# A rare case of metastatic ovarian carcinoma originating from primary intrahepatic cholangiocarcinoma. Case report

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**Summary**

*Background*: A rare case of metastatic ovarian carcinoma arising from intrahepatic cholangiocarcinoma is reported and the literature reviewed.

*Case*: A 49-year-old woman presented with ascites and a left pelvic mass. Optimal debulking surgery was carried out including a segmental resection of segment 5/6 of the liver. Histopathology confirmed an intrahepatic cholangiocarcinoma metastatic to the ovaries and omentum.

*Conclusion*: Distinguishing a metastatic tumor from a primary ovarian tumor is critical for appropriate management. A high index of suspicion intraoperatively and subsequent expert pathological review are essential in making the correct diagnosis.

*Key words:* Metastatic ovarian carcinoma; Intrahepatic cholangiocarcinoma.

## Introduction

Approximately 5-6% of all ovarian tumours are metastatic from other organs, most frequently from the female genital tract, the breast or the gastrointestinal tract [1]. The best known gastrointestinal tract tumour metastasizing to the ovaries is signet ring cell adenocarcinoma, also known as the Krukenberg tumor. These are almost always gastric in origin [2], and have the classic mucin-filled signet ring cells. However, other cases of metastases from the gastrointestinal tract to the ovaries do not have this classic appearance. Most of these are from the colon, less commonly from the small bowel, and a few cases of primary hepatobiliary carcinoma and gall bladder carcinoma metastasizing to the ovaries have been reported.

Cholangiocarcinomas are relatively rare tumours, and there have been case reports in the literature of extrahepatic and gall bladder cholangiocarcinoma metastasizing to the ovaries [3, 4]. To our knowledge, however, this is the first case report of an intra-hepatic cholangiocarcinoma presenting as a case of advanced ovarian carcinoma.

## Case report

A 49-year-old woman presented with a 2-week history of abdominal pain. Clinically there was no jaundice but abdominal and pelvic examination revealed gross ascites and a left pelvic mass. CT scan showed a 4 x 3 cm left adnexal mass of soft tissue density, omental caking and small volume ascites (Figure 1). A small lesion of heterogeneous attenuation was seen in the right lobe of the liver, which showed delayed filling of contrast suggestive of a hemangioma (Figure 2). The CA-125 was 928 U/ml, CEA < 0.5 ug/l and AFP was 2.4 ug/l. Preoperative full blood count, renal and liver function were all normal.

At laparotomy, both ovaries were replaced by nodular tumour; there was extensive nodular peritoneal disease and ascites. A large omental cake was noted, extending to a 5 cm mass on the surface of segment 5 of the liver. The gall bladder wall was thickened but the cystic duct appeared normal. A total hysterectomy, bilateral salpingo-oophorectomy, total omentectomy, and wedge segmental resection of segment 5/6 of the liver was performed. Optimal debulking was achieved with residual disease of < 5 mm nodules over the bowel mesentery and military disease over the diaphragmatic surfaces.

At the gross pathology examination, the wedge of liver measured 6 x 9.5 x 6 cm with a gall bladder 2.3 x 2.3 x 5.5 cm included. There was a white tumor mass 5 x 3 x 4.5 cm within the wedge extending close to the liver capsule and grossly 1 cm from the surgical resection margin (Figure 3). A few small satellite nodules were seen in one area and there was focal infiltration of the tumor into the gall bladder bed. Both ovaries were moderately enlarged to 5 and 5.5 cm in maximum diameter respectively and showed nodular outline with extensive replacement by firm white tumor tissue. The tumor was disposed as multiple nodules, many of which were confluent (Figure 4). There were also tumor deposits in the utero-vesical peritoneal fold and in the omentum. Microscopic examination showed that the liver contained multiple foci of adenocarcinoma, including some within the liver capsule. These comprised mainly small oval tubules, with occasional larger glands, small solid clusters, trabeculae and cords (Figure 5). Among the smaller deposits, the tumor tended to be located within expanded portal tracts, with the bulk of the malignant glands adjacent to the hepatic plate. Intraductal spread of tumor was seen, and there were a few bile ductules showing dysplasia and carcinoma-in-situ (Figure 6). Perineural spread was identified.

