Abstract. Hepatoid adenocarcinoma of the stomach (HAS) is a rare type of gastric cancer with an extremely poor prognosis. The current study reports a rare case of HAS, characterized by gastric cancer and infiltration of cancer cells into the left liver lobe, as well as lymphadenectasis. The expression of α-fetoprotein (AFP) was markedly increased in the tumor cells of the liver neoplasms. A gastric biopsy indicated highly, moderately and poorly differentiated papillary adenocarcinoma. The patient underwent two cycles of chemotherapy with oxaliplatin (130 mg; day 1) and capecitabine (2 mg, twice daily; days 1-14). At 7 weeks after the chemotherapy, an expanded gastrectomy and radical resection of left lung lobe were performed on the operable lesion. AFP expression was significantly decreased following the procedure. A literature review was also conducted by searching PubMed/Medline, indicating that surgery and chemotherapy may positively affect the outcomes of HAS patients.

Introduction

Hepatoid adenocarcinoma is an extrahepatic tumor with an incidence of 0.38-0.73% (1). The occurrence of this malignancy has been described in several organs, including the lungs, gallbladder, esophagus, uterus and stomach (2). Hepatoid adenocarcinoma of stomach (HAS) refers to a rare type of gastric carcinoma characterized by a distinct morphology and elevated α-fetoprotein (AFP) levels (3). The diagnosis of HAS is largely depend on the pathological analysis. In 1981, Kodama et al (4) initially described two histologic types of AFP-producing gastric carcinoma with medullary or papillotubular arrangements. Subsequently, Ishikura et al (5) proposed the term ‘hepatoid adenocarcinoma of the stomach’ for primary gastric carcinomas characterized by hepatoid differentiation and the production of large amounts of AFP. At present, the prognosis of HAS is rather poor and according to a literature search of PubMed/Medline between January 2001 and December 2013, only a few cases of this disease have been reported (Table I) (6-8). The current study reports a case of HAS, and summarizes the treatment and outcome for the disease.

Case report

A 70-year-old male patient presented to Shaoxing People's Hospital (Shaoxing, China) due to muscle weakness and palpitations lasting for 2 months. No abnormalities were noted during the physical examination. During laboratory tests, fecal occult blood was noted, and the patient's AFP level was 14,399.9 ng/ml (normal range, 0-13.4 ng/ml). Ultrasound examination indicated an occupying lesion in right upper quadrant. Computed tomography imaging was performed, revealing gastric cancer and infiltration of cancer cells into the left lobe of the liver, as well as lymphadenectomy of the group 1 and 3 nodes (Fig. 1A). Gastroscopy and pathological tests revealed irregular bulges in the gastric antrum and oedema in the peripheral mucous membrane. In addition, highly-differentiated adenocarcinoma cells were observed. On this basis, the patient was diagnosed with adenocarcinoma of the gastric antrum (Figs. 1B and 2A). The diagnosis of HAS was primarily based on the presence of the following aspects: papillary adenocarcinoma of high, moderate or low grade; mucinous adenocarcinoma; undifferentiated carcinoma and poorly differentiated hepatocellular carcinoma combined with presence of hyaline bodies; poorly differentiated hepatocellular carcinoma and hyaline body-like structures in the liver cancer specimen. Two cycles of chemotherapy with oxaliplatin (130 mg; day 1) and capecitabine (2 mg, twice daily; days 1-14) were administered.

At 7 weeks after chemotherapy, resection of the stomach and external lobe of the left liver were conducted, during which a tumor mass measuring ~2.0x1.5x1.0 cm was observed in gastric corpus. Meanwhile, a gastric biopsy revealed an ulcerating tumor (4.0x3.0x1.5 cm) from the gastric angle to the gastric antrum, and infiltration of cancer cells into left liver (4.0x3.0x3.0 cm). No postoperative complications were
Biopsy of liver indicated adenoid carcinoma with no infiltration of cancer cells in the incisal margins, and no lymph node metastasis (Fig. 2B and C). The immunohistochemistry results were AFP(+), cytokeratin (CK) 19(+), CK7(-) and CK20(-). Biopsy of gastric samples indicated adenocarcinoma (Fig. 2D); the immunohistochemistry results were AFP(-), c-erbB-2(+), E-cadherin(+), epidermal growth factor receptor(+), Ki-67 (+65%), CK7(+) and CK20(+). AFP levels were measured on postsurgical days 9 and 30 at 116.7 and 17.3 ng/ml, respectively. Subsequently, chemotherapy was performed 3 weeks after the after surgery. The chemotherapy regimen, was 130 mg oxaliplatin on day 1 plus 2 mg capecitabine, twice daily, on days 1-14, for two cycles. The patient survived during 7 months of follow-up, at which point the AFP levels were 10.4 ng/ml.

