Obstructive Jaundice Secondary to Metastatic Cancer: A Review

by S. Patel, N. Kheterpal, R. Patwardhan, and J. Levey

Jaundice due to metastatic cancer is much more common than originally appreciated. Studies have shown that up to 21% of malignant biliary obstructions are a result of distant primary malignancies metastatic to the pancreaticobiliary system. Jaundice due to biliary stasis occurs from either the diffuse hepatic parenchymal infiltration of malignant cells causing obstruction of the small intrahepatic biliary ducts or by compression of the larger extrahepatic ducts. The latter form of obstruction can be due to intraluminal invasion within the submucosal layer of the bile duct or from external compression secondary to enlarged tumor-infiltrated periportal lymph nodes and masses or pancreatic parenchymal lesions. The clinical differentiation of primary and secondary pancreatic-biliary tumors can be difficult. In fact many of these patients who present with jaundice are initially misdiagnosed with primary cholangiocarcinoma or pancreatic carcinoma. It is important to make this distinction due to the therapeutic implications. Some authors have actually shown improved survival in patients with metastatic disease compared to those with primary pancreatic or biliary duct cancers. The most common primary cancers to metastasize to the pancreaticobiliary system are stomach, colon, breast, kidney, and lung (2–5). Other reported primary tumors causing metastatic biliary obstruction include malignant melanoma, lymphoma, gallbladder, ovary, duodenum, esophagus, liver, cervix, uterus, muscle, prostate, bone, and brain.

The possibility of metastatic tumor should be considered in all patients with obstructive jaundice, especially if a previous malignant lesion has been identified. Improved imaging (MRI) and biopsy techniques (EUS with FNA) should be helpful in distinguishing primary and metastatic biliary cancer. In this article we will review the characteristics of the common primary tumors causing metastatic biliary obstruction.

GASTRIC CANCER

Despite its decline in incidence over the past few decades, gastric cancer is still the second most common cancer worldwide. Approximately one-half of patients with gastric cancer are not surgical resection candidates due to advanced disease at presentation. Those who undergo potentially curative resections have a high rate of both local and distant recurrence.

Gastric cancer spreads locally within the gastric wall infiltrating into the submucosa early in their development. The presence of nodal metastases is very closely related to depth of local invasion. With mucosal invasion...

(continued on page 27)
sion, lymph nodes are involved in 0% to 7% and in 15% to 30% of lesions involving the submu-
cosa (6). Gastric cancer that invades the muscular propria is called advanced carcinoma.
Once it reaches the serosa of the stomach it also spreads via the peritoneal cavity. The progres-
sion of lymph node spread can be categorized into three tiers. The first level, N1 nodes, are 
perigastric nodes (Figure 3A, groups 1–6) followed by N2 nodes (Figure 3B, groups 7–11) which are found along the celiac axis and finally to the N3 nodes, which include the hepatoduode-
nal ligament nodes, paraaortic nodes, and those around the origin of the middle colic and superior mesenteric arteries. This staging is the logic behind the extensive local resections that have been 
developed for surgical excision.

Obstructive jaundice is frequently present in patients with advanced gastric carcinoma and is among the more common causes of malignant biliary obstruction by metastatic cancer (4–7). Bile duct obstruction in advanced gastric carcinoma is predominantly due to metastatic lymphadenopathy in the hepatoduodenal ligament around the level of the cystic duct (4). Standard gastric surgery with lymph node dissection for gastric carcinoma does not remove N3 lymph nodes along the hepatoduodenal ligament. Despite this, malignant obstruction after gastrectomy is rare occurring in only 1.4%–2.3% of patients (4,6). Obstructive jaundice in these patients also can be due to benign post-surgical causes. Imaging via endoscopic retro-
grade cholangiography can be challenging, however, due to surgeries such as Billroth II reconstruction.

