Metastatic hepatoid adenocarcinoma of the stomach: a case report and review of the literature


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Abstract

Hepatoid adenocarcinoma (HAC) is defined as an extrahepatic tumor with hepatocyte differentiation. Hepatoid adenocarcinoma of the stomach (HAS) is a rare type of gastric cancer characterized by unique clinico-pathological features and a poor prognosis. We report a case of a metastatic HAS with a review of the literature.

Critical words

Hepatoid Adenocarcinoma; Gastric Cancer; Chemotherapy

Background

Hepatoid adenocarcinoma (HAC) is defined as an extrahepatic tumor with hepatocyte differentiation and may be associated with high plasmatic levels of alpha-feto-protein (AFP). Histology confirms the diagnosis [1].

Hepatoid adenocarcinoma of the stomach (HAS) is a rare type of gastric cancer characterized by unique clinico-pathological features and a poor prognosis. Stomach and esophagus are the most frequent sites but other localizations may be seen such as ovary, uterus, and lungs [2]. In 1970, Bourreille et al. provided the first description of an AFP-producing gastric tumor [3].

Ishikura et al. introduced in 1985 the term of the HAC when reporting seven cases of gastric adenocarcinoma with high serum levels of AFP [1].

Regarding the scarcity of this disease, literature is mostly based on case reports or small case series. Thus, both diagnosis and treatment of this entity remain challenging especially for metastatic HAS.

We report a case of a metastatic HAS with a review of the literature.

Case report

We present the case of a 32-year-old woman, who complained of abdominal pain. Physical examination found an epigastric hard and painful mass. Abdominal ultrasound revealed many hepatic masses evoking hemangiomas.

Abdominal magnetic resonance imaging showed an
enlarged liver with many masses and nodules measuring from 1 to 13 cm consistent with metastases. Gastric endoscopy showed ulcerative antral lesions. A biopsy was performed. The pathological examination concluded to an undifferentiated adenocarcinoma.

However, serum AFP was very high 1500 (normal level <40) leading us to perform a liver biopsy. CEA was under limit of normal. Pathologic examination and revision of the gastric sample showed typical hepatocyte cells. Immunohistochemistry study was negative to CK7, CK20, Chromogranin, and Synaptophysin. It finally concluded to a metastatic HAS.

The patient underwent chemotherapy. She received six cycles of XELOX (Capecitabine and Oxaliplatin) with a complete clinical and biological response and radiological partial response estimated to 45% according to RECIST 1.1 criteria. We opted to maintenance chemotherapy using six cycles of Capecitabine with clinical, biological and radiological stable disease. The systemic treatment was well tolerated. Twenty months after the diagnosis, the patient died of the disease.

**Discussion**

HAC is defined as an extrahepatic tumor with hepatocyte differentiation with potentially high levels

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**Table-1: Reported cases of metastatic HAS**

<table>
<thead>
<tr>
<th>Case</th>
<th>Author/year</th>
<th>Nationality</th>
<th>Age/Sex</th>
<th>Metastases</th>
<th>AFP/CEA</th>
<th>Gastric surgery</th>
<th>Chemotherapy</th>
<th>Response</th>
<th>OS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Shima da/2002</td>
<td>Japanese</td>
<td>71/F</td>
<td>Liver</td>
<td>5190/NA</td>
<td>No</td>
<td>Cisplatin/Paclitaxel</td>
<td>Complete response</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>Shima da/2002</td>
<td>Japanese</td>
<td>63/M</td>
<td>Liver</td>
<td>156/NA</td>
<td>No</td>
<td>Weekly paclitaxel</td>
<td>Complete response</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>Chiba/2005</td>
<td>Japanese</td>
<td>47/M</td>
<td>Liver</td>
<td>606.8/ULN</td>
<td>Yes</td>
<td>5FU/Cisplatin/Etoposide</td>
<td>Partial response</td>
<td>14 months</td>
</tr>
<tr>
<td>4</td>
<td>Takayama/2007</td>
<td>Japanese</td>
<td>64/M</td>
<td>Liver</td>
<td>1497.8/727</td>
<td>No</td>
<td>Doxorubicin/Mytomycin/5FU</td>
<td>stable</td>
<td>9 months</td>
</tr>
<tr>
<td>5</td>
<td>Takahashi/2009</td>
<td>Japanese</td>
<td>51/M</td>
<td>Liver</td>
<td>91/N/A</td>
<td>No</td>
<td>Cisplatin/Capecitabine</td>
<td>Complete response</td>
<td>7 years</td>
</tr>
<tr>
<td>6</td>
<td>Lin/2009</td>
<td>Chinese</td>
<td>56/F</td>
<td>Liver</td>
<td>9457/NA</td>
<td>Yes</td>
<td>FOLFIRI/Bevacizumab</td>
<td>stable</td>
<td>20 months</td>
</tr>
<tr>
<td>7</td>
<td>Galvez-Mulnoz/2009</td>
<td>European</td>
<td>75/M</td>
<td>Liver/Nodes</td>
<td>4500/460</td>
<td>Yes</td>
<td>Sorafenib</td>
<td>Progression</td>
<td>8 months</td>
</tr>
<tr>
<td>8</td>
<td>Ye/2013</td>
<td>Chinese</td>
<td>54/M</td>
<td>Lung</td>
<td>99/ULN</td>
<td>Yes</td>
<td>Cisplatin/Capecitabine</td>
<td>Complete response</td>
<td>20 months</td>
</tr>
<tr>
<td>9</td>
<td>Ye/2013</td>
<td>Chinese</td>
<td>61/F</td>
<td>Spleen</td>
<td>&gt;500/00/ULN</td>
<td>No</td>
<td>Gemcitabine</td>
<td>Progression</td>
<td>18 months</td>
</tr>
<tr>
<td>10</td>
<td>Ahn/2013</td>
<td>Korean</td>
<td>68/M</td>
<td>Liver</td>
<td>NA/N/A</td>
<td>Yes</td>
<td>Cisplatin S-1</td>
<td>Complete response</td>
<td>9 years</td>
</tr>
<tr>
<td>11</td>
<td>Nagai/2014</td>
<td>Japanese</td>
<td>62/M</td>
<td>Liver</td>
<td>NA/N/A</td>
<td>Yes</td>
<td>Paclitaxel/Carboplatin/Sorafenib</td>
<td>Partial response</td>
<td>2 years</td>
</tr>
</tbody>
</table>