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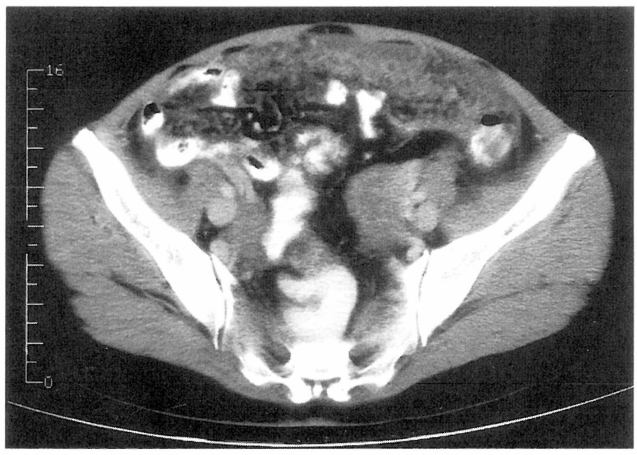


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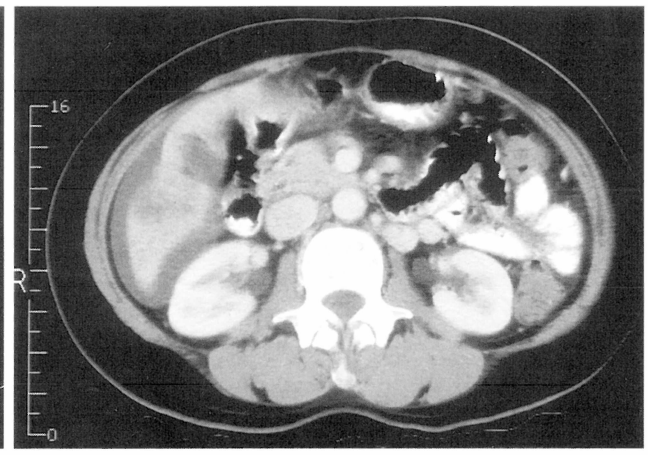


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Figure 1. — CT scan showing a 4 x 3 cm left adnexal mass of soft tissue density and omental caking.
Figure 2. — CT scan showing a small lesion of heterogeneous attenuation in the right lobe of the liver.

The tumor had spread to the soft tissue of the gall bladder bed but not into the gall bladder wall. Metastatic tumor deposits were seen in a lymph node as well as in the soft tissue of the resection margin of the cystic duct. Both ovaries showed nodular deposits of tumor, many of which were confluent. The tumor comprised oval and angular tubules resembling those in the liver (Figure 7). A tendency for the center of the tumor deposits to show necrosis and hyalinization was noted. There was tumor involvement of the ovarian surface. Metastatic deposits to the omentum and utero-vesical peritoneal fold were also confirmed microscopically, and there were deposits identified in the right paratubal tissue and falciform ligament of the liver.

## Discussion

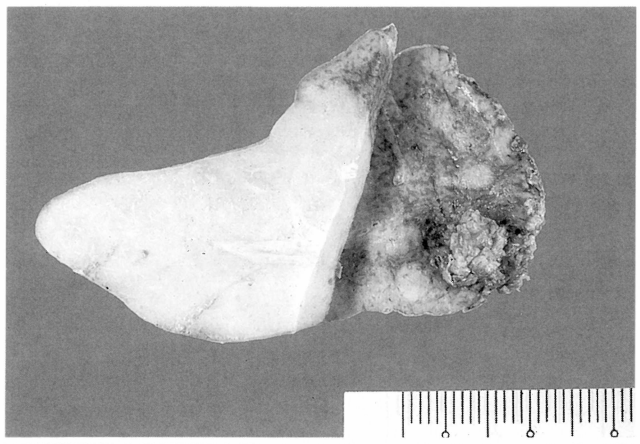
A variety of tumors metastasize to the ovary and the majority of those, which are clinically significant, originate in the gastrointestinal tract [5]. Metastatic tumors are important because the misinterpretation of those cases encountered as surgical pathology specimens may have important adverse consequences for the patient. The recognition of the metastatic nature of an ovarian tumour depends on several factors: (1) the awareness of the frequency with which metastases occur and simulate a variety of primary tumours, (2) a detailed clinical history, (3) a thorough clinical and operative search by the gynecologic oncologist for a primary tumour outside the ovary and for other sites of tumour spread, and (4) a careful evaluation of the gross and microscopic features of the ovarian tumour by the pathologist [5].