The treatment goal in patients with jaundice due to advanced gastric carcinoma is palliation. Biliary drainage can be accomplished with the placement of plastic or expandable metallic stents with patency rates of three and eight months respectively. The median survival in these patients after biliary drainage is approximately two months (7). Anecdotal reports

---

**Table 1**

<table>
<thead>
<tr>
<th>Tumor</th>
<th>Frequency %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary</td>
<td></td>
</tr>
<tr>
<td>Pancreas</td>
<td>80</td>
</tr>
<tr>
<td>Bile Duct</td>
<td>5</td>
</tr>
<tr>
<td>Ampullary</td>
<td>1</td>
</tr>
<tr>
<td>Duodenum</td>
<td>1</td>
</tr>
<tr>
<td>Secondary (porta hepatis)</td>
<td></td>
</tr>
<tr>
<td>Gastric</td>
<td>10–50</td>
</tr>
<tr>
<td>Colon</td>
<td>20–40</td>
</tr>
<tr>
<td>Melanoma</td>
<td>15</td>
</tr>
<tr>
<td>Breast</td>
<td>10</td>
</tr>
<tr>
<td>Lung</td>
<td>1</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>1</td>
</tr>
<tr>
<td>Secondary (pancreas)</td>
<td></td>
</tr>
<tr>
<td>Kidney</td>
<td></td>
</tr>
<tr>
<td>Lung</td>
<td></td>
</tr>
</tbody>
</table>

---

(continued from page 24)

![Image](image-url)

**Figure 1.** Breast carcinoma metastatic to the duodenal wall resulting in biliary obstruction was diagnosed at ERCP. This patient survived over 4 years after endoscopic biliary drainage, radiation therapy, and chemotherapy.

(continued on page 32)
Obstructive Jaundice Secondary to Metastatic Cancer

A SPECIAL ARTICLE

(continued from page 27)

Figure 2. Squamous cell carcinoma of the cervix metastatic to the porta hepatitis. A) extrinsic compression of the biliary tree at the porta hepatitis. (B) endoscopic biliary drainage with a metallic stent. (C) histopathology of mass at porta hepatitis confirming metastatic cervical carcinoma.

have shown some prolongation of survival with external and intraluminal radiation therapy in comparison to biliary drainage alone (8). Hemoglobin and total serum bilirubin levels on admission have been shown to be independent risk factors predicting survival (7). Some authors therefore advocate reserving the use of metallic stents with radiation therapy for patients with a normal hemoglobin level and a lesser degree of jaundice.

COLON CANCER

Colorectal cancer is the second leading cause of cancer deaths in the United States. Over the past few years our understanding regarding the genetics of colorectal cancer has improved immeasurably. This has led to improvements in screening techniques as well as medical and surgical therapy. Despite these advances, the overall five year mortality from colorectal cancer remains around 40%.

The liver is the most common organ of distant metastases from colorectal cancer. Patients with hepatic metastases have a median survival of six to 12 months. Chemotherapy improves survival to 12 to 18 months (9). Surgical resection of isolated liver metastases can offer long term survival and potentially a cure in patients with disease limited to the liver. Repeat liver resection has been shown to be safe and effective in the management of recurrent disease.

Jaundice is a common late feature of advanced colon cancer and usually signifies extensive hepatic metastasis. In this setting the onset of jaundice carries a grave prognosis with a median survival of approximately one month (10). There exists, however, a small subgroup of

Figure 3A and 3B. N1 nodes and N2 nodes.

32 PRACTICAL GASTROENTEROLOGY • SEPTEMBER 2004
patients whose jaundice is due to extrahepatic biliary obstruction. Obstruction generally occurs from metastatic lymphadenopathy at the level of the common bile duct or higher in the porta hepatic compressing the common hepatic duct. These periporal nodal metastases can occur frequently without tumor in the liver. In this setting the prognosis is more favorable with a median survival of 23 months. Biliary bypass with gastrojejunostomy in patients with extrahepatic obstruction from metastatic colon cancer offers palliation of symptoms and prolongs life (3). This compares favorably to obstruction secondary to pancreatic and periampullary cancer in which the survival rates are three to five months and are not lengthened by biliary drainage procedures.

Studies have shown that colorectal cancer can spread along intact basement membranes of biliary epithelial cells (11). Metastatic colon cancer has the ability to replace normal biliary mucosa making its differentiation from primary cholangiocarcinoma challenging. The clinical and radiographic findings of these two entities can mimic one another. Distinction is made generally by careful histologic examination. The clinical manifestation of this process is slow generally occurring 45 months from the resection of the primary colonic carcinoma. Distinguishing metastatic colon cancer with intrabiliary growth from primary cholangiocarcinoma is important as it can have significant treatment implications. Intrabiliary extension of metastatic colon cancer into the hepatic ducts can be an unexpected obstacle for the surgeon and may prohibit curative resection.

