Metachronous Bilateral Pulmonary Metastases from Cancer of the Ampulla Duodeni

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We present a 76-year-old man who underwent two lung resections for metastases originating from cancer of the Ampulla duodeni, 9 years-after pancreaticoduodenectomy (PD) with lymphadenectomy. PD was performed in 2002; histological examination of the original tumor revealed a stage III tubular adenocarcinoma (pT3, N0, M0). Repetitive lung resection was performed in 2007 (left S8) and 2011 (right S1 and extirpation of a pericardial cyst). Although rarely performed, resection of bilateral pulmonary metastases from carcinoma of the papilla of Vater was done to improve the patient’s chances for long-term survival.

Keywords: cancer of the ampulla duodeni, papilla of Vater carcinoma, pulmonary metastases, pericardial cyst

Introduction

Cancer of the Ampulla duodeni is a rare malignancy of the gastrointestinal tract, and its 5-year survival rate has been reported to be between 40% and 60%.1,2 Local recurrence and hepatic metastases are two major causes of treatment failure, although cases in which carcinoma of the papilla of Vater metastasizes to different organs, including the lung, are not rare. However, reports on the surgical resection of pulmonary metastases from cancer of the Ampulla duodeni are very rare. Herein we describe a patient who underwent metachronous bilateral lung resection for metastases from carcinoma of the Ampulla duodeni after PD.

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Case Report

A 67-year-old man underwent PD for cancer of the Ampulla duodeni with obstructive jaundice in December 2002 (Fig. 1A). He had no history of drinking or smoking and his past medical and family histories were unremarkable. Histological examination revealed a well-to-moderately differentiated adenocarcinoma, which was classified as pT3N1M0, stage III (Fig. 1B). Blood chemistry data were unremarkable; the expected perioperative icterus and tumor markers: carcinoembryonic antigen, squamous cell carcinoma-related antigen and carbohydrate antigen19-9 were all within normal limits.

The patient was asymptomatic, but during follow-up in December 2006, abdominal computed tomography (CT) revealed a 12-mm nodular shadow in left lung segment 8 (S8). Chest X-ray and CT showed a tumor in the left S8 of the lung as well as a homogenous mediastinal nodule in the right side of the mediastinum (Fig. 1C and 1D). The mediastinal tumor, which had a very low CT value of 17 Hounsfield Units and was not enhanced, was diagnosed as a pericardial cyst and examined further (Fig. 2A). Because neither local recurrence nor liver metastases were detected, the patient underwent a left thoracoscopic partial resection of the left S8 of the lung,
in January 2007. Histopathologic findings of the resected tumor revealed adenocarcinoma with tubular projection and metastases from carcinoma of the papilla of Vater. The patient underwent six cycles of systemic chemotherapy with 1200 mg gemcitabine (GEM) and 120 mg oral tegafur, gimeracil and oteracil potassium (S-1) daily for 2 years. After pulmonary resection, we provided follow-up care at our out-patient clinic. Chest CT revealed a 4-mm nodular shadow in the right S1 of the lung, in November 2010. In May 2011, the tumor was further enlarged, and the chest CT showed a well-defined, 6-mm tumor in the right S1 of the lung, but the mediastinal tumor had not changed (Fig. 2B). The patient refused confirmatory bronchoscopy. Initially, we considered that the lung tumor was either primary or metastatic lung cancer. Even if there were pulmonary metastases from cancer of the Ampulla duodeni, we considered surgery because, during a follow-up period of 4 years, there was no evidence of recurrence at an extrapulmonary site, such as the primary site or the liver. Thoracoscopic partial resection with finger palpitation from the access port and extirpation of the mediastinal tumor were then performed. Histologically, the tumor, consisting of eosinophilic tall columnar cells proliferated, forming tubular structures (Fig. 2C). In addition, the lung tumor and cancer of the Ampulla duodeni both showed similar immunostaining properties: cytokeratin (CK) 7-negative, TTF-1-negative/CEA-positive, and CK 20-positive (Fig. 2D). These findings led to the pathological diagnosis of pulmonary metastases from cancer of the Ampulla duodeni. Macroscopically the mediastinal tumor was a cystic lesion containing clear fluid. Histologically, a single layer of flat cells lined the thin-walled cyst, resulting in the pathological diagnosis of pericardial cyst. Although postoperative chemotherapy was recommended and administered to lower the risk of recurrence, the patient chose oral 120 mg S-1 per day for 1 year. Ten years after the PD, the patient remained free of recurrence.

Fig. 1 (A) Macroscopic findings of carcinoma of the Ampulla duodeni. (B) Histological findings of tubular adenocarcinoma of cancer of Ampulla duodeni (hematoxylin and eosin staining). (C) After the first lung resection, the chest X-ray showed a well-defined tumor in the left lower lung field. (D) Chest CT revealed a tumor in the left lung.
Cancer of the Ampulla duodeni is a rare malignancy (0.2%) of the gastrointestinal tract, and its 5-year survival rate after curative resection has been reported to range between 40% and 60%. PD is the preferred surgical approach, as cancer of the Ampulla duodeni is amenable to resection. Its operative mortality rate is 5% satisfactory cardiopulmonary function and clean surgical margins. Local recurrence and hepatic metastasis are two major causes of treatment failure. On multivariate analysis, 5-floururacil (5-FU)-based adjuvant chemoradiation has been significantly associated with improved overall survival when adjusted for age, gender, institution, T-stage, tumor size, node status, and grade. Additionally, lymph node involvement is the only other variable associated with overall survival on multivariate analysis, with node-positive patients experiencing a significantly increased risk of death.

