Hepatoid carcinoma of the ovary: Characteristics of its immunoreactivity. A case report

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Summary

Alpha-fetoprotein producing tumors other than hepatoma and germ cell tumors have been widely reported, especially in carcinoma with hepatoid differentiation (hepatoid carcinoma). Hepatoid carcinoma has mostly been found in the stomach, but also occurs in many other organs. A rare case of hepatoid carcinoma of the ovary is presented. A 57-year-old Taiwanese woman was admitted because of lower abdominal pain. Magnetic resonance imaging showed a 10 cm right adnexal mass. She underwent a total hysterectomy and bilateral salpingo-oophorectomy with omentectomy. A right ovarian mass measuring 13 x 9 x 8 cm was found. Microscopic examination showed characteristic features for hepatoid carcinoma. Immunohistochemical staining was performed on the tumor using a panel of eight markers (AFP, p-CEA, CD10, Hep Par 1, thyroid transcription factor-1, CK7, CK19 and CK20). This study contradicts the theory that hepatoid carcinoma derives from the surface epithelium of the ovary. Hepatoid carcinoma of the ovary commonly contains a population of clear cells, which may lead to the misdiagnosis of yolk sac tumor or clear cell adenocarcinoma that may arise in many anatomic sites. Histologically, it is also difficult to distinguish hepatoid carcinoma from hepatoid yolk sac tumor. In such cases, demonstration of CD 10, Hep Par 1, membraneous patterns of p-CEA and CK7 would be invaluable for characterizing the tumor as hepatoid carcinoma. More studies are needed to confirm this observation.

Key words: Hepatoid carcinoma; Alpha-fetoprotein; Hepatocyte antigen; CD10; p-CEA; Thyroid transcription factor 1.

Introduction

Alpha-fetoprotein (AFP) producing tumors other than hepatoma and germ cell tumors have been reported, especially in carcinoma with hepatoid differentiation (hepatoid carcinoma). Hepatoid carcinoma (HC) has mostly been found in the stomach [1, 2]. HC of the ovary is rare. Only a few cases have been reported in the literature [3-8]. An additional case of HC of the ovary is herein reported. This case provided the opportunity to study its immunoreactivity using a panel of eight immunohistochemical markers.

Case Report

A 57-year-old Taiwanese woman was admitted to the hospital in July 2000, with lower abdominal pain for two month's duration. Her medical history included one spontaneous abortion and four fullterm pregnancies. She had experienced menopause at the age of 52 years. On pelvic examination, the uterus was normal in size. A large right adnexal mass was palpable. Magnetic resonance imaging (MRI) showed a 10 cm right adnexal mass with solid and cystic components (Figure 1). Her serum alpha-fetoprotein concentration was raised to 24,879 ng/ml. The patient underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy and omentectomy. Cytology from pelvic washing was negative.

The patient did not receive adjuvant chemotherapy or radiation therapy, and was doing well when she was last seen in July, 2003. Her serum level of alpha-fetoprotein was < 20 ng/ml.

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Pathology

The right ovarian mass measured 13 x 9 x 8 cm. The external surface was smooth and intact. The cut surface showed multiple cystic areas containing bloody fluid. The solid part was soft and yellowish with foci of necrosis. The left ovary, both fallopian tubes and the uterus were grossly unremarkable and no tumor seeding was found in the omentum.

Microscopically, the tumor cells were polygonal with a trabecular arrangement resembling hepatoma. They had abundant eosinophilic cytoplasm with large nuclei and prominent cherry red nucleoli (Figure 2).

Immunohistochemical studies and results

Paraffin blocks from the case of HC and a hepatoid yolk sac tumor (HYST) in the pathology file were used for the immunohistochemical studies.