of alpha-feto-protein (AFP) [4]. Pathological examination confirms the diagnosis when it founds typical hepatocyte cells and detects by immunohistochemical study an overexpression of AFP [4].

HAS is a rare subtype of gastric tumors characterized by hepatoid differentiation and high serum levels of AFP [3]. The pathogenesis is still unclear. It may be due to a cellular transdifferentiation from glandular to hepatoid type [4].

The implication of H. Pylori infection in this subtype is not established. Patients are usually adults, aged from 44 to 87 years. There is a male predominance with a sex ratio about 2:3. Most frequent symptoms are unspecific including epigastric pain and asthenia [5].

To our knowledge, only fourteen cases of metastatic hepatoid gastric carcinoma were described in the literature including our patient. The table below (Table-1) summarizes information on these cases [6-14].

<table>
<thead>
<tr>
<th>Case No</th>
<th>Author</th>
<th>Country</th>
<th>Age</th>
<th>Gender</th>
<th>Tumor Site</th>
<th>AFP</th>
<th>Treatment</th>
<th>Outcome</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>Simmet/2017</td>
<td>European</td>
<td>64</td>
<td>M</td>
<td>Liver</td>
<td>2600/ULN</td>
<td>No</td>
<td>Complete response</td>
<td>9 years</td>
</tr>
<tr>
<td>13</td>
<td>Simmet/2017</td>
<td>European</td>
<td>60</td>
<td>F</td>
<td>Liver</td>
<td>6700/0/176</td>
<td>No</td>
<td>Progression</td>
<td>23 months</td>
</tr>
<tr>
<td>14</td>
<td>Mokrani/2018</td>
<td>Tunisian</td>
<td>33</td>
<td>F</td>
<td>Liver</td>
<td>1500/ULN</td>
<td>No</td>
<td>Partial response</td>
<td>20 months</td>
</tr>
</tbody>
</table>

Most frequent sites of metastases are nodes and the liver. In our case, the patient presented with voluminous hepatic metastases and a high serum level of AFP.

Curative surgery when early detection is possible may be associated with healing. Treatment of localized tumors consists of radical surgery when feasible followed by adjuvant chemotherapy including 5FU, leucovorin, Cisplatin and Epirubicin [5].

EGFR, KRAS, and BRAF mutations were frequently reported as well as overexpression of HER, which implies the possible use of targeted therapies in the metastatic setting [15].

In our case, those mutations have not been assessed. Compared to gastric carcinomas with no hepatoid differentiation, the prognosis is worse with a global 5-year-survival rate of 9% [5].

Conclusion
HAS is a rare and aggressive subtype of gastric tumors characterized by a hepatoid differentiation and potentially increased AFP serum levels. Management of metastatic disease is controversial. We reported the case a metastatic HAS treated by XELOX.

Additional systemic treatments are yet to be explored to overcome the poor global prognosis. In this context, targeted therapies represent an interesting alternative especially due to the many molecular mutations.

References