The cancer of the Ampulla duodeni is categorized by its histological differentiation (i.e., intestinal versus pancreatobiliary), with the pancreatobiliary type being more frequent. Several gastrointestinal markers, such as CKs, apomucins (MUC), and proteins, have been shown to differentiate subtypes of cancer of the Ampulla duodeni. Intestinal types generally express CK20, and pancreatobiliary tumors usually stain positive for MUC1, and MUC5a and CK7. Furthermore, cancer of the Ampulla duodeni with intestinal differentiation typically contains microsatellite instabilities similar to those of colon cancer. In addition, intestinal differentiation predicts significantly better overall survival than does pancreatobiliary differentiation, appearing to be one of the strongest prognostic parameters for cancer of the Ampulla duodeni. Since our case showed an intestinal subtype histologically, as evidenced by positive CK20 and 7 staining, a good course was expected.

Overall, the liver is the most common site of metastases, found in 24.7% of all patients. Liver metastases are often numerous and associated with a poor prognosis.
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The peritoneum is the second most common site of metastases, present in 5.9% of all patients. Lung metastases are found in 4.8% of all patients, making it the third most common site of metastatic spread.

Concerning lung metastases, there have been few cases in which pulmonary resections for metastases from cancer of Ampulla duodeni have been summarized (Table 1).4-8) For metastatic colorectal carcinoma, a complete resection can offer the only chance of cure. Long-term survival can be expected after complete resection of pulmonary metastases arising from colorectal cancer, especially in patients with solitary metastasis.

In unresectable local or metastatic cancer, chemotherapy can be applied, although the lack of large randomized controlled trials prevents the choice of any particular treatment as a standard.9) 5-FU and mitomycin (MMC), GEM-Capecitabine (CAP), and GEM-oxaliplatin (Oxa) are the most commonly used medicines to treat cancer of the Ampulla duodeni, but the best combination and protocol remain to be identified. In Japan, a combination of uracil and ftorafur (UFT) or S-1 has been commonly used. Even with such treatments, metastatic/advanced cancer of the Ampulla duodeni has a poor prognosis, with an overall survival rate of 2 years, ranging from 5% to 10%.

Conclusion

We describe a surgical case of pulmonary metastases from carcinoma of the Ampulla duodeni. At least empirically, surgery is the treatment of choice to improve rates of long-term survival in such patients.

Disclosure Statement

None of the authors have a vested commercial affiliation that could be construed as a conflict of interest with regards to this data or manuscript, nor did the study utilize external grants or funds for its conduction.

References


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Table 1 Cases of lung resection due to cancer of the Ampulla duodeni metastases

<table>
<thead>
<tr>
<th>Author</th>
<th>Age</th>
<th>Sex</th>
<th>Liver meta.</th>
<th>Lung site</th>
<th>Lung surgery</th>
<th>Adjuvant chemo Tx.</th>
<th>Post lung surg. chemo Tx.</th>
<th>Death/Alive After PD</th>
<th>CK20 Intestinal</th>
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<tbody>
<tr>
<td>Nakayama</td>
<td>69</td>
<td>F</td>
<td>+</td>
<td>rS5</td>
<td>r middle L</td>
<td>UFT</td>
<td>None</td>
<td>A, 3 yr</td>
<td>N.D.</td>
</tr>
<tr>
<td>Moriya</td>
<td>60</td>
<td>F</td>
<td>+</td>
<td>rS1 IS2,3</td>
<td>Partial</td>
<td>5-Fu MMC</td>
<td>None</td>
<td>D, 12 yr</td>
<td>N.D.</td>
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<tr>
<td>Nakajima</td>
<td>70s</td>
<td>F</td>
<td>–</td>
<td>rS2</td>
<td>r upper L</td>
<td>UFT</td>
<td>S-1</td>
<td>A, 4 yr 4 m</td>
<td>–</td>
</tr>
<tr>
<td>Goto</td>
<td>51</td>
<td>M</td>
<td>–</td>
<td>rS8</td>
<td>r lower L</td>
<td>None</td>
<td>None</td>
<td>A, 4 yr 9 m</td>
<td>+</td>
</tr>
<tr>
<td>Giakoustidis</td>
<td>53</td>
<td>F</td>
<td>–</td>
<td>l upper</td>
<td>Partial→l Pn</td>
<td>GEM/Oxa</td>
<td>GEM/Cap</td>
<td>A, 7 yr</td>
<td>+</td>
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<tr>
<td>Our</td>
<td>71</td>
<td>M</td>
<td>–</td>
<td>lS8</td>
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<td>GEM→S-1</td>
<td>A, 10 yr</td>
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PD: pancreaticoduodenectomy; CK: cytokeratin; r: right; l: left; L: lobectomy; UFT: ftorafur; N.D.: not discuss; 5-Fu: 5-flurouracil; MMC: mitomycin; Pn: pneumonectomy; GEM: gemcitabine; Oxa: oxaliplatin; Cap: capecitabine