Hepatoid Adenocarcinoma Of The Stomach – A Rare Pathological Entity

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Abstract
Hepatoid adenocarcinoma is a rare cancer with an extremely poor prognosis. Here, we describe two cases referred to our hospital with suspected gastric cancer. Gastrointestinal endoscopy revealed lesions in the stomach. Biopsy from the lesions was reported as adenocarcinoma. Both the patients underwent exploratory laparotomy. One was an operable lesion and the other was an inoperable lesion. Total gastrectomy was done in the operable lesion and feeding jejunostomy was done in the inoperable case. Histologically, both turned out to be hepatoid adenocarcinomas. Retrospective analysis showed the serum levels of alphafetoprotein (AFP) are markedly elevated in both cases. We describe this rare entity of hepatoid adenocarcinoma of the stomach, and review the literature concerning the clinicopathological aspects of the cases.

Keywords
Gastric cancer, Hepatoid adenocarcinoma, Alpha Feto Protein, Stomach

Introduction
Alfa Feto Protein (AFP) producing tumors have been reported in several different organs. Gastric hepatoid adenocarcinomas are the most common of these tumors.(1) The first report of AFP producing gastric carcinoma was by Bourreille et al.(2). The incidence is reported to be 1.3%–15% of all gastric carcinomas (3-7). It was Ishikura et al.(8,9) who proposed the term “hepatoid adenocarcinoma of the stomach” for primary gastric carcinomas that are characterized by both hepatoid differentiation and the production of large amounts of AFP. In this report, we describe two cases of hepatoid adenocarcinomas of the stomach, with a review of the literature.

Case I
A 76 year old female patient was evaluated for upper abdominal pain of one month duration and generalized weakness and malena of 2 weeks duration. Clinical evaluation revealed pallor and a lump in the upper abdomen of size 20x20 cm in left hypochondrium. Upper gastrointestinal endoscopy revealed an ulcerative growth in the body of the stomach along the lesser curvature. Biopsy from the lesion showed the lesion to be moderate to poorly differentiated adenocarcinoma. CT scan of the abdomen showed a 14x13.5 cm lesion arising from the lesser curvature of the stomach and abutting the tail of pancreas with enlarged perigastric and para aortic nodes (Figure 1). There was an associated left ovarian tumor of size 8x5 cm. Exact site of origin of the mass lesion was doubtful. The radiological features were suggestive of a Gastrointestinal Stromal Tumor.
tumour. Liver was normal in size and texture and there was no ascites. At laparotomy the liver was normal and there was no ascites. There was a 25x30 cm mass arising from lesser curvature of the stomach which was well encapsulated. It was exophytic in nature and it was in contact with transverse mesocolon and the pancreas was stretched out over the tumour. There was a left ovarian mass of size 10x5 cm limited to ovary alone. A total gastrectomy (Figure 2) and left oophorectomy was done. Post operative period was uneventful.

Pathology

The histopathological evaluation of both the lesion showed hepatoid differentiation. Section from the neoplasm showed cells arranged in tubular pattern and in sheets. Individual cells were large with moderate to abundant pale eosinophilic cytoplasm and pleomorphic vesicular nucleus with large prominent nucleoli. Intervening delicate vascular channels were noted (Figure 3). On immunohistochemistry, tumor cells were showing diffuse cytoplasmic positivity for AFP (Figure 4) and negative for CK7, CK20 and CD30. Serum AFP estimation was done in both patients and was found to be more than 10,000 ng/ml. Hence a final diagnosis of hepatoid adenocarcinoma was made.

