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A case report of Hepatoid Carcinoma of the Ovary with peritoneal metastases treated with cytoreductive surgery and hyperthermic intraoperative intraperitoneal chemotherapy without systemic adjuvant therapy

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ABSTRACT

BACKGROUND: Hepatoid Carcinoma of the Ovary (HCO) is a rare subtype of ovarian cancers where malignant cells undergo hepatoid metamorphic changes and cytologically resemble hepatocytes. There are many case reports of HCO in the literature, and patients with these tumors are almost uniformly treated with palliative debulking and conventional adjuvant chemotherapy. To our knowledge, there is only one case report of HCO complicated by peritoneal dissemination that was treated with cytoreductive surgery plus hyperthermic intraperitoneal chemotherapy (CRS plus HIPEC), followed by adjuvant chemotherapy.
CASE SUMMARY: A 47-year-old female presented with vague lower abdominal pain. Work-up included imaging studies and biopsies for histopathology which confirmed the diagnosis of hepatoid ovarian carcinoma with synchronous liver metastasis and peritoneal dissemination, without evidence of extraperitoneal disease. She underwent a cytoreductive surgery plus hyperthermic intraperitoneal chemotherapy (CRS plus HIPEC) with curative intent. Complete cytoreduction was achieved (CC-0). Postoperatively, the patient elected to forgo adjuvant therapy. She continues to be closely followed through clinical and radiological surveillance. On her most recent follow-up visit, she achieved 22 months of disease-free survival.
CONCLUSION: CRS plus HIPEC can be considered as a promising curative approach for HCO with peritoneal dissemination in absence of extraperitoneal disease. Further studies are warranted to determine the role of adjuvant chemotherapy in this relatively rare entity.

1. Case report

This case was prepared and reported in line with the CARE criteria [1]. Our patient is a 47-year old female with no significant past medical or surgical history, BMI of 31 kg/m2, who presented initially with vague lower abdominal pain, not associated with any gastrointestinal symptoms including nausea, vomiting, constipation or diarrhea. Her clinical exam confirmed the presence of a lower abdominal mass on deep palpation. She underwent computed tomography imaging that showed an ill-defined, heterogeneous, left lobe liver lesion measuring 4.2 × 4.7 cm, with multiple enhancing soft tissue masses in the lower abdomen and pelvis coalescing to a maximum diameter of 10 cm. Magnetic resonance imaging revealed peritoneal dissemination in the left and right lower quadrants and in the hypogastric region. (Figs. 1 and 2). Laboratory work demonstrated an alpha-veto protein (AFP) level of 6669 ng/mL and CA-125 level of 144 U/mL. Further work-up did not demonstrate any pulmonary or extraperitoneal metastases. Preoperative Peritoneal Carcinomatosis Index (PCI) was calculated according to Sugarbaker's criteria [2,3] and revealed a score of 11The decision was made to proceed with CRS plus HIPEC. CRS, including left partial hepatectomy, was completed with complete cytoreduction (CC score = 0). HIPEC was conducted using Cisplatin 45 mg/L infused throughout the peritoneum in a closed-abdomen technique for 90 min at 42°. Her postoperative hospital stay was only remarkable for a pelvic abscess that required drainage. She was discharged in a good state on day 14. After extensive discussion with the multidisciplinary treating team, the patient opted to forgo any adjuvant chemotherapy following her discharge.

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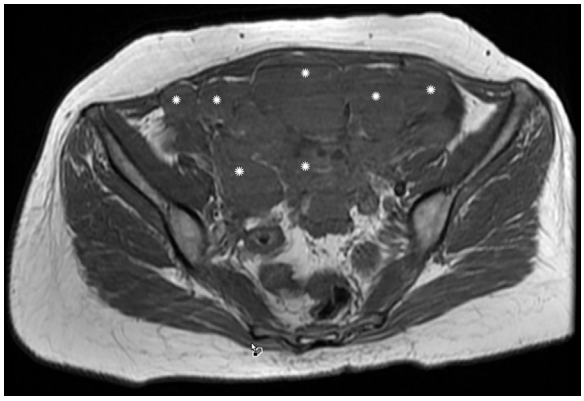

Fig. 1. T2-weighed MRI of the pelvis. Pelvic complex mass with bilateral adnexal involvement and omental invasion (asterisk).

