Occult Gallbladder Carcinoma Presenting as a Primary Ovarian Tumour: a Case Report and Review of Literature

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Abstract

The ovary is a common site of metastasis from various organs. However, little is known about gallbladder carcinoma metastasising to the ovaries and presenting as a primary ovarian tumour. We report a case of a metastatic gallbladder carcinoma which mimicked a primary ovarian tumour in a 31-year-old woman who presented with menstrual symptoms and an ovarian mass without obvious signs and symptoms related to gallbladder carcinoma. Postoperatively histopathological examination diagnosed primary ovarian germ cell tumour for further chemotherapy. However, postoperative re-evaluation with radiology suggested the possibility of a primary gallbladder carcinoma. Exact diagnosis could only be made after repeat histopathological evaluation of the ovarian mass.

Keywords Gallbladder carcinoma · Ovarian metastasis · Adenocarcinoma of the ovary

Introduction

The ovary is a relatively frequent site of metastasis from various organs, especially the pancreas and gastrointestinal tract. Rarely, the metastasis may precede detection of the primary site and may present as an ovarian tumour [1]. Only few cases of metastasis from the gallbladder to ovaries have been reported in the literature [2–13]. Some of these cases were initially misdiagnosed as primary ovarian tumours. We report a patient who was operated for an ovarian cyst, pathological examination showed granulosa cell tumour, but later was found to have primary in the gallbladder. A review of literature has been carried out to search for the important features in such cases.

Case Report

A 31-year-old woman with menorrhagia, operated 10 days ago for removal of ovarian cyst, was referred with histopathological report showing granulosa cell tumour (GCT) with focal invasion outside the capsule of right ovarian mass. She did not have any gastrointestinal symptoms. She had a vaginal delivery 3 years ago. Examination showed no icterus. Ultrasonography of the abdomen revealed a hypoechoic area in V hepatic segment. This hypoechoic area was ill-defined, measuring about 2.5×2.1 cm, and communicating with gallbladder wall. The gallbladder wall showed gross thickening, predominantly in the neck and proximal part, with extension to cystic duct until the level of confluence of common hepatic duct. Multiple enlarged lymph nodes, largest measuring 2.1×1.4 cm, were seen in the pre-aortic region and the aorto-caval region above the origin of renal vessels. The uterus showed seedling fibroids. The left ovary was normal and the right ovary was absent. Multislice axial post contrast computerised tomography scan of the abdomen (Fig. 1) showed gross dilatation of the intrahepatic and common hepatic bile ducts, radiating from the porta hepatis. Irregular, heterogeneously enhancing, eccentric thickening of the wall of the gallbladder was seen with loss of surrounding fat planes and infiltration of the adjacent segment V of right lobe of the liver, representing the primary malignancy of the gallbladder.

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Fig. 1 Axial contrast-enhanced CT images at the level of the hepatic hilum. Images (a) and (b) show gross dilatation of the intrahepatic and common hepatic bile ducts radiating from the porta hepatis. Images (c) and (d) show an irregular heterogeneously enhancing eccentric wall thickening of the gallbladder with loss of surrounding fat planes and infiltration of the adjacent segment V of right lobe of the liver representing the primary malignancy of the gallbladder. Few enhancing lymph nodes can also be seen adjacent to the head of the pancreas

Few enhancing lymph nodes were seen adjacent to the head of the pancreas. Serum levels of bilirubin and liver enzymes were normal at admission but started to rise thereafter. At initial assessment, serum total bilirubin level was 5.7 mg/dl, and serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), and alkaline phosphatase were 424 U/l, 556 U/l, and 839 U/l respectively. Serum levels of tumour markers were elevated (CA 125 = 228.9 U/ml; CEA = 15.57 ng/ml; CA19-9 = 524.9 U/ml) except those for germ cell tumour (LDH = 411 U/ml; alpha feto protein = 0.86 ng/ml; beta hCG = 3.31 mIU/ml). Coagulation and renal parameters were normal. Ultrasound-guided biopsy of hepatic lesion revealed metastatic mucin-secreting carcinoma. Review of slides of ovarian tumour was reported as metastatic adenocarcinoma to the ovary. Immunohistochemistry results were strongly positive for cytokeratin (CK)-7, CK-20, and CEA, and negative for vimentin. Based on CT scan and immunohistochemistry reports, gallbladder carcinoma was considered as the primary diagnosis. As the serum bilirubin levels were rising, endoscopic retrograde cholangiopancreatography and stenting was attempted. First and second parts of the duodenum were narrowed due to infiltrating growth. Ampulla could not be reached because of extraneous compression and hence, the procedure was abandoned. Percutaneous transhepatic cholangiography and biliary

drainage was done. In view of stage IVB gallbladder carcinoma, she received chemotherapy with gemcitabine and carboplatin. She is on regular follow-up.

