells). Apparently, these have specific hepatic genes in a repressed state that are activated during the carcinogenesis process, expressing cells with a hepatic phenotype. This theory is sustained by the fact that the liver and the pancreas are both derived from the same embryonic germinal layer. However, hepatoid carcinomas also occur in organs of different embryonic origin.[5] According to a study conducted by Rao et al, in animal models, this author concluded that the cellular transdifferentiation process was possible through the activation of quiescent genes and the consequent synthesis of new and different gene products. This fact thus makes it possible to consider that hepatoid differentiation represents an ability of cells in general, which under certain conditions (e.g. influence of carcinogens), undergo multi-phenotype differentiation with a preponderance for subsequent progenies.[5,8]

We conclude by confirming that the relevance of this case resides in its rarity, and the need to consider it when making a differential diagnosis between pancreatic or peripancreatic tumors, particularly those with high AFP.[9,10] ■

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