**BREAST CANCER**

Invasive breast cancer is the most common malignancy in women and accounts for 15% of all cancer deaths. Improved screening has led to earlier detection with only 1%–5% of patients having metastatic disease at presentation. This coupled with improved treatment regimens have reduced overall breast cancer mortality. However, the rate of recurrence after initial therapy remains substantial. In patients treated for early stage disease, the recurrence rate is the highest within the first five years but can occur up to thirty years after the diagnosis. Although 15% to 40% of recurrences involve the chest wall and axillary or supraclavicular nodes, breast cancer can metastasize to any organ in the body.

Breast cancer is generally thought to be a systemic disease even at the time when initial treatment is started. Jaundice in patients with breast cancer is usually a result of metastatic disease replacing liver parenchyma. The onset of jaundice in this setting is an ominous sign with a mean survival of only one month (12). However, while liver metastases can be a cause of jaundice in a breast cancer patient, there exists a largely unrecognized group of patients whose jaundice is caused by obstruction of extrahepatic bile ducts by nodal metastases. The time interval between initial diagnosis and jaundice due to extrahepatic obstruction tends to be longer at a mean of 16 months (2). Obstruction of the biliary tree has been shown to occur anywhere between the porta hepatis and the duodenal wall (2,12,13,14). This fact is important because in these patients with normal liver function, relief of biliary obstruction using surgical bypass or biliary stenting extends survival to over a year (2,14). Furthermore, since breast cancer reduces with radiation, it is preferable in this situation to achieve immediate relief of jaundice by transhepatic intubation of the biliary tree followed by radiation to the portal nodes (13).

Patients with extra-hepatic metastatic obstruction from breast cancer are being recognized increasingly and should be treated vigorously, especially since patients without liver parenchymal involvement have a greater survival (median six months) than those with liver involvement (median 1.8 month) (2). The use of novel chemotheraphy, hormonal therapy and irradiation in conjunction with biliary decompression may lead to even more prolonged survival and requires further study.

**KIDNEY**

The appearance of metastases many years after nephrectomy is a well-known feature of renal cell carcinoma (RCC). Most recurrences appear two to three years after surgery, but late recurrences have been commonly reported. In a study by McNichols, et al, 11% of patients who survived 10 years or more after nephrectomy developed metastases(14). These clinical observations have led to the development of long-term surveillance protocols for patients who have undergone nephrectomy for RCC.

Renal cell carcinoma is the most common primary neoplasm to metastasize to the pancreas, accounting
Obstructive Jaundice Secondary to Metastatic Cancer

A SPECIAL ARTICLE

Table 2

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Interval between 1° dx and jaundice</th>
<th>Treatment</th>
<th>Survival with Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastric</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chu, et al</td>
<td>41</td>
<td>21.8 months</td>
<td>(38) Biliary drainage: (36) with PTC: (1) with operative t-tube: (1) with endoprosthesis</td>
<td>70 days</td>
</tr>
<tr>
<td>Colon</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Warshaw, et al</td>
<td>8</td>
<td>13 months</td>
<td>(8) Biliary drainage: (4) with surgical bypass: (1) with t-tube: (1) with PTC: (2) with XRT</td>
<td>18 months</td>
</tr>
<tr>
<td>Riepel, et al</td>
<td>8</td>
<td>45 months</td>
<td>(7) Surgical resection</td>
<td>—</td>
</tr>
<tr>
<td>Breast</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Popp, et al</td>
<td>7</td>
<td>40 months</td>
<td>(1) Surgical bypass alone: (1) Surg + chemotherapy: (1) Surg + radiation therapy: (1) PTC + radiation therapy: (3) Radiation therapy alone</td>
<td>17 months</td>
</tr>
<tr>
<td>Kopelson, et al</td>
<td>26</td>
<td>16 months</td>
<td>(6) Radiation therapy alone: (3) XRT + surgical bypass + chemo: (7) Chemo + surgical bypass</td>
<td>6 months</td>
</tr>
<tr>
<td>Kidney</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ghavamian, et al</td>
<td>11</td>
<td>9.7 years</td>
<td>Surgical resection</td>
<td>4.6 years</td>
</tr>
<tr>
<td>Hirota, et al</td>
<td>49</td>
<td>11 years</td>
<td>Surgical resection</td>
<td>13 months</td>
</tr>
<tr>
<td>Lung</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Johnson, et al</td>
<td>5</td>
<td>—</td>
<td>(5) Chemotherapy alone</td>
<td>&gt;12 months</td>
</tr>
</tbody>
</table>