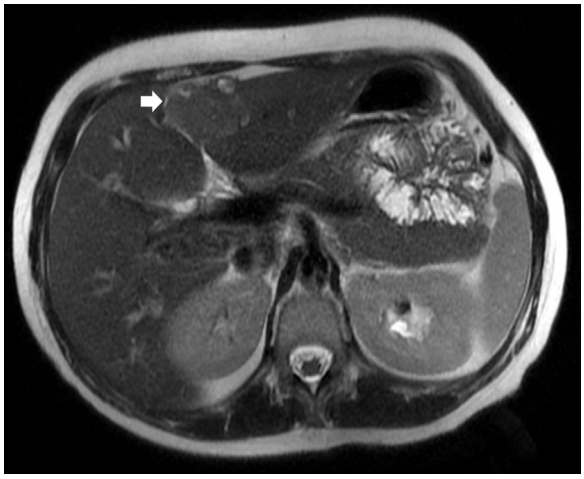

Fig. 2. T1-weighed MRI of the abdomen. 4.2 × 4.7 cm liver metastasis in the anterior left lobe (arrow).

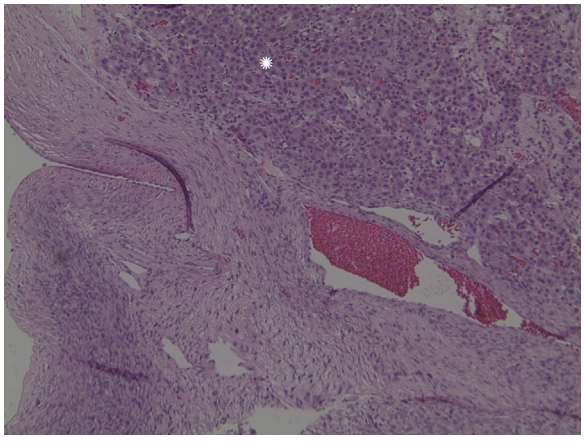

Fig. 3. Ovarian parenchymal carcinoma with classic hepatoid morphology (asterisk); uniform, cuboidal cells with eosinophilic cytoplasm.

The pathology report confirmed the presence of hepatoid polygonal malignant cells in the ovarian stroma (Fig. 3) with multiple organ involvement. Malignant cells had strong expression of Hep Par 1, glypican-3, and cytokeratin 7, 8, and 18, whereas cytokeratin 20 was not detected. Negative margins were achieved on the hepatectomy specimen, and there was no evidence of cirrhosis in liver.

She underwent serial surveillance imaging every 6 months postoperatively, and achieved 22-months disease-free survival without evidence of intra- or extra-peritoneal recurrence. Her follow up laboratory work showed normalization of AFP and CA-125, and the patient was satisfied with the overall outcome of the procedure The timeline of the patient's diagnosis and treatment course is demonstrated in Table 1.

2. Discussion

HCO is a rare malignancy that arises primarily in the ovary, first described in 1987 by Ishikura and Scully [4]. They reported five cases of HCO, two of whom had liver metastases including one who had other abdominal dissemination, similar to our patient. The determination of the tumor's origin was largely based on clinical manifestation and histopathological features of the specimen, where the lack of squamous, cholangiocellular, or adenofibromatous differentiation would strongly suggest an ovarian origin with hepatoid morphology.

The most prominent microscopic features of HCO are the well demarcated, cuboidal tumor cells arranged in trabeculae or sheets, with eosin staining cytoplasm and hyaline globules on periodic Acid-Schiff. [5]

HCO tumors uniformly stain positive for AFP which is usually found to be elevated in the serum as well [6]. It is critically important to distinguish HCO from hepatoid yolk sac tumors (HYST) and metastatic hepatocellular carcinoma (HCC). The former can be fairly easily ruled out by the absence of Hep-Par 1, a well-characterized positive marker for hepatocellular differentiation, abundant in hepatocytes and hepatoid tumors [7]. On the contrary, discrimination between HCO and metastatic HCC can be extremely challenging, especially in the case of synchronous hepatic and ovarian involvement. The tumor's origin can be judged according to clinical and pathological facts as mentioned above. Moreover, inhibin positivity has been proposed as a marker to discern HCC-derived cells [8].