The relative frequency of metastatic tumours among all ovarian tumours is difficult to establish accurately for several reasons: (1) some studies are based on autopsy findings while others are based on operative findings, (2) some studies are based on incidental asymptomatic metastases while others are based on clinically symptomatic metastases, (3) some studies do not differentiate between synchronous and metastatic lesions, and (4) there are racial differences in specific cancer susceptibility. However the figure for the frequency of metastatic ovarian carcinoma that is most meaningful to the gynaecological oncologist is one that expresses the probability that an ovarian neoplasm found on exploration of a pelvic or abdominal mass is metastatic; this is about 6 [6] to 7% [7].

There is a paucity of information in the literature concerning the ovarian spread of tumours originating from the gall bladder, intra- and extra-hepatic bile ducts. A series published by Young and Scully [3] described six cases of gall bladder carcinoma with ovarian metastases. In three of these cases, the gall bladder tumour and ovarian metastases were detected simultaneously. A case report by Sharma [4] reported another case of carcinoma of the common bile duct presenting with metastatic ovarian carcinoma. The common bile duct primary was detected one month after laparotomy for what was at initial histology a primary ovarian carcinoma. Histopathology review subsequently confirmed a cholangiocarcinoma.

Biliary tree carcinomas are divided into intrahepatic (cholangiocarcinomas) and extrahepatic tumours. The proximal bile duct is the most frequent site for malignancy, accounting for up to 76% of bile duct tumours [8]. Proximal tumours above the hepatic bifurcation may not cause jaundice, which is otherwise the commonest presenting feature. Metastatic disease is evident in about 30% of patients, 10% of whom have peritoneal spread [3]. Ovarian metastases are rare, and likely represent "drop metastasis" as seen in most other pelvic metastases from adenocarcinoma [4]. The median survival in untreated cases is six months and the usual cause of death is liver failure due to disease progression of the primary lesion.

The gross and microscopic appearance of the ovaries had the features usually described for metastatic tumors i.e., bilateral involvement, lobulated outline, multiple nodular deposits within the ovarian parenchyma, ovarian surface involvement and a histological appearance unlike the usual primary ovarian carcinomas. The greatest challenge in this case was to determine if the liver tumor was a primary tumor or a metastatic deposit from an unknown



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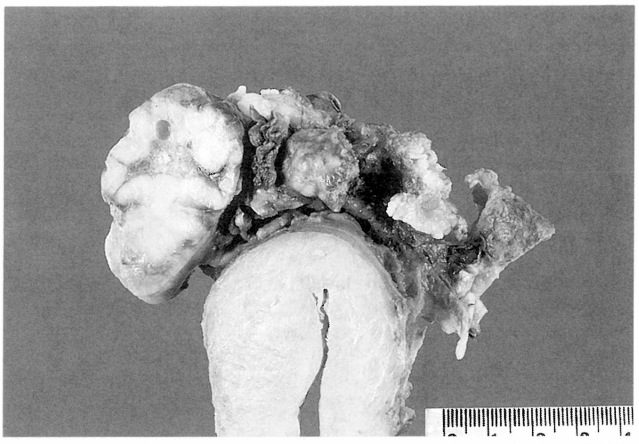

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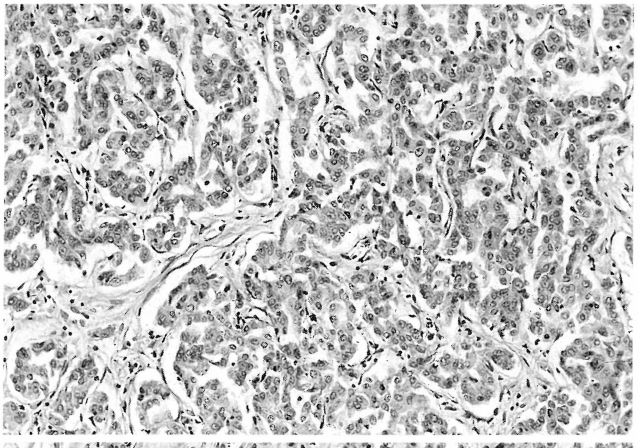

