Case Report:

Hepatoid adenocarcinoma of stomach: a morphological curiosity

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ABSTRACT

Hepatoid adenocarcinoma is a rare histological form of gastric cancer with a poor prognosis. We describe a 53-year-old woman who presented to the surgical gastroenterology outpatient department with a history of abdominal pain, vomiting and loss of appetite for one month. Laboratory investigations revealed anaemia (haemoglobin 5.6 g/dL). On gastrointestinal endoscopy, an ulceroproliferative growth was seen in the pylorus with gastric outlet obstruction. Endoscopic biopsy was suggestive of a well differentiated adenocarcinoma. Computed tomography of abdomen revealed irregular circumferential thickening of pylorus with perigastric and common hepatic nodes without distant metastasis. Patient underwent radical subtotal gastrectomy. The final histopathology was reported as hepatoid adenocarcinoma. Further immunohistochemistry with alpha-foetoprotein showed intense cytoplasmic positivity. She was treated with adjuvant Macdonald regimen. She developed liver metastasis eight months after surgery and received palliative chemotherapy. She died 13 months after surgery. Our experience and previous reports suggest that hepatoid adenocarcinoma is an aggressive cancer. Radical surgery and chemotherapy still remain the main stay of treatment.

Key words: *Adenocarcinoma, Stomach neoplasms, Alpha foeto-protein, Stomach, Immunohistochemistry*

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INTRODUCTION

Hepatoid adenocarcinoma of the stomach (HAS) is a rare subtype of gastric cancer with poor prognosis. Only few case reports and small case series have been previously reported. Ishikura et al first described HAS in 1985.[1] We report our experience with a case and review of literature highlighting the histopathogical aspect and aggressive nature of HAS.

CASE REPORT

A 53-year-old female presented to the surgical gastroenterology outpatient department with abdominal pain, vomiting and loss of appetite for one month. On physical examination, she had pallor. Per abdomen examination did not reveal any palpable mass or organomegaly. Laboratory testing revealed haemoglobin 5.6 g/dL. Gastrointestinal endoscopy showed an ulceroproliferative growth in the pylorus with gastric outlet obstruction. Endoscopic biopsy was suggestive of a well differentiated adenocarcinoma. Contrast-enhanced computed tomography (CECT) of abdomen revealed irregular circumferential thickening of pylorus with perigastric and common hepatic nodes without any evidence of distant metastasis. (Figures 1 and 2). She received two packed red cell transfusion prior to surgery. She underwent radical subtotal gastrectomy. Post-operative course was uneventful. Histopathology of excised specimen revealed Grade III HAS with negative resected margins. Pathological staging was reported as pT2 N3b. Microscopy showed that the lesion was composed of polygonal cells arranged in solid

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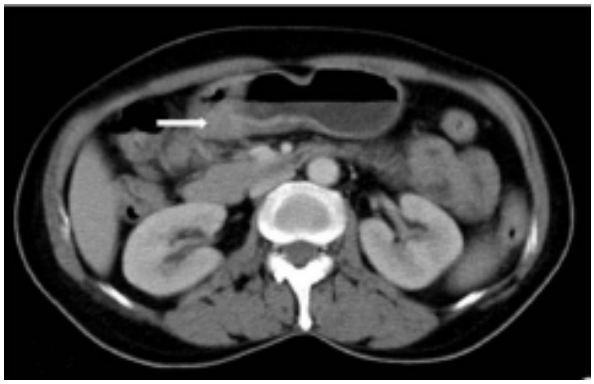

Figure 1: CECT abdomen (axial section) showing enhancing thickening in pylorus (arrow)
CECT = contrast enhanced computed tomography

