

# Papillary adenocarcinoma gallbladder with simultaneously detected bilateral ovarian metastases: A Case Report

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## Abstract

Gallbladder and bile ducts are rare sources of metastatic tumor in the ovary. There are few reports of a primary tumor in the gallbladder with bilateral ovarian involvement discovered simultaneously. Herein, we report a case of 38 year old female, presenting with symptoms of gallbladder mass, and on Magnetic Resonance Imaging ovarian masses were also detected. A gallbladder carcinoma with Krukenberg tumor involving bilateral ovaries was suspected. Histopathological examination of the resected specimen revealed a papillary adenocarcinoma gallbladder with tumor of similar histology in both ovaries. No signet ring cells were seen on microscopic examination in any of the involved sites.

"Krukenberg tumors" by definition, are metastatic signet ring cell adenocarcinoma of the ovary. They are usually bilateral, characterized grossly by solid multinodular enlargement of ovaries and microscopically by diffuse infiltration by signet ring cells, which should occupy at least 10% of the neoplasm, and contain abundant neutral and acidic mucin. Hence, bilateral ovarian metastasis, as in our case, is not always a Krukenberg tumor at the histological level.

## INTRODUCTION

The ovaries are one of the common sites for involvement by metastatic tumors. In few of these cases, simultaneous detection of the primary tumor is possible intraoperatively or preoperatively through imaging modalities. The tumors metastasizing to ovary arise most commonly from the gastrointestinal tract, which includes stomach, large bowel and appendix. Metastasis from the breast, uterus and skin are also known. However, primary tumors detected in the gall bladder or hepatobiliary tract are relatively rare, with very few case reports available.

The best known metastatic tumor in the ovary is a Krukenberg tumor. The diagnosis of this tumor requires the presence of diffuse infiltration by signet ring cells containing abundant neutral and acidic mucin (mostly sialomucins). Signet ring cell adenocarcinomas of various anatomic sites tend to metastasize to the ovaries much more commonly than adenocarcinomas of other histologic types from the same sites.

A metastatic tumor in the ovary can also simulate a primary epithelial tumor at the macro and microscopic level, and this may lead to difficult diagnostic problems in patients having an occult primary lesion elsewhere.

## CASE PRESENTATION

A 38 year old female patient presented in this hospital with complaints of abdominal pain off and on since one year. Pain was in the central quadrant, gradual in onset, increasing in severity and radiating to the back. It was not associated with nausea and vomiting. The pain aggravated after having food, and there was no relieving factor. Simultaneous with pain, the patient also noticed distension of abdomen, which was gradual in onset and progressive. There was associated anorexia, indigestion and constipation. Gradual loss of weight and weakness was also present. Yellowish discoloration of eyes and yellow colored urine was present since one and half month, but the patient did not notice any alteration in color of stools. There was no history of smoking or alcohol intake. However, she had history of tobacco chewing.

On examination, there was mild abdominal distension and mild icterus. No dilated veins or abnormal pigmentation was seen. On palpation abdomen was tense with tenderness in the right hypochondrium. The liver edge was palpated 2.5 cm below the costal margin. Bilateral adnexal masses were also appreciated. On percussion, shifting dullness was present.

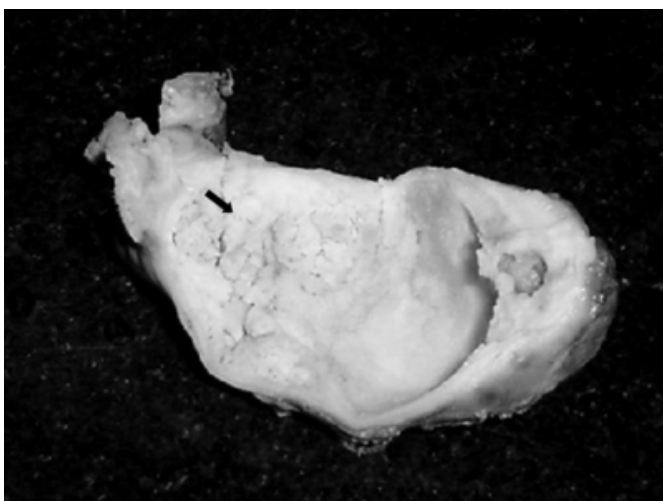
Laboratory investigations revealed conjugated hyperbilirubinemia, with increased liver enzymes and

alkaline phosphatase. CA-125 level was elevated. Ultrasonography showed mildly enlarged liver with mild intrahepatic biliary radicle dilatation. The gallbladder was filled with multiple calculi and sludge. Both common hepatic duct and common bile duct were dilated. Moderate ascitis was also present. Magnetic Resonance Imaging revealed enlarged gall bladder with marked irregular and nodular circumferential thickening, along with an ill defined mass in the region of the neck. In addition, there were large complex solid cystic masses involving both ovaries. Thick septations were noted in the ovarian masses. Based on these findings, a pre operative diagnosis of carcinoma gall bladder with Krukenberg tumour (bilateral adnexa) was made, and subsequently bilateral adnexal excision, cholecystectomy and Roux-en-Y hepaticojejunostomy was performed.