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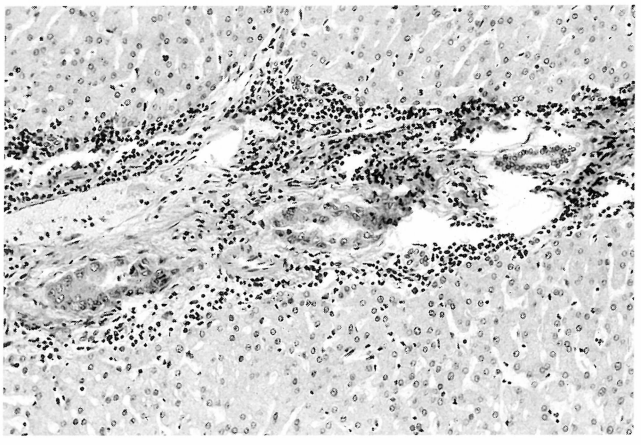

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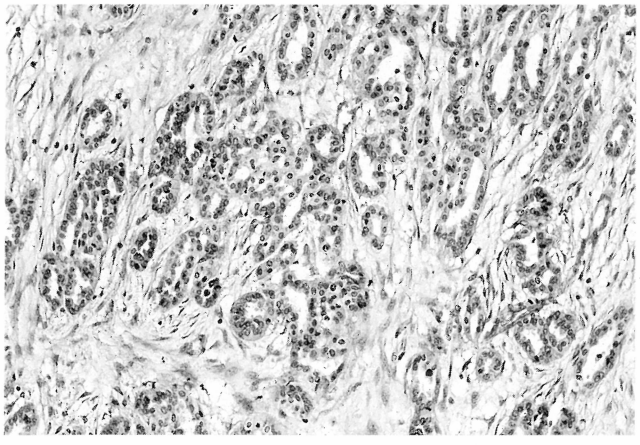

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Figure 3. — Wedge of liver showing a solid white tumor mass with a few small satellite nodules.
Figure 4. — Section of hysterectomy specimen showing tumor deposits within an ovary and peritoneal fold. Ovarian deposits are multinodular and confluent. Opposite ovary appeared similar.
Figure 5. — Microscopic section of liver tumor showing confluent small malignant glands.
Figure 6. — Microscopic section of liver showing portal tract with bile duct lined by normal epithelium on the right and dysplastic glandular epithelium with features of carcinoma-in-situ in center and left.
Figure 7. — Microscopic section of ovarian tumor showing adenocarcinoma histologically similar to the liver tumor (see Figure 5).

primary site, presenting with simultaneous ovarian and liver metastases. Distinguishing a primary intrahepatic cholangiocarcinoma from metastatic adenocarcinoma, especially from a primary in the gall bladder, extrahepatic biliary tree, pancreas or breast, can be very difficult. At present, there are no specific tumor markers useful in distinguishing cholangiocarcinoma from other forms of adenocarcinoma. The diagnosis therefore depends on exclusion of primary tumors in other sites. The presence of dysplastic change in nearby bile ducts or ductular epithelium favors a primary in the liver and this was present in this case. The absence of tumor in the intestine and extrahepatic bile ducts at surgery, a normal pancreas on CT scan and normal breasts on clinical examination also support the impression that the tumor was a primary in the liver.

We believe this to be the first reported case of intrahepatic cholangiocarcinoma with a clinical presentation mimicking advanced stage ovarian carcinoma. Distinguishing a metastatic ovarian tumour from a primary ovarian tumor is critical for appropriate management. To optimize outcome, the diagnosis must be made at an early stage. A high index of suspicion in the presence of atypical surgical distribution of disease and subsequent expert pathological review are essential in arriving at the correct diagnosis.

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