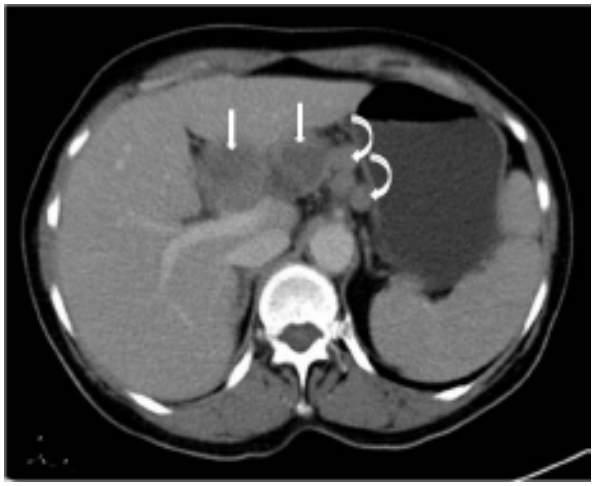

Figure 2: CECT abdomen axial section showing enlarged perigastric (curved arrow) and necrotic common hepatic (arrow) lymph nodes

sheet and trabecular pattern with focal glandular exhibition. The neoplastic cells resembled hepatocytes. These cells showed pleomorphic vesicular nuclei and moderate amount of eosinophilic cytoplasm (Figure 3). There were presence of hyaline globules which were periodic acid Schiff (PAS) positive (Figures 4A and 4B) Immunohistochemistry (IHC) showed intense cytoplasmic positivity for alpha foetoprotein (AFP) and alpha-1-anti-trypsin. (Figures 5A and 5B) Patient received adjuvant Macdonald regimen. She developed liver metastasis eight months after surgery. Subsequently she received palliative chemotherapy for the same (intravenous epirubicin 50 mg/m^2, oxaliplatin 130 mg/m^2 on day 1 followed by oral capecitabine 625 mg/

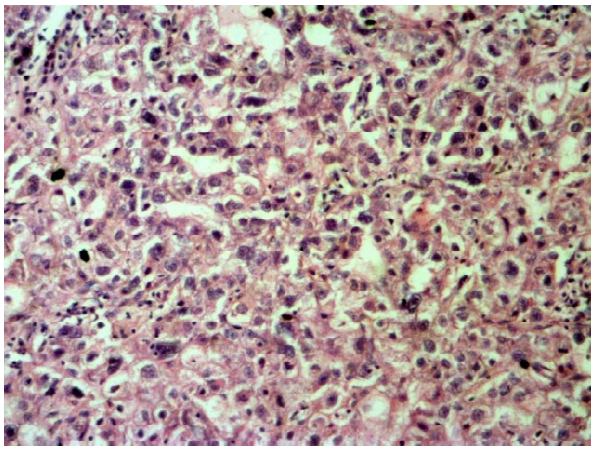

Figure 3: Photomicrograph showing neoplastic polygonal cells with moderate amount of eosinophilic cytoplasm resembling hepatocytes ,increased mitotic activity and inflammatory cell infiltrate (Haematoxylin and eosin $\times$ 100)

m^2 twice daily from day 1- 21, every 21 days). She expired 13 months after surgery.

DISCUSSION

HAS is a rare subtype of gastric cancer. The reported incidence varies from 0.17 to 15 %[2-5] and is common in elderly males.[2-6] The youngest case was reported in a 12-year-old boy.[7] HAS was first described by Ishikura et al in 1985 for gastric carcinomas showing hepatoid differentiation and producing large amount of AFP.[1,5] Hepatoid adenocarcinomas have also been reported in other organs, such as oesophagus, jejunum, colon, rectum, gall bladder, lung, peritoneum, urinary bladder, renal pelvis, pancreas, ovaries, uterus and papilla of vater.[6,8]

Preoperative diagnosis is difficult as patients present with symptoms similar to other digestive cancers.[9] Epigastric pain and generalized fatigue caused by anaemia are common symptoms.[8] Most studies suggest antrum as the most common site for HAS.[8] In a recent study,[4] the tumour was located in cardia in 42.1%, body in 36.8% and in antrum in 21.1%. Serum AFP levels decrease rapidly after gastrectomy and definitive diagnosis is made by characteristic histopathological features and