The resected gallbladder measured 6x3x3 cm, with congested external surface. On opening, the wall was found to be thickened, and a grey white growth was seen involving the region of the neck and extending to involve almost the entire mucosal surface of the gallbladder (Figure 1). The wedge of the liver, measuring 3x2 cm, was grossly normal. The size of the right and left ovarian masses were 13x10x6 cm and 8x6x5 cm respectively. The capsular surface showed multinodularity (Figure 2) along with bilateral surface implants. The fallopian tubes were identified measuring 4 cm and 2.5 cm respectively. Both the ovaries on slicing showed solid areas and cysts filled with grayish mucinous material.

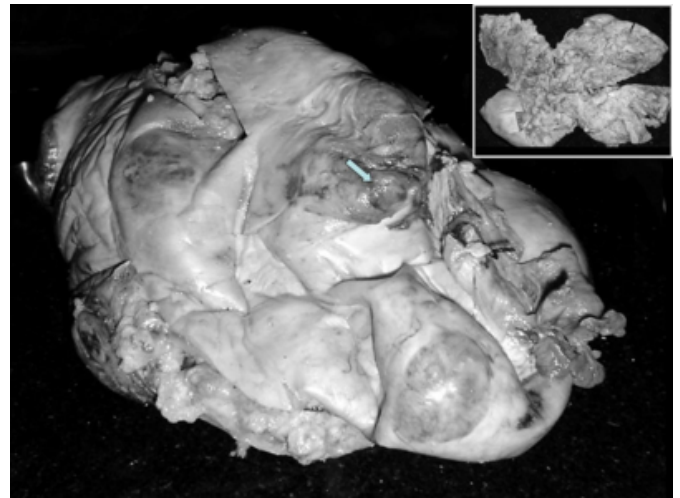
#### **Figure 1**

Figure 1: Resected specimen of gallbladder with neck mass (arrow).



#### **Figure 2**

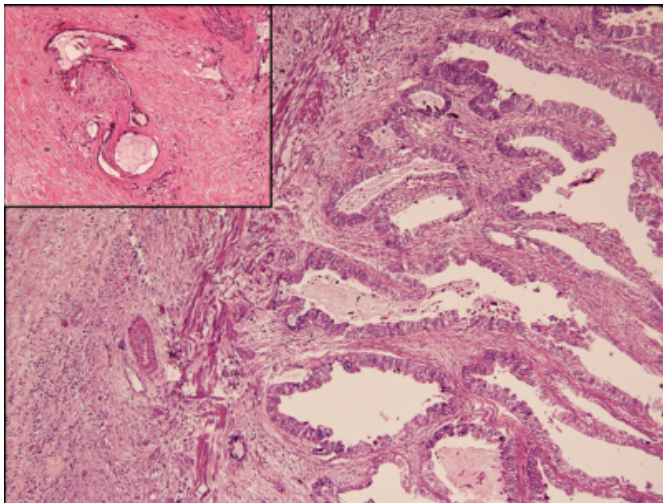
Figure 2: Gross photograph showing capsular surface of the right ovary (arrow showing nodularity); Inset: Cut surface.



Multiple sections examined from the gall bladder showed a papillary adenocarcinoma (Figure 3). The tumor cells were arranged in papillary and glandular configuration. Perineural and intraneural invasion were seen (Figure 3, inset). The tumor was infiltrating up to serosa and into the adjacent underlying liver parenchyma. Sections from both right and left ovaries also showed an epithelial tumor with predominant papillary arrangement, multiple cystic spaces and extracellular mucin. A thin rim of ovarian stroma was seen at the periphery of the tumor (Figure 4). Surface implants in bilateral ovaries were confirmed microscopically. Both the fallopian tubes were free of tumor. After the surgical procedure, the patient has been on regular follow up for the last one year, and at present she is doing well.

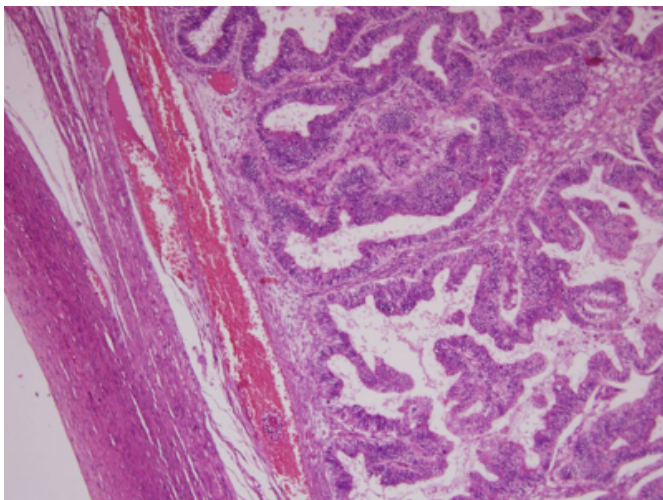
**Figure 3**

Figure 3: Papillary adenocarcinoma gallbladder (H&E, x200); inset showing perineural invasion. (H&E, x400)



