A case of hepatoid carcinoma of the ovary

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Summary

A 50-year-old female was admitted with abdominal distention. Her serum CA125 level was elevated. Ultrasonography and computerized tomography showed adnexal tumoral masses with intraperitoneal metastases but no hepatic parenchymal involvement. She was operated on and histopathological and immunohistochemistry findings indicated ovarian hepatoid tumor. We present this case of ovarian hepatoid tumor and discuss the two-year disease progression from diagnosis to death.

Key words: Hepatoid tumor; Ovary.

Introduction

Hepatooid carcinoma is a rare malignant tumor defined as a primary extrahepatic tumor that morphologically mimics hepatocellular carcinoma. Its occurrence has been described in several organs, including the ovary. Differentiating the tumor is not only challenging but also critical, because treatment modalities and operative strategies depend on the exact nature of the hepatoid cancer. Here, we present a rare case of hepatoid carcinoma of ovary.

Case Report

A 50-year-old, regularly menstruating woman, gravida 11 and parity 7, was admitted to Uludag University Medical Faculty Department of Obstetrics and Gynecology with complaints of abdominal distention and pain for 15-20 days. She had undergone appendectomy 23 years before and coronary bypass surgery three months previoulsy; she was on coumadin treatment. A left adnexal pelvic mass was palpated, however the margins were obscure due to abdominal distention. The external genitalia, vagina, cervix, and uterus were normal. The cervical smear was benign. Her hemoglobin level was 9.1 g/dl, leukocyte count 8000 K/µl, and the platelet count was 512,000 K/µl. The levels of other blood laboratory parameters were as follows: serum fasting glucose, 84 mg/dl; urea, 48 mg/dl; creatinine, 1.1 mg/dl; AST, 27 U/l; AIT, 16 U/l; total protein, 6.8 g/dl; and albumin, 4.0 g/dl. The serum levels of tumor markers were as follows: CA 15.3, 11.5U/ml; CA 19.9, 2.5 U/ml; CA 125, 538 U/ml; CEA, 2.1 ng/ml; and AFP, 1.7 ng/ml. The tumor marker levels were obtained again after three days, and the values were 10.5 U/ml, 2.5 U/ml, 638 U/ml, 2.2 ng/ml, and 1.5 ng/ml, respectively.

Transvaginal ultrasonography (TVS) revealed a right adnexal mass measuring 85 × 41 mm with solid and cystic components, which measured a maximum of 21 × 15mm, occupying the Douglas pouch. The uterus and endometrium were normal but pelvic ascites was present. The liver, gallbladder with the entire biliary system, intestines, spleen, bilateral kidneys, and suprarenal glands were normal; however, abdominal ultrasonography (US) revealed the presence of 2 cm perihepatic fluid and 8 mm fluid in the Morrison pouch.

Abdominopelvic computerized tomography (CT) was performed 20 days after US, and it revealed a 15 x 10 cm septated mass with solid components. Massive ascites and widespread peritoneal implants were detected. The liver, gallbladder with the entire biliary system, pancreas, intestines, spleen, bilateral kidneys, and suprarenal glands were normal. Thoracic CT revealed bilateral 3 cm pleural effusion and atelectasis in the left lung. Pleurocenthesis was performed and cytological findings were benign.

The patient was diagnosed with ovarian carcinoma and consequently underwent surgery. Three liters clear serous of ascitic fluid were aspirated. left ovarian (10 x 8 cm) and right ovarian (7 x 6 cm) multilobulated cystic masses were found to obliterate the Douglas pouch. The omental cake and 7 x 8 cm tumoral masses invading the wall of the rectum, the hepatic and splenic flexures of the transverse colon and cecum were observed. The tumoral mass on the hepatic flexure was found to invade the adjacent liver capsule superficially. Three separate tumoral masses measuring 2 x 3 cm were detected on the ileum. In addition, a 5 x 6 cm tumoral mass was noted on the greater curvature of the stomach, but it did not invade the lumen. The entire peritoneum, diaphragm, and mesentery harbored tumoral implantations, measuring from a few millimeters to a few centimeters. The surgical treatment comprised total abdominal hysterectomy, bilateral salphingo-oophorectomy, omentectomy, tumor excision from the pelvis and ileostomy. The tumoral masses on the gastrointestinal tract were planned to be removed with interval debulking.

Peritoneal cytology was positive for adenocarcinoma. Histopathology revealed solid groups and papillary structures of polygonal atypical epithelial cells that exhibited course and fine chromatin and prominent nucleoli in the nucleus and large cytoplasm. Histopathological diagnosis was: (1) hepatoid carcinoma of the right and left ovaries with invasion into the uterine serosal surface and focal involvement of the myometrium and (2) metastatic carcinoma of the omentum. Microscopy of the tumorous ovaries revealed oval or polygonal atypical epithelial cells with large eosinophilic cytoplasm and a hyperchromatic and pleomorphic nucleus with numerous atypical mitotic figures in fibrous stroma (Figure 1). Tumor cells were arranged in cords; there were solid areas with intermingling necrotic areas. Intracytoplasmic PAS-positive diastase-resistant globules were noted. Bile stains did not show pigments. Immunohistochemical staining revealed that the tumoral cells were positive for CK, EMA, AFP, CK-7 and CA125, and were focally and weakly positive for α-1 antitrypsin and negative for P1AP, HCG, GCDFP, chromogranin-A, S-100, calretinin, CK20, CEA, CD10, and 19-9.