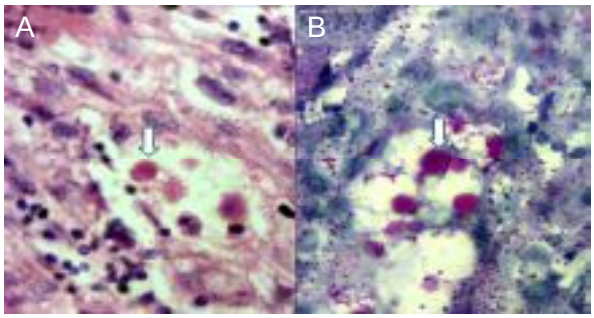

Figure 4: Photomicrograph showing neoplastic cells with presence of hyaline globules (arrow) (Haematoxylin and eosin x 400) **(A)**, (Periodic acid Schiff × 400) **(B)**

not on AFP production.[5] In our case we did not estimate serum AFP pre-operatively.

The characteristic histopathological features are areas of adenocarcinoma with hepatoid-like foci.[6,8] The cells are large and polygonal with prominent nucleoli, prominent cell borders, central nuclei and abundant cytoplasm.[6,9] The morphology of tumour foci resembles hepatocellular carcinoma.[8] These tumours show positivity for AFP, carcinoembryonic antigen, alpha 1-antitrypsin and alpha 1-antichymotrypsin on IHC.[6,8,9] Positive AFP staining on histopathology varies from 73.7% - 91.6 %.[4,9] Our case showed the characteristic hepatoid morphology with presence of hyaline globules and the histopathological diagnosis was supported by immunohistochemical findings.

CECT abdomen features include a large polypoid appearance, heterogenous contrast enhancement of the asymmetrical gastric wall thickening, liver metastasis and regional lymphadenopathy.[5] Morphological appearance of enhancement pattern on CT may assist in distinguishing HAS from other types of advanced gastric carcinoma.[5]

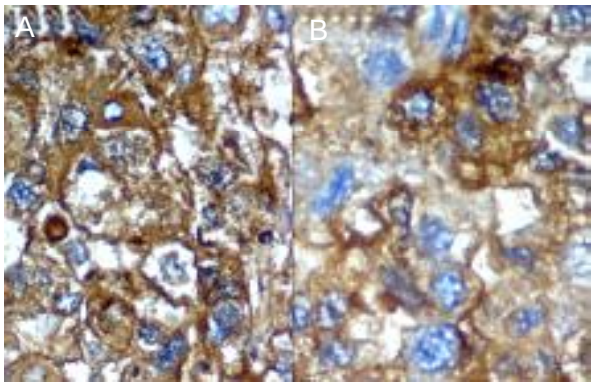

Figure 5: Immunohistochemistry (IHC) showing intense cytoplasmic positivity for alpha foetoprotein (x 400) **(A)**, intense cytoplasmic positivity for alpha-1 antitrypsin (× 400) **(B)**

Radical surgery with negative margins remains the main stay of treatment in the absence of distant metastasis. Currently, there are no standard regimens for HAS and chemotherapy response is poor compared to common gastric adenocarcinoma regimens.[4] Some studies suggest adjuvant chemotherapy and radiotherapy according to gastric cancer indications as no specific data are available for HAS.[8]

The prognosis of HAS is poorer than gastric adenocarcinoma in published literature. Most HAS patients are either metastatic at presentation[4,6,8] or have shorter interval between gastrectomy and metastasis.[8,9] Liu et al[10] reported 1, 3, 5 year survival rates of HAS to be 30%, 13% and 9% and whereas corresponding survival rates with gastric adenocarcinoma were 95%, 57% and 38%.[10] In a recent study[4] both 3- and 5 -year survival rates reached 30% and lymph node status was significantly related to survival. After R0 resection, patients with N0 or N1, had a higher chance of cure than N2 or N3 disease.[4]

In conclusion, HAS is a rare subtype of gastric cancer with unique histopathological features and poor prognosis. Radical surgery and adjuvant chemotherapy still remain the main stay of treatment.

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