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Case Report

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.

Keys 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

Table-1: Reported cases of metastatic HAS

Case	Author /year	Nationality	Age /Sex	Metastases	AFP/ CEA	Gastric surgery	Chemotherapy	Response	OS
1	Shimada/2002	Japanese	71/F	Liver	5190/ NA	No	Cisplatin/Paclitaxel	Complete response	-
2	Shimada/2002	Japanese	63/ M	Liver	156/ NA	No	Weekly paclitaxel	Complete response	-
3	Chiba/ 2005	Japanese	47/ M	Liver	606.8 /ULN	Yes	5FU/Cisplatin/Etoposide	Partial response	14 months
4	Takayema/2007	Japanese	64/ M	Liver	1497. 8/727	No	Doxorubicin/Mytomicin/5FU	stable	9 months
5	Takahashi/2009	Japanese	51/ M	Liver	91/NA	No	Cisplatin/Capecitabine	Complete response	7 years
6	Lin/2009	Chinese	56/F	Liver	9457/ NA	Yes	FOLFIRI/Bevacizumab	stable	20 months
7	Galvez-Mulnoz/2009	European	75/ M	Liver/Nodes	4500/ 460	Yes	Sorafenib	Progression	8 months
8	Ye/2013	Chinese	54/ M	Lung	99/ULN	Yes	Cisplatin/Capecitabine	Complete response	20 months
9	Ye/2013	Chinese	61/F	Spleen	>50000/ULN	No	Gemcitabine	Progression	18 months
10	Ahn/2013	Korean	68/ M	Liver	NA/NA	Yes	Cisplatin S-1	Complete response	9 years
11	Nagai/ 2014	Japanese	62/ M	Liver	NA/NA	Yes	Pacltaxel/Carboplatin/Sorafenib	Partial response	2 years

12	Simmet/ 2017	European	64/ M	Liver	2600/ ULN	No	Cisplatin/Etoposide	Complete response	9 years
13	Simmet/ 2017	European	60/F	Liver	6700 0/176	No	Cisplatin/Etoposide	Progression	23 months
14	Mokrani /2018	Tunisian	33/F	Liver	1500/ ULN	No	Capecitabine/Oxaliplatin Maintenance by Capecitabine	Partial response	20 months

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 trans-differentiation 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].

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.

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