The antibodies used in this study are listed in Table 1. Sections were cut at 4 μm, deparaffinized in xylene and rehydrated in graded ethanol. Staining was performed in a Dako Auto-Stainer. Appropriate positive and negative tissue controls were used throughout. Immunoreactivity was evaluated according to the intensity of the tumor cell staining (0-3+), as well as the percentage of tumor cells that were stained. The tumor cells were considered unequivocally positive if > 10% of the tumor cells reacted with any intensity. The results of the immunohistochemical studies are summarized in Table 2. In HC, the tumor cells showed positive reactivity for Hep Par 1, AFP, CD10, CK7, and p-CEA, but negative for thyroid transcription factor 1 (TTF-1), CK19, and CK20 (Figures 3-7). In the yolk sac tumor, the neoplastic cells were positively stained for p-CEA, AFP, and CK19, with a membranous pattern; while the immunoreactivity was negative for CK7,CK20, Hep Par 1, CD10 and TTF-1.

Fig. 1

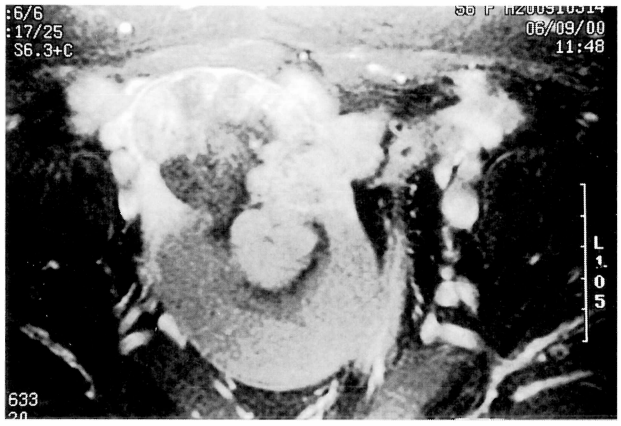


Fig. 2

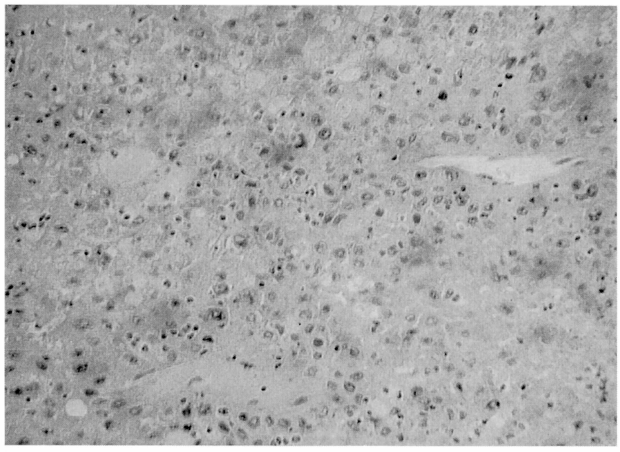


Figure 1. — A large 10 cm right adnexal mass with solid and cyctic component.

Figure 2. — Hepatoid carcinoma of the ovary. Trabeculae of neoplastic cells resembling hepatocytes (hematoxylin and eosin stain x 100).

Table 1. — *List of antibodies used.*

Antibody	Type	Dilution	Source
TTF-1	Monoclonal	1:200	DAKO
Hep Par 1	Monoclonal	1:100	DAKO
AFP	Polyclonal	1:500	DAKO
CD 10	Monoclonal	1:5	Novocastra
p-CEA	Polyclonal	1:60	DAKO
CK19	Monoclonal	1:100	DAKO
CK20	Monoclonal	1:20	DAKO

Table 2. — *Results of immunoreactivity.*

Hepatoid	Adenocarcinoma	Yolk sac tumor
TTF-1	negative	negative
Hep Par 1	3+, diffuse cytoplasmic, granular	negative
AFP	!+, focal, cytoplasmic	3+, focal, cytoplasmic
CD 10	3+ diffuse cytoplasmic, granular	negative
p-CEA	3+ diffuse, membranous	2+, focal, cytoplasmic
CK19	negative	2+, focal membranous
CK20	negative	negative
CK7	2+, focal, cytoplasmic	negative

Discussion

In 1993, Wennerberg *et al.* [9] reported the development of a new monoclonal antibody designated hepatocyte paraffin 1 (Hep Par 1), which has been shown to be highly specific for identification of hepatic phenotype. In the present case, the tumor cells were diffusely and intensely immunoreactive for Hep Par 1 (Figure 3). In contrast, Hep Par 1 immunoreactivity was negative in HYST.