**Figure 4**

Figure 4: Metastasis in the ovary by tumor bearing similar morphology; compressed ovarian stroma is seen at the periphery. (H&E, x200)



## DISCUSSION

The ovary is a common site of metastatic deposits, well known among which is the Krukenberg tumor. Identification of signet ring cells containing demonstrable intracytoplasmic mucin and occupying at least 10% of the tumor is essential for this diagnosis. These tumors are bilateral in more than 80% of instances. Approximately two thirds of the primary tumors arise from the stomach<sup>4, 5</sup>; other sites in order of frequency include appendix, large bowel, breast, small intestine, rectum, with reports of primary also from gallbladder, biliary tract, pancreas, ampulla of Vater, cervix, and urinary bladder/urachus<sup>5</sup>. Primary tumors of

histomorphological types other than signet ring cell adenocarcinomas less frequently have distant metastasis<sup>5</sup>. In a study by Hamed F et al<sup>7</sup>, including 9 patients with extragenital tumors metastatic to ovary, 7 were microscopically Krukenberg tumors. All these cases had bilateral enlarged ovaries with solid appearance. Of the primary tumors detected in these patients, 4 were of gastric origin, 2 from the colon, 1 from the gallbladder and 1 from the breast. Hence, from the literature it is evident that ovarian metastasis arising from a gall bladder primary is quite rare.

Microscopically, most gallbladder carcinomas are adenocarcinoma. Gallbladder carcinoma has a greater propensity to invade the adjacent liver tissue, to lesser extent stomach and duodenum. It metastasizes frequently to liver and lymph nodes. Young RH et al<sup>1</sup> reported 6 cases in which ovarian metastases from carcinoma gall bladder and extrahepatic bile ducts were discovered during the life of the patient. Five of the cases had bilateral ovarian involvement, and in three cases, primary tumor in the gall bladder and metastasis in the ovary were discovered simultaneously. Grossly, the tumor size in one of the cases was 13 cm with multiloculated cystic appearance, simulating primary mucinous ovarian tumor. Other tumors were up to 6.5 cm in diameter. In our case, the primary lesion in gallbladder and bilateral ovarian metastasis were detected simultaneously. The ovaries were 13x10x6 cm and 8x6x5 cm in size, with multinodularity and surface implants. On slicing, solid areas along with multiple cystic spaces and extracellular mucin were seen. Histology revealed a tumor with complex papillary architecture, similar to the papillary adenocarcinoma seen in gall bladder. The ovaries in Krukenberg tumor are usually asymmetrically enlarged, with a bosselated contour and capsular surface free of adhesions or surface implants. Surface implants, as seen in our case, favor the macroscopic diagnosis of other metastatic tumors to the ovary<sup>5</sup>. Again at the histological level also, due to the absence of signet ring cells, this case did not qualify for the diagnosis of Krukenberg tumor, though the same was suspected preoperatively through clinical and imaging modalities.

Ovarian metastases from pancreatobiliary and gallbladder carcinomas can have histological resemblance with a primary ovarian epithelial tumor<sup>3, 6</sup>, and differentiating metastasis from primary ovarian neoplasms is important in situations where the primary tumor is very small, without

producing significant symptoms, and hence can escape detection. Carcinoma metastatic to the ovary has a very poor prognosis. Features helpful in establishing the metastatic nature include bilateral involvement, surface implants, multinodularity and extra ovarian spread. Lee KR et al<sup>8</sup>, in addition mentioned infiltrating pattern of stromal invasion as one of the features favoring metastasis. Less frequent findings present almost exclusively in metastatic lesions were a nodular invasive pattern, ovarian hilar invasion, single cell invasion, signet ring cells, vascular invasion and microscopic surface mucin. On the other hand, factors favoring primary mucinous tumors were expansile pattern of invasion, complex papillary pattern, size >10 cm, smooth external surface, benign and borderline appearing areas, microscopic cystic glands and necrotic luminal debris. In our case, though bilateral ovarian metastasis was suspected pre-operatively through clinical features and imaging studies, additional features of metastasis like bilateral surface implants, multinodular appearance and infiltrating pattern of stromal invasion were also documented later.

To conclude, a papillary adenocarcinoma gallbladder with simultaneous detection of bilateral ovarian metastases has been seldom documented. Possibility of metastatic carcinoma should be excluded in cases of doubtful ovarian masses and bilateral involvement. This is particularly important for occult primary lesions from the prognostic and therapeutic point of view.

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