Discussion

For patients with HAS, the initial symptoms are usually upper abdominal pain (9); more rarely, individuals may also exhibit melena. On pathological evaluation, elevated AFP is commonly noted in these patients. In such cases, the AFP is reported. Biopsy of liver indicated adenoid carcinoma with no infiltration of cancer cells in the incisal margins, and no lymph node metastasis (Fig. 2B and C). The immunohistochemistry results were AFP(+), cytokeratin (CK) 19(+), CK7(-) and CK20(-). Biopsy of gastric samples indicated adenocarcinoma (Fig. 2D); the immunohistochemistry results were AFP(-), c-erbB-2(+), E-cadherin(+), epidermal growth factor receptor(+), Ki-67 (+65%), CK7(+) and CK20(+). AFP levels were measured on postsurgical days 9 and 30 at 116.7 and 17.3 ng/ml, respectively. Subsequently, chemotherapy was performed 3 weeks after the after surgery. The chemotherapy regimen, was 130 mg oxaliplatin on day 1 plus 2 mg capecitabine, twice daily, on days 1-14, for two cycles. The patient survived during 7 months of follow-up, at which point the AFP levels were 10.4 ng/ml.

Discussion

For patients with HAS, the initial symptoms are usually upper abdominal pain (9); more rarely, individuals may also exhibit melena. On pathological evaluation, elevated AFP is commonly noted in these patients. In such cases, the AFP is
typically significantly reduced compared with the baseline levels following surgery and chemotherapy.

The diagnosis of HAS is largely dependent upon hematoxylin and eosin (H&E) staining and immunohistochemical staining. When stained with H&E, HAS typically exhibits similar features to hepatocellular carcinoma. In addition, proliferation of polygonal tumor cells is observed in trabecular and intestinal-like structures. For the differential diagnosis, immunohistochemical staining is required. In the current case, AFP expression was confirmed using immunohistochemical staining, as shown in Fig. 2E.

All articles cited in the Medline/Pubmed database between January 2001 and December 2013 were searched using the terms ‘hepatoid adenocarcinomas of stomach’, ‘AFP-producing tumor’ and ‘AFP-producing gastric cancer’. AFP expression was also used as a marker for the subsequent treatment. In the present study, AFP expression levels were stable during the 7-month follow-up.

In summary, HAS is a rare type of carcinoma with poor prognosis. The current study presented a case of HAS occurring in a 70-year-old male, and summarized the treatment outcomes of the chemotherapy and/or gastrectomy in previous studies of this disease. The present results indicated surgery and chemotherapy may positively affect the outcome of similar patients. As the number of cases is still limited, further randomized controlled trials are necessary to confirm the efficacy of this treatment for HAS.

**References**


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**Table I. Literature review from January 2001 to December 2013**

<table>
<thead>
<tr>
<th>Author (reference no.)</th>
<th>Gender</th>
<th>Age (years)</th>
<th>AFP</th>
<th>Treatment</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gálvez-Muñoz et al (7)</td>
<td>Male</td>
<td>75</td>
<td>Positive</td>
<td>Palliative total gastrectomy; palliative chemotherapy with cisplatin and capecitabine (6 cycles)</td>
<td>Alive at 8 months post surgery</td>
</tr>
<tr>
<td>Ahn et al (6)</td>
<td>Male</td>
<td>68</td>
<td>Positive</td>
<td>Billroth II subtotal gastrectomy; palliative chemotherapy with cisplatin and capecitabine; second-line palliative chemotherapy with fluororacil, leucovorin and irinotecan</td>
<td>Alive during 21 months of follow-up</td>
</tr>
<tr>
<td>Ye et al (8)</td>
<td>Male</td>
<td>58</td>
<td>Positive</td>
<td>Distal gastrectomy; epirubicin, oxaliplatin and fluorouracil (6 cycles)</td>
<td>Alive at 20 months post surgery</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>54</td>
<td>Positive</td>
<td>Total gastrectomy with lymph node dissection; oxaliplatin plus fluorouracil adjuvant chemotherapy (6 cycles); paclitaxel and capecitabine (2 cycles)</td>
<td>Deceased at 18 months post surgery</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>61</td>
<td>Positive</td>
<td>Chemotherapy with oxaliplatin plus S-1</td>
<td>Deceased at 8 months after treatment</td>
</tr>
<tr>
<td>Present study</td>
<td>Male</td>
<td>70</td>
<td>Positive</td>
<td>Expanded gastrectomy and radical resection of left lung lobe; chemotherapy using oxaliplatin and capecitabine</td>
<td>Alive during 7 months of follow-up</td>
</tr>
</tbody>
</table>

*Search of Pubmed/Medline for English language articles using terms ‘hepatoid adenocarcinomas of stomach’, ‘AFP-producing tumor’ and ‘AFP-producing gastric cancer’. AFP, α-fetoprotein.*