For hepatocellular carcinoma (HCC), immunoreactivity with polyclonal CEA (p-CEA) shows a characteristic canalicular pattern with a sensitivity ranging from 50% to 90% and a specificity of almost 100%. In the present case, p-CEA was strongly positive with a membraneous pattern which was less specific as compared to p-CEA with a canalicular pattern. In HYST, the neoplastic cells were focally positive with a cytoplasmic pattern.

CD 10 is expressed in both normal and neoplastic liver tissue, where it exhibits characteristic canalicular or membraneous patterns similar to the one observed with the antibody against p-CEA [10]. In the present case, a cytoplasmic granular pattern was observed when the antibody against CD 10 was used, while it was negative in HYST. A cytoplasmic granular pattern has never been reported, and the significance of such is unknown.

Nuclear immunoreactivity of TTF 1 has been proven useful as a marker of lung and thyroid carcinoma in biopsy specimens [11]. In contrast, cytoplasmic staining with TTF 1 antibodies has not been studied systematically. This pattern of staining has been demonstrated in the cytoplasm of hepatocellular carcinoma [12]. They were both negative in HC and HYST.

HC of the ovary is very rare. In 1987, Ishikura and Scully first recognized this entity [3]. They postulated that HC is most likely a variant of a common epithelial carcinoma. In a study by Scurry *et al.* [9], they found imperceptible merging of the hepatoid and papillary components, supporting the theory of a surface epithelial origin of HC.

Tochigi *et al.* [7] also reported three cases of HC admixed with a common surface epithelial carcinoma. Using immunohistochemical studies, they demonstrated that HC cells had a hepatocytic phenotype, but shared the cytokeratin profile with the common surface epithelial carcinoma. Their findings suggested that HC of the ovary was probably derived from carcinoma of the surface epithelial origin by a process of neometaplasia or transdifferentiation. The immunohistochemical study of the present case contradicts this theory; the neoplastic cells were reactive for hepatocytic antigen, but negative for ovarian epithelial antigen.

HC of the ovary commonly contains a population of clear cells, which may lead to the misdiagnosis of yolk sac tumor or clear cell adenocarcinoma that may arise in many anatomic sites. Histologically, it is also difficult to distinguish HC from HYST. In such cases, demonstration

g. 3

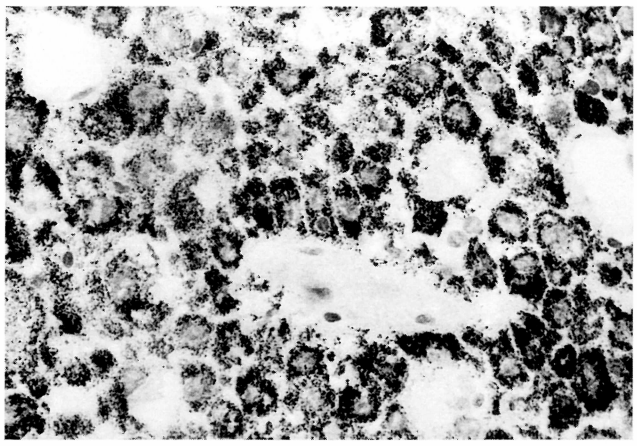
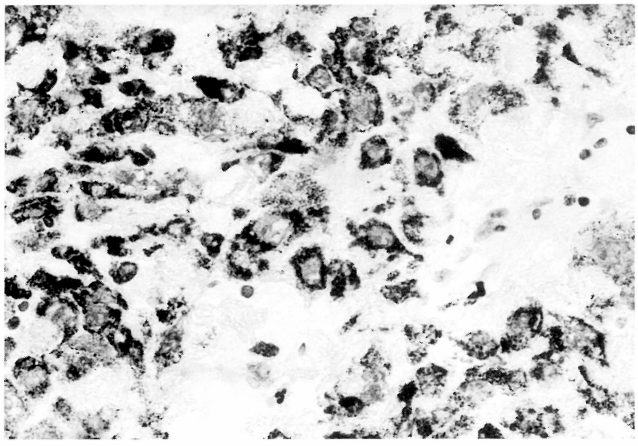