Extrahepatic tumors with hepatoid morphology most commonly arise in the stomach [9,10], and less commonly in other viscera. HCO is considered a rare entity with 33 cases documented since Ishikura and Scully's report [4,6,8,11–33], described in both pre- and post-menopausal females between 35 and 78 years old. The vast majority of patients are found to have advanced disease (stage III/IV) at the time of diagnosis. HCO is particularly known to be locally and regionally aggressive. Metastatic disease most commonly manifests as peritoneal seeding and intraabdominal visceral metastasis and less frequently as distant hematogenous spread. In addition to the current report, one case was managed surgically with CRS plus HIPEC using paclitaxel as an intraoperative agent [26]. The patient achieved a complete cytoreduction (CC = 0), and was further treated with adjuvant chemotherapy consisting of paclitaxel and carboplatin. The documented disease-free survival was 28 months. In another case report sorafenib was used due to paclitaxel intolerance, however was unsuccessful in halting the disease progression [8].

Interestingly, our patient experienced a significant recurrence-free survival of 21 months documented by radiologic and laboratory testing following the use of a different HIPEC agent and waiver of adjuvant therapy. This observation raises the query of whether such a long-term outcome in HCO is more contingent on complete cytoreduction rather than adjuvant regimens in the absence of extraperitoneal disease. This would be in contrast to other ovarian carcinomas with peritoneal dissemination, such as germ cell tumors, whose mainstay of treatment is the adjuvant or neoadjuvant chemotherapy regardless of the completeness of debulking and irrespective of the size of residual disease [34].

Table 1
The timeline of diagnosis, treatment, and follow up of our patient.

August 22nd, 2014	Initial presentation with vague lower abdominal pain
August 29th, 2014	Abdominal ultrasound revealed a liver lesion and lower abdominal mass
September 5th, 2014	Abdominal CT revealed an ill-defined left hepatic lobe mass with multiple enhancing soft tissue masses in lower abdomen and pelvis coalescing at 10 cm
September 7th, 2014	Abdominal MRI confirmed the above findings and detected peritoneal carcinomatosis
September 12th, 2014	CT-guided biopsy of the pelvis mass was positive for malignancy and consistent with HCC/HCO
September 13th, 2014	Laboratory work showed elevated AFP and CA-125
October 10th, 2014	Patient consulted for CRS plus HIPEC
October 15th, 2014	Abdominal MRI was repeated: no evidence of disease progression
October 20th, 2014	CRS plus HIPEC
October 22nd, 2014	Discharge from ICU
October 27th, 2014	Pelvic abscess requiring IR drainage
November 4th, 2014	Discharge from hospital
January 14th, 2015	Abdominal MRI was negative for recurrence. AFP and CA-125 normalized.
April 13th, 2015	Abdominal MRI was negative for recurrence. Tumor markers were normal.
July 13th, 2015	Abdominal MRI was negative for recurrence. Tumor markers were normal.
October 19th, 2015	Abdominal MRI was negative for recurrence. Tumor markers were normal.
April 14th, 2016	Abdominal MRI was negative for recurrence. Tumor markers were normal.
August 8th, 2016	Abdominal MRI was negative for recurrence. Tumor markers were normal.

In conclusion, HCO remains a rare diagnosis and all evidence available in the literature is based on case reports and series. At this time, there is no consensus regarding the optimal management of HCO, given the lack of high-level evidence. Current management relies on systemic chemotherapy or immunomodulation with various levels of success as reported above. The combination of surgical debulking and systemic therapy has been proposed in one case report. Our current report confirms that CRS plus HIPEC can be applied as a promising, and possible curative, option for this disease. What we propose as a learning point is that adjuvant therapy may be waived safely in this patient population if complete cytoreduction is achieved and in absence of extraperitoneal spread. Further evidence is necessary to confirm these findings.

Conflicts of interest

The authors have no financial disclosures nor conflicts of interest to report.

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Ethical approval

Ethical approval was not required for this case report presentation.

Consent

Informed consent obtained from the patient.

Author contribution

Samer A. Naffouje: Study design, data collection, writing the paper.Richard R. Anderson: Histologic analysis, confirmation of pathology findings.George I. Salti: Surgical procedure (CRS plus HIPEC), follow up plan.

Guarantor

George I. Salti.

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