Discussion

Hepatoid adenocarcinomas are rare malignant tumours characterized histologically by hepatoid differentiation. Hepatoid adenocarcinomas can arise from any organ in the human body. Stomach is one of the most common sites affected by these tumors and the first such

Fig. 2 : Gastrectomy specimen showing the tumour

Case II

A 60 year old male patient was evaluated for abdominal pain and upper gastrointestinal symptoms. Upper gastrointestinal endoscopy revealed an ulcerated nodular lesion in the body of the stomach. Biopsy from the lesion showed the lesion to be adenocarcinoma of stomach. CT scan of the abdomen showed an irregular wall thickening in body and pylorus of stomach, abutting left lobe of liver. There was no ascites or liver metastasis. There was a focal loss of fat planes with pancreas and multiple enlarged perigastric lymph nodes. At laparotomy, a tumour was found involving the whole of stomach. The lesion was adherent to pancreas posteriorly and there were large perigastric nodes and small omental deposits. There was no liver metastasis. As the tumour was inoperable, definitive procedure could not be done and a feeding jejunostomy was done for the patient. A biopsy was taken from the omental deposit.

Fig. 3 : H&E staining showing the hepatoid differentiation

Fig. 4 : IHC showing positivity for AFP
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The report was published by Bourreille et al. in 1970(2). The term “hepatoid adenocarcinoma of the stomach” was coined by Ishikura et al.(8,9). The term was coined to denote all tumours that not only show hepatoid differentiation but also produce AFP(10-14). But later on, Nagai et al.(15) noted that AFP production was not a prerequisite for the diagnosis of hepatoid adenocarcinoma. Based on this we can presume that there are two variants of hepatoid adenocarcinoma – AFP-producing and non AFP-producing. Both cases that we report here are AFP-producing hepatoid adenocarcinomas which can be called “classical hepatoid adenocarcinomas”. The “non-classical hepatoid adenocarcinomas” are the ones that show hepatoid differentiation but do not produce AFP. It also needs to be noted that non-hepatoid adenocarcinomas can also produce AFP. Another characteristic feature of classical hepatoid adenocarcinomas is the immunohistochemical staining of AFP. Immunohistochemical positivity for AAT, ACT, and bile can be seen in certain cases but these findings are non-specific(15). The two cases reported here have classical histological features of hepatoid differentiation with immunohistochemical staining of AFP and both patients have elevated AFP making them classical AFP-producing hepatoid adenocarcinomas.

A major area of concern in cases of hepatoid adenocarcinoma is the exact site of origin. Majority of the patients have liver metastasis at presentation. So it becomes difficult to differentiate between primary hepatoid adenocarcinoma of the stomach and metastatic deposits in the stomach from a primary in the liver. In the two cases reported here the patients were not having liver metastasis and hence it can be concluded that both were primary hepatoid adenocarcinomas of the stomach.

Review of literature shows that only about 85 cases have been described by the term “hepatoid adenocarcinoma of the stomach”(15,16,17). Most of the reports have been case reports with Nagai et al reporting on 15 patients(15). The average age of the patients has been 63.5 years, and the male-to-female ratio has been 58:25. Antrum was the commonest site of the tumour (60.2%). The average serum AFP level was 51130.1 ng/ml. Most of the patients present with symptoms common to all gastric malignancies like epigastric pain and general fatigue, because of anemia. Most patients present at an advanced stage with early gastric cancers accounting for a few cases. In most of the reported patients, metastases to the liver and/or lymph nodes were detected preoperatively.

Even early stage hepatoid adenocarcinoma has an extremely poor prognosis, because of the frequent occurrence of liver and/or lymph node metastases(15,16,17). Most of the patients died within 2 years of surgery. The reasons for the poor prognosis are not clearly understood. Hepatoid adenocarcinoma produces AAT, ACT in addition to AFP. AAT and ACT have immunosuppressive and protease-inhibitory properties that enhance invasiveness. Most patients develop liver metastasis within a year after surgery(17). The role of adjuvant chemotherapy is not well-established. There have been reports of response to chemotherapy in some cases. Therefore, even if hepatoid adenocarcinoma is diagnosed, curative resection and further chemotherapy are recommended.

Both patients in our cases are into their 2nd month of follow-up. In view of the advanced age, the first patient was not been given any adjuvant therapy and is on follow-up only and the inoperable case is on palliative chemotherapy with 5 Fu and cisplatin.