Fig. 4



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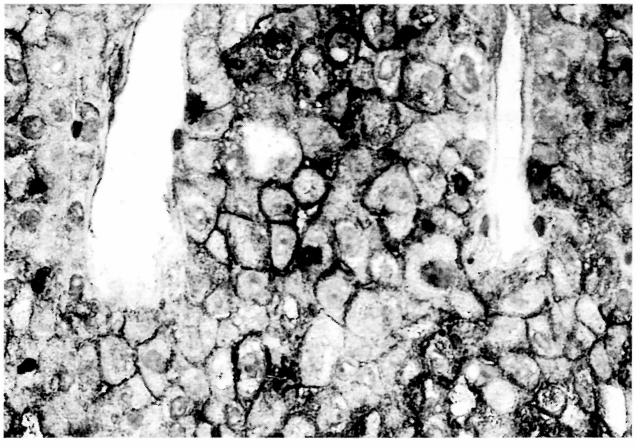
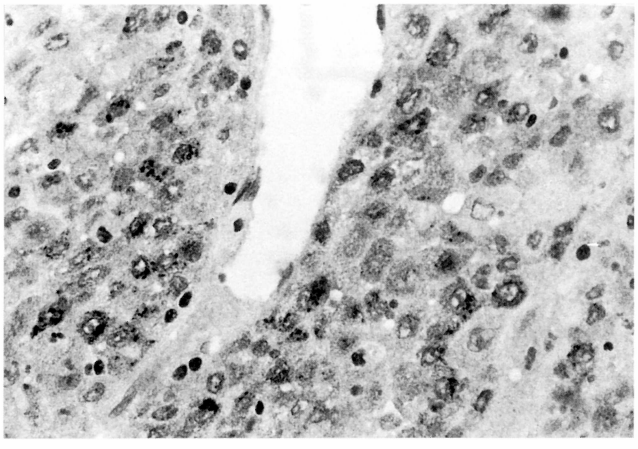


Fig. 6



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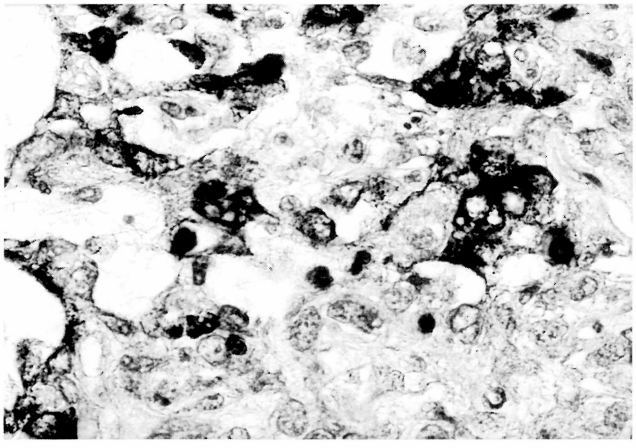

Figure 3. — Intense, diffuse granular cytoplasmic immunoreactivity in malignant cells (hepatocyte paraffin 1 x 400).

Figure 4. — Intense, diffuse, granular, cytoplasmic immunoreactivity (CD10 x 400).

Figure 5. — Intense, diffuse membraneous immunoractivity (p-CEA x 400).

Figure 6. — Scattered tumor cells immunoractive for AFP x 400.

Figure 7. — Focal strong cytoplasmic immunoreactivity for p-CEA (hepatoid yolk sac tumor x 400).

of CD 10, Hep par 1, CK7 and a membranous pattern of p-CEA with negative CK19 would be invaluable to characterize the tumor as a hepatoid carcinoma. More studies are needed to confirm this observation.

In conclusion, HC of the ovary is a rare tumor. It is possible to differentiate HC from HYST using immunohistochemical staining. In this study, we demonstrated that the neoplastic cells share the hepatocyte phenotype, and contradict the theory that they derive from a surface origin as previously reported in the literature [3, 7, 9].

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