This suggests that RCC has both a rapid and slow type of growth pattern. Growth is slow in most cases of RCC with late metastases, particularly those with pancreatic metastases. Chemotherapy, hormonal therapy, and radiotherapy have generally proved ineffective for primary renal cell carcinoma or metastatic deposits. Despite the early promising results of immunotherapy, a complete response occurs in less than 15%, emphasizing that this is a disease best treated with complete resection of the primary and metastatic lesions where possible. When metastatic disease is limited to the pancreas, surgical resection has improved the five-year survival rate to 29%–35% (19,20). These results are better than the survival rates for those

(continued on page 39)

for 2% to 3% of all pancreatic malignancies(16). Pancreatic metastasis of renal cell carcinoma is symptomatic in only 50% of cases. These patients present with jaundice generally due to compression of the intrapulmonary portion of the common bile duct by a metastatic lesion in the head of the pancreas. The mean interval between diagnosis of the primary RCC and discovery of pancreatic metastases has been shown to be 9.7 years (17) This long disease-free interval suggests a slow biological tumor growth pattern.

The mode of spread of renal cell carcinoma to the pancreas is unclear. The possible routes discussed in the literature include lymphogenous and hematogenous spread. Lymphogenous spread may occur by retrograde lymph flow secondary to infiltration of the retroperitoneal lymph nodes by the tumor. It also appears that there are some lymphatic routes from the head of the pancreas to the dorsal side of the renal artery (18). Hematogenous spread may occur via portacaval shunts.

Diagnosis is generally aided by the use of contrast-enhancing computed tomography. Due to their hypervascularity, metastatic RCC lesions appear well-defined and hyperattenuated relative to pancreatic tissue. This vascular appearance differs from primary pancreatic carcinoma which tend to be hypovascular lesions and therefore non-enhancing on CT. The most reliable method of diagnosis remains pancreatic biopsy, however it carries a higher risk of hemorrhage in RCC.

Survival of patients with metastatic RCC in general is usually poor with a five-year survival rate of 2.7% (19).
with primary pancreatic cancers. For these reasons, aggressive surgical management of pancreatic metastases due to renal cell carcinoma is warranted. Excision of all metastases evident on radiographs and during surgical exploration should be attempted while preserving as much function of the pancreas as possible.

**LUNG**

Lung cancer is currently the most common cause of cancer mortality in the United States and throughout the world. Small cell lung cancer (SCLC) represents 15% to 25% of all lung cancers and occurs almost exclusively in smokers. It is distinguished from non-small cell lung cancer by its rapid doubling time, high growth fraction, and the early development of metastases. Approximately 70 percent of patients present with overt metastatic disease at the time of diagnosis. Despite the relative chemosensitivity of SCLC, patients with extensive stage disease rarely enjoy prolonged relapse-free survival.

Patients with metastatic small-cell lung cancer can present with jaundice. Jaundice is usually due to diffuse hepatic parenchymal involvement, but can also be a result of extrahepatic biliary obstruction from a pancreatic metastasis. The former is associated with a poor prognosis with a mean survival of three months, while the latter has been shown to be chemosensitive offering rapid palliation and an improved survival of over a year (21). The use of novel combination chemotherapy and irradiation in conjunction with biliary decompression may lead to even more prolonged survival and requires further study.

**CONCLUSION**

Metastatic carcinoma is a recognized cause of malignant biliary obstruction. If obstructive jaundice occurs in the setting of a previous malignancy, one must strongly consider the cause as secondary to metastases. Biliary obstruction can be a result of a wide array of metastatic malignancies and can present at any level of the biliary tree. Interestingly, some groups of patients with metastatic biliary obstruction may have a survival advantage when compared to patients with primary malignant biliary obstruction. Although the approach to biliary drainage is largely the same, metastatic biliary obstruction should be identified because of the impact on subsequent medical and surgical therapies.

**References**