Discussion

The incidence of ovarian metastasis from different organs is nearly 5 to 15% [6]. Although Albores-Saavedra [14] has reported the incidence of gallbladder carcinoma metastasising to ovaries to be about 6%, a description of only few such cases could be found in the literature [2–13]. Seventy-five percent of patients with gallbladder cancer are older than 65 years [15]. In the vast majority of patients (>75%), the source of this chronic inflammation is cholesterol gallstones, which increases the risk of gallbladder cancer four- to fivefold [16].

Of the 30 cases reported, eight patients presented with ovarian masses [3, 5, 9–11, 17] and clinico-radiological findings in five of them mimicked a primary ovarian tumour [3, 6, 9], as in our case. With preoperative radiological investigations, diagnosis could not be established in four of these cases [4–6, 10] and few were misdiagnosed as primary ovarian tumour, even on histology [5, 6], as seen in our case too. A majority of such patients in all the published reports had non-specific abdominal or pelvic symptoms (pain, distension, or mass). In our report, a young woman without any gall

Table 1 Summary of published cases of gallbladder carcinoma with ovarian metastasis

Author	Age (years)	Clinical presentation	Initial detection	Laterality
Meriden [2]	56–69	Abdominal pain, pelvic mass, bowel obstruction	Secondary	Bilateral
Khunamompong [3]	47–83	Abdominal pain, vaginal bleeding, pelvic mass	Primary in 3, synchronous in 5	Bilateral
Ayhan [4]	33	Abdominal pain	Simultaneous	Unilateral
Jain [5]	45	Pelvic mass	Simultaneous	Bilateral
Jarvi [6]	82	Abdominal pain	Simultaneous	Bilateral
Carlomagno [7]	38	Abdominal distension	–	Bilateral
Ricks [8]	63	Pelvic mass, virilisation	–	Bilateral
Young [9]	33–72	Abdominal pain, pelvic mass	Primary first in 1, ovarian first in 1	Bilateral
Miyagui [10]	43	Confusion	Simultaneous	Bilateral
Taranto [11]	52	Pelvic mass	Primary	Bilateral
Petru [1]				Bilateral
Kumar [12]	35, 62	Abdominal mass	Simultaneous	Bilateral
Sun [13]	84	Pelvic mass	Secondary	Bilateral

stones or gastrointestinal symptoms presented to the clinician with only the menstrual symptoms. Initial report of ovarian tumour as GCT could be because GCT can mimic other pathologies as they are often filled with serous fluid or clotted blood and may be mistaken for mucinous cystadenoma or cystadenocarcinoma. Though Call-Exner bodies are said to be present in 30–60% of adult GCTs, the moderately differentiated type, which includes a diffuse, “sarcomatoid” growth pattern is very similar to adenocarcinoma on histopathological examination [18].

Jaundice or other symptoms, related to gallbladder carcinoma with secondaries to the ovary, were observed in only few cases [3, 5, 18] in the literature and serological markers such as alkaline phosphatase, CA19-9, CEA, and CA-125 were found to be variable [3–6, 9, 11, 17] in these reports.

In our case, high index of suspicion in view of presence of gallbladder wall thickening radiologically led to re-examination of the ovarian specimen by a different pathologist, revealing metastatic adenocarcinoma to the ovary. The differential diagnosis of mucinous ovarian carcinoma remains an intriguing challenge for the pathologist, especially when the ovarian mass is metachronous. Both microscopy and immunohistochemistry are useful in distinguishing primary from metastatic disease. Cytokeratine expression is routinely performed because CK7 staining is present in virtually all primary ovarian tumours, and CK20 is very frequently expressed in colorectal and gastric tissue. However, CK7 positivity is also present in many gastrointestinal tumours, and about 75% of primary mucinous ovarian cancers have patchy CK20 staining [19].

This report raised interesting issues. First, metastatic tumours to the ovary are usually bilateral, but it was unilateral in our case. Second, intraperitoneal dissemination of primary

gallbladder cancer is uncommon [1, 3–12, 16]. Third, patients with ovarian metastases from primary gallbladder cancer seldom have typical symptoms [3–5]. Pathologic evaluation, especially frozen pathology, may still diagnose them as ovarian cancer [3]. In Table 1 [2–13], we summarised the data of the currently available cases of primary gallbladder carcinoma mimicking advanced-stage ovarian cancers. Accurate preoperative diagnosis of primary gallbladder carcinoma with ovarian metastases is reported as <30% [3]. During surgery for ovarian masses, the upper abdomen should be evaluated [20]. Intraoperative ultrasound, frozen section may be performed to assess any suspicious growth.

Outcome in our case is poor. Unlike primary ovarian cancer [21], role of surgery is limited. Radiotherapy or chemotherapy provides little improvement [22].

Conclusions

Gallbladder carcinoma should be added to the known list of origins of metastatic tumours to the ovary. Pathologists should maintain high index of suspicion and adequate sampling is required of ovarian masses. Knowledge of the extent to which metastasis may mimic a primary ovarian tumour and its differentiating histological features may help in correct diagnosis.

Compliance with Ethical Standards

Consent Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Conflict of Interest The authors declare that they have no conflict of interest.

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