The final diagnosis was Stage IIIc ovarian hepatoid carcinoma, and chemotherapy with 75 mg/m^2 cisplatin and 135 mg/m^2 paclitaxel was started. Although the patient's serum

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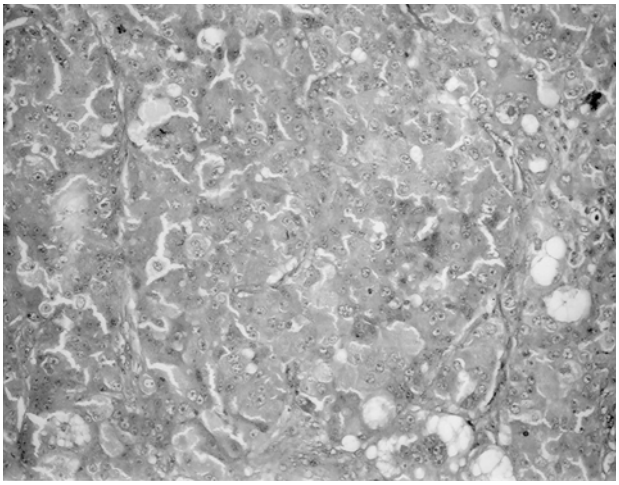

Figure 1. — Stained section of the hepatoid tumor (H&E x 400).

CA125 level was normal by the third course of chemotherapy, there were 3 cm tumoral masses at the caecum, transverse colon, rectum, greater curvature of the stomach, ileum, and mesentery. There was no suspicious lesion in the hepatic parenchyma, but tumoral implants were observed over the hepatic capsule and around the spleen. Ascites persisted but the amount had decreased. Positron-emission tomography (PET) confirmed the findings of abdominopelvic US and CT. The patient was considered unsuitable for cytoreduction by the general surgeons, and the remaining courses of chemotherapy were administered. After the completion of six courses of chemotherapy the lesions, although minimally decreased in size, were persistent on abdominopelvic CT. The chemotherapy regimen was changed to 75 mg/m^2 cisplatin and 1000 mg/m^2 gemcitabine. Following the sixth course of second-line chemotherapy, no tumoral mass, except that on the rectum, was detected. There was a 2.5 cm segmentary thickening of the sigmoid colon, which constricted the lumen. Her serum CA125 level was 17.3 U/ml. Surgery for the constricting lesion on the sigmoid wall was decided on. Laparotomy was performed, and following tumoral masses were observed: 4 × 3 cm mass on the rectosigmoid junction and a 3 × 2 cm mass on the sigmoid colon, both completely invading the wall and entering the lumen, a 4 × 3 cm mass on the splenic flexure, a 5 × 4 cm mass on the hepatic flexure of the transverse colon, and a 3 × 3 cm mass on the greater curvature of the stomach. There were multiple peritoneal implantations. The general surgeons agreed that it was an inoperable case, and biopsy samples were obtained from the appendices epiploicae. Histopathology findings revealed metastatic carcinoma with the same histological pattern of the primary. Her serum CA125 level was 95.6 U/ml, and she was administered six courses of 50 mg/m^2 liposomal doxorubicin as the third-line chemotherapy.

Three months after the last course of chemotherapy, she was admitted for nausea, vomiting, cough, and dyspnea. Based on physical examination findings and complete blood count and chest X-ray reports, she was diagnosed with pneumonia. Abdominopelvic CT revealed multiple metastases within the abdominal cavity, with a maximum size of 4 x 3 cm. Despite antibiotic therapy, she developed sepsis and renal failure. She died 24 months after the diagnosis of hepatoid carcinoma.

Discussion

The term "hepatoid carcinoma" is used for tumors arising in extrahepatic tissues but resembling hepatocellular carcinoma both histologically and immunohistochemically in its staining for AFP. It was first defined as a separate entity by Ishikura and Scully in 1987 [1]. In the literature, hepatoid carcinoma has been reported as ovarian cancer in 17 cases, uterine cancer in four cases, and follopian tube cancer in one case [2-4]. It has a poor prognosis with a maximum one-year survival of 40% [5].

The tumor cells express AFP and therefore patients have a high serum AFP level [6, 7]. Although our patient was positive for AFP in immunohistochemical staining, her serum AFP levels were never high.

In the differential diagnosis, hepatic parenchymal involvement was not detected either at diagnosis or during disease progression until death by US, CT, and PET. Therefore, primary hepatocellular carcinoma of the liver was excluded. An increased serum CA125 level in our case was another finding supporting the histopathological diagnosis of the ovarian surface epithelial origin of the hepatoid tumor. Yolk sac tumor of the ovary, which is usually observed in females in their early reproductive age, is an AFP-related tumor that should be considered in the differential diagnosis. In our case, the tumor did not appear as an endodermal sinus or yolk sac tumor either macroscopically or histopathologically.

Immunohistochemical staining is a rather helpful technique for determining the primaries of some tumors that have obscure behavior and spread, and is useful in the differentiation of hepatoid tumors. However, because the tumor is rare, there may be some variations in the immunohistochemical findings of hepatoid ovarian carcinoma. Some authors have reported positivity of AFP and CEA and negativity for CK7, CK20, and chromogranin (2); nevertheless, CEA was negative and CK7 was positive in our case.

A limited number of cases are reported in the literature and our case shows that the behavior of an ovarian hepatoid tumor is rather aggressive and that its prognosis is poor.

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