Secondary Tumors of the Ampulla of Vater: A Tale of Two Cases

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We report two cases of women with metastatic cancers to ampulla of Vater. The first was 91 years old and presented with severe anemia, due to upper gastrointestinal bleeding. She had history of renal cell cancer treated with nephrectomy 8 years ago and diagnosis confirmed to be metastasis of renal cell cancer to ampulla of Vater. The second patient was 54 years old with breast cancer, metastasis and developed obstructive jaundice; diagnosis confirmed to be breast metastasis in the ampulla of Vater. Secondary tumors of the ampulla of Vater due to breast cancer and renal cell cancer are rare findings and prognosis can be poor.

Abstract

Keywords
- ampulla of Vater
- breast cancer
- renal cell cancer

Introduction

The ampulla of Vater has unique anatomy and physiological function. For instance, its main function is regulation of bile flow into the duodenum and preventing its reflux back into the biliary and pancreatic ducts. Anatomically, it is situated in the second part of duodenum, closely related to last portion of the pancreatic duct and final portion of common bile duct. Therefore, ampulla of Vater is usually affected by cancer from pancreas, biliary system, and duodenum. Despite the fact that primary neoplasm of ampulla of Vater is rare, most common primary cancer is ampulla of Vater carcinoma (AVC), which usually occurs between the ages of 60 to 70 years. AVC is shown to be involved in 30% of pancreatico-duodenectomies and 20% of all tumors involved in obstruction of the common bile duct. The main types of AVC are pancreatobiliary and intestinal type. These subtypes have different pathogenic and clinical characteristics. Other rare primary cancers of ampulla of Vater include neuroendocrine, adenosquamous, and papillary types. The metastasis to ampulla of Vater is quite rare indeed and the clinical presentations can also be quite variable. In 2017, Sarocchi et al showed in their literature review of 32 cases published between 1989 and 2017 that the metastasis to ampulla of Vater though quite unusual, but if they do occur, then the primary cancer is usually from malignant melanoma, renal cell carcinoma, and breast cancer.

Case Presentation

Case 1
The first patient was a 91-year-old female and presented to the medical assessment unit with shortness of breath, tiredness, and loss of appetite. Eight years ago, she had right nephrectomy as part of treatment of renal cell cancer and was subsequently discharged from the Urology, as she was deemed to be in remission. Past medical history included hypertension, osteoarthritis, and hypothyroidism. There was no previous history of NSAIDs use or alcohol intake. She was found to have severe anemia with hemoglobin levels of 71 g/dL (normal reference range 120–130) (Table 1). She was treated with blood transfusion and other supportive
measures. Subsequent endoscopy showed presence of ulcerating lesion in the ampulla of Vater (►Fig. 1). Computed tomography scan (CT) showed the presence of mass in the ampulla of Vater (►Figs. 2), which was biopsied during endoscopy. Histological assessment of the biopsy specimens confirmed the presence of metastasis from renal cell cancer (►Fig. 3). Patient was discharged home after the endoscopic management. Unfortunately, few weeks later she was re-admitted with another episode of upper gastrointestinal bleeding and the decision was to undertake palliative care only this time. Due to her underlying comorbidities and frailty, endoscopic therapy or angioembolization was deemed unsuitable via interventional radiology. Consequently, only palliative care was instituted. She sadly passed away after a few days.

Case 2
The second patient was a 54-year-old female with known breast cancer and bone metastasis. Past medical history included Crohn’s disease, which was in remission on Pentasa maintenance therapy 2 g/d. She developed jaundice few weeks before the presentation and CT scan showed biliary dilation and axial view of CT scan showed large soft tissue in the ampulla of Vater (►Figs. 4, 5) (►Table 1). Subsequent endoscopic retrograde cholangiopancreatography (ERCP) showed large, obstructive lesion in ampulla of Vater (►Fig. 4). The histological examination of the biopsy specimen from the lesion taken during the endoscopy confirmed the presence of metastasis of breast cancer to ampulla of Vater (►Fig. 5). The bile duct could not be cannulated during ERCP and therefore she underwent PTC (percutaneous transhepatic cholangiography) and was successfully stented radiologically, causing dramatic resolution of her cholestasis. She was subsequently put on an alternative regime of chemotherapy by the oncologist for her breast cancer and is making satisfactory progress both clinically and radiologically, with significant regression of her primary disease. She is still doing well a year after diagnosis with the radiologically inserted stent in situ, and no recurrence of biliary obstruction. However, the prognosis remains guarded.

