CASE REPORT

Case Report: Primary pure clear cell gastric carcinoma

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Abstract
Clear cell carcinoma has been described in numerous anatomic sites, but the renal location is the most frequent. Its occurrence in the stomach is exceptional. Here, we report the case of a 51-year-old woman who presented with epigastric pain of four months. The upper gastrointestinal endoscopic examination revealed a polypoid tumor of the greater curvature of the stomach. Biopsies showed a poorly differentiated carcinoma with a signet-ring cell component. The CT scan revealed a polypoid mass of the vertical part of the greater gastric curvature. There was no renal lesion. A distal subtotal gastrectomy was performed, and the post-operative course was uneventful. The gross exam showed a 6.5 cm, polypoid ulcerated tumor of the antrum. Histological analysis showed a clear cell gastric carcinoma. The immunohistochemical study, performed to rule out a metastasis from renal carcinoma, showed that tumor cells didn't express CD10 and vimentin. We therefore retained the diagnosis of a primary gastric clear cell carcinoma. Pure primary clear cell carcinomas of the stomach are exceedingly rare and are associated with a poor prognosis. Immunohistochemistry is the cornerstone of the diagnosis of these tumors to rule out metastases from a renal clear cell carcinoma.

Keywords
Clear cells, gastric cancer, gastrectomy
Introduction

Clear cell carcinoma (CCC) generally develops in organs originating from the Mullerian system, such as the lower urinary and female genital tracts\(^1\). Its occurrence in the gastrointestinal tract is uncommon, and cases occurring in the stomach are exceedingly rare\(^2\). Clear cytoplasm, and hence clear cells, are the result of intracellular accumulation of glycogen, lipid, water, or mucin\(^3\). Due to its rarity, the clinicopathological and biological behaviors of this entity remain unclear.

Until now, only a few cases of gastric CCC have been reported in the English literature. These reports generally included gastric carcinoma with focal clear cell changes. We report herein the third case of a pure gastric CCC.

Case report

We report the case of a 51-year-old north African woman, who presented with a history of epigastric pain of four months. The abdominal examination found mild epigastric tenderness but no palpable mass. The upper gastrointestinal endoscopic examination revealed a polypoid tumor of the greater curvature of the stomach measuring 6 x 4 cm (Figure 1). Biopsies were performed using digestive endoscopic biopsy forceps. The anatomopathological examination showed a poorly differentiated carcinoma with a signet-ring cell component. No immunohistochemical examination was performed.

A CT scan of the thorax and abdomen, performed as part of the extension assessment, showed a pedicled budding mass with endoluminal development of the vertical part of the greater gastric curvature measuring 6 x 4 x 5 cm (Figure 2). Otherwise, it did not show evidence of any renal tumor or hepatic or pulmonary localization.

In order to reduce tumor volume and improve the R0 resection rate, the patient received four courses (one course per two weeks) of perioperative chemotherapy with 5-fluorouracil (2600 mg/m\(^2\)), folinic acid (350 mg), oxaliplatin (85 mg/m\(^2\)) and docetaxel (50 mg/m\(^2\)) according to the FLOT regimen, administrated through a totally implantable venous access port via the internal jugular left vein. Then the patient underwent distal subtotal gastrectomy with a manual Roux-en-Y esophagojejunostomy, via a midline incision. This was the procedure of choice of the clinical lecturer who performed the intervention in case of proximal gastric cancer.

Gross examination revealed an ulcerated polypoid tumor with endoluminal development. The histological examination showed an invasive tumor arranged in lobules, clusters, and nests within a highly vascularized stroma (Figure 3a). There were necrotic changes. Tumor cells had abundant clear cytoplasm and well-defined cytoplasmic borders. The nuclei had marked atypia and prominent eosinophilic nucleoli (Figure 3b). The tumor infiltrates to the subserosa without serosal invasion. Moreover, we noted the absence of vascular emboli, perineural tumor invasion and lymph node metastasis. Periodic acid-Schiff and alcian blue stains were negative. An immunohistochemical study was performed to rule out a renal origin. The tumor cells were negative for CD10 and vimentin. They were positive for cytokeratin with diffuse cytoplasmic and membranous staining. The diagnosis of primary gastric CCC in its pure form was made.

Figure 1. Upper gastrointestinal endoscopic examination showing a polypoid yellowish tumor of the greater curvature of the stomach.

Figure 2. CT scan of the abdomen revealing a pedicled budding mass with endoluminal development located in the vertical part of the greater gastric curvature.
The postoperative course was uneventful and the patient was discharged on the fifth postoperative day on analgesic treatment and low-molecular-weight heparin for thirty days. The patient received four courses of adjuvant chemotherapy (FLOT regimen). The CT scan done after six months showed no local or distant recurrence.

Discussion
A CCC can develop in various organs, and the most common sites are the kidneys and the female genital tract. Its occurrence in the gastrointestinal tract is uncommon. Only few case reports or small series have been described in the colon, pancreas, and the biliary system.

Even though the presence of clear cell changes in gastric carcinoma has been reported in 8.5% of cases, the pure form of CCC of the stomach is an extremely rare oncologic entity. There is no specific reference to CCC in the latest WHO classification of gastric carcinoma. This entity has not been well documented, with only limited literature available on the topic.

Regarding the clinical characteristics, Kim et al. have demonstrated, in a large cohort study, that gastric carcinomas with clear cell changes were associated with younger age and tended to be located in the gastric antrum. However, Ghotli et al. showed that gastric CCC had a predilection for the gastroesophageal junction. Moreover, these tumors are polyoid and histologically characterized by a tubulo-papillary pattern. These features are consistent with the characteristics of the tumor in our case, which was polyoid and located in the vertical part of the greater gastric curvature.

What makes this case remarkable is that the present tumor is made of 100% clear cells. Kim et al. reported 65 cases and defined CCC as a carcinoma composed of more than 5% of clear cells. To the best of our knowledge, only Terada and Yamada et al. have reported the pure form. It has been shown that the presence of clear cell changes is an independent indicator of poor prognosis since it is associated with advanced depth of invasion, presence of lymphovascular tumor emboli, and lymph node metastases, compared to gastric adenocarcinoma without clear cell changes.

Advances made in techniques used for pathological examination and immunohistochemistry made the diagnosis of gastric CCC easier. Immunophenotypically, it has been demonstrated that CCC carcinoma shows overexpression of cyclin D1. It has also been noted that clear cell tumors of the stomach may produce alpha-fetoprotein (AFP) in the serum and within the tumor. In our case, AFP was not measured.

Recently, hepatocyte nuclear factor-1b (HNF-1b) has been accepted as a unique biomarker of CCC for tumors of the female genital tract, bladder, and pancreas. In the stomach, carcinomas with clear cell changes also show increased positive immunostaining of HNF-1b as it has a role in cellular glycogen synthesis. Nevertheless, until now, there has been no reports about the role of HNF-1b in gastric adenocarcinomas.

Due to its rarity, there are no therapeutic guidelines for CCC. It is managed like conventional gastric carcinomas, and its surgical treatment depends on its localization. In our case, the tumor was located in the vertical part of the great gastric curvature and necessitated total gastrectomy.

Conclusions
Pure primary CCC of the stomach are exceedingly rare and are associated with a poor prognosis. Immunohistochemistry is the cornerstone of the diagnosis of these tumors to rule out metastases from a renal CCC.
Data availability
All data underlying the results are available as part of the article and no additional source data are required.

Consent
Written informed consent for publication of their clinical details and clinical images was obtained from the patient.

References

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