**Table 1** Showing hemoglobin level, liver functions, and plasma calcium for the two patients

<table>
<thead>
<tr>
<th></th>
<th>Case 1 (renal cell cancer)</th>
<th>Case 2 (breast cancer)</th>
<th>Normal reference range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb</td>
<td>63</td>
<td>109</td>
<td>110–150 g/dL</td>
</tr>
<tr>
<td>ALT</td>
<td>12</td>
<td>529</td>
<td>1–34 mmol/L</td>
</tr>
<tr>
<td>GGT</td>
<td>16</td>
<td>1,185</td>
<td>0–37 mmol/L</td>
</tr>
<tr>
<td>ALP</td>
<td>75</td>
<td>916</td>
<td>30–130 mmol/L</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>9</td>
<td>122</td>
<td>3–21 mmol/L</td>
</tr>
<tr>
<td>Plasma calcium</td>
<td>2.43</td>
<td>2.18</td>
<td>2.2–2.6 mmol/L</td>
</tr>
</tbody>
</table>

Abbreviations: ALP, alkaline phosphatase; ALT, alanine aminotransferase; GGT, gamma-glutamyl transferase; Hb, hemoglobin.

**Discussion**

The total number of renal cell cancer with metastasis to ampulla of Vater according to Sarocchi et al was 11. In seven
of these patients, upper gastrointestinal bleeding was the main presentation. This is similar to the clinical presentation in the first case. The average time from diagnosis of renal cell carcinoma till metastasis to ampulla of Vater is around 10 years.² This is also almost similar to our case report as metastasis to ampulla of Vater occurred 8 years after the diagnosis of renal cell carcinoma. Renal cell cancer is highly vascular and can therefore present with significant gastrointestinal bleeding and/or anemia.⁵,⁶ This also can make upper gastrointestinal endoscopy difficult as taking of biopsies may need special expertise to avoid fatal bleeding. It is worth mentioning, that renal cell carcinoma can also present with obstructive jaundice.⁷ Since the publication of Sarocchi et al in 2017, other four case reports were published.⁶,⁸,¹⁰ Therefore, the total case reports of renal cell carcinoma with metastasis to ampulla of Vater including our report will be 16 cases.
Breast cancer with metastasis to ampulla of Vater can present with upper gastrointestinal bleeding, jaundice, nausea, and vomiting. The presentation in the second case was with obstructive jaundice. The average time from diagnosis of breast cancer till metastasis to ampulla of Vater was around 3 years. In the second case, the metastasis to ampulla of Vater was found 3 years from the diagnosis of breast cancer.

BRCA1 and BRCA2 mutations are established markers for hereditary breast and ovarian cancer, and it can also be associated with increased risk of other rare cancers like cancer of pancreas. Importantly, Pinto et al identified high frequency of germline BRCA2 mutations in metastatic ampullary cancers as well. This may raise the potential in future of using molecular biology techniques in combination with imaging alone to diagnose these cases, without resorting to performing hazardous endoscopies, or where taking of biopsy can result in fatal complications or is inappropriate. The possible learning points from these two cases are: (1) Metastasis to ampulla of Vater is very rare. More common neoplastic involvement of papilla is extension from pancreatic or biliary tumors; (2) Common cancers with metastasis to ampulla of Vater are malignant melanoma, renal cell cancer, and breast cancer; (3) Common presentations include obstructive jaundice or upper gastrointestinal bleeding. Taking biopsies from renal cell cancer can be quite hazardous as it is highly vascular; (4) Germline BRCA2 mutations can be found in metastatic ampullary cancers from breast cancer as well.

Authors' Contribution
J.A., A.K., M.H.A., and R.M. wrote the manuscript. All authors edited the manuscript and approved the final version. M.H.A. is the article guarantor.

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Informed Consent
Informed and written consent was obtained for both cases reported in this manuscript.

Conflict of Interest
None declared.

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