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Case Report
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Primary adenosquamous carcinoma of the stomach

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ABSTRACT

Adenosqamous carcinoma of the stomach is a rare subtype, accounting for less than 0.4 % of cases of gastric cancer. It is aggressive and tends to be present in advanced stages with a worse prognosis than typical gastric adenocarcinoma. This case is interesting because of its rarity and histogenesis. Based on the fact that clinically and endoscopically, it resembles intestinal-type adenocarcinoma, histopathology is required to make definitive diagnosis. Presented here is a case report of a 70-year-old male that presented with the features of gastric outlet obstruction. Distal gastrectomy with D1 duodenectomy showed adenosquamous carcinoma at the distal end of the stomach with metastatic deposits in 4/6 perigastric lymphnodes. With immunohistochemistry, the squamous component demonstrated CK5/6 positivity and the adenocarinoma component was positive for CK7.

Key words: *Adenosquamous carcinoma, stomach*

Introduction

Adenosquamous carcinoma (ASC) is an invasive carcinoma of a rare subtype that occurs throughout the gastrointestinal tract [1]. Primary ASC of the stomach is rare with an incidence that varies from 0.04 - 0.7 %, mostly affecting Asians [2-5]. Most reported cases are from Japan with similar reports being sparse from other parts of the world. The male to female ratio is 4:1 and usually manifests in the elderly. Based on the fact that clinically and endoscopically, it resembles intestinal-type adenocarcinoma, histopathology is required to make definitive diagnosis. There has been much debate on the origin of these tumors as the tumor cells are not indigenous to the organ [3]. Primary gastric ASC exhibits early tumor progression and metastasizes extensively to other abdominal organs compared to typical gastric adenocarcinoma. We report this case because of its rarity and unique histopathology.

Case Report

A 70-year-old man presented with features of gastric outlet obstruction to the surgical services unit of the Kempegowda Institute of Medical Sciences (KIMS), Bangalore, India. Routine blood investigations indicated mild anemia. Upper gastrointestinal endoscopy revealed an ulceroproliferative mass in the distal part of the stomach. Pathology of distal gastrectomy with D1 duodinectomy specimen demonstrated an ulceroproliferative tumor with a broad base measuring approximately 3.5 cms, Borrman type 3[6], at the gastroduodenal junction with dilatation and relative

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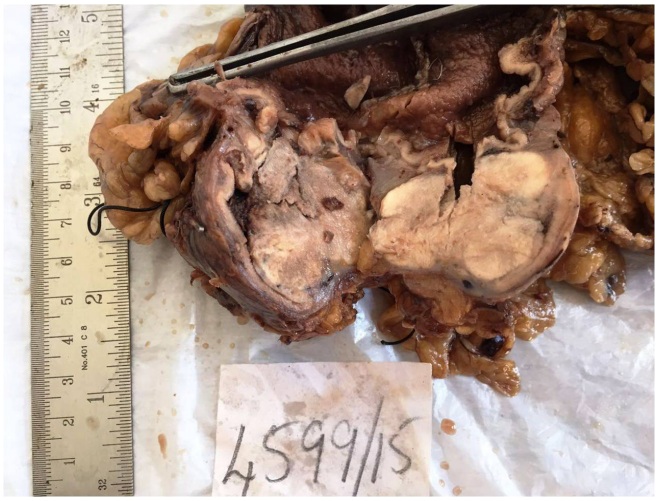

Figure 1. Ulceroproliferative gray white mass in the distal stomach infiltrating the entire thickness.

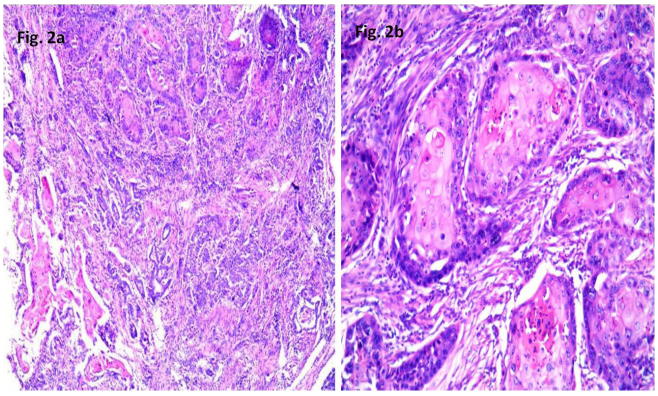

Figure 2. (A) Microscopy showing squamous and adenocarcinoma components with gradual transition [H and E×4]. **(B)** Squamous component with keratinizing masses [H and E×10].

flattening of the mucosal folds above it. The tumor had a cauliflower-like appearance, with gray white coloring, friable infiltrating the entire thickness of the gastric wall (Figure 1). Roughly six lymph nodes were identified in the omentum.

Microscopy exhibited a mixture of squamous (nearly 70%) and adenocarcinoma (roughly 30%) components with gradual transition between the two. Both components were well- to moderately-differentiated (Figure 2A). The squamous component was identified based on the keratinizing cell masses and intercellular bridges (Figure 2B), and the tumor was infiltrating entire gastric wall. There was extensive lymphovascular and perineural invasion (Figure 3A). The rest of the uninvolved stomach showed moderate chronic gastritis. No intestinal metaplasia or *Helicobacter Pylori* was noted. Proximal surgical margin was free of tumor, and the distal surgical margin featured lymphovascular emboli. The radial margin was positive for tumor. Four out of six lymph nodes were positive for tumor, with both squamous and adenocarcinoma components present in equal proportion (Figure 3B). Immunohistochemical staining revealed strong cytoplasmic positivity for CK5/6 in the squamous component (Figure 4A) and CK7 positivity in the adenocarinoma component (Figure 4B).

Discussion

Gastric ASC was first reported in1905 by Rolleston and Trevor [1]. Clinical manifestations of ASC are similar to those of primary adenocarcinoma of the stomach. Hence, histopathological examination is required for definitive diagnosis. The criteria for definitive diagnosis of ASC of the stomach are: (1) confirmation of the presence of a mixed pattern of carcinoma outside the cardia without oesophageal involvement; (2) absence of ASC in other organs; and (3) presence of an SCC is squamous cell carcinoma (SCC) component in over 25% of tumor mass [7]. In our case, the tumor was present at the distal end of stomach; microscopically, the SCC component constituted over 70% of tumor mass and the patient did not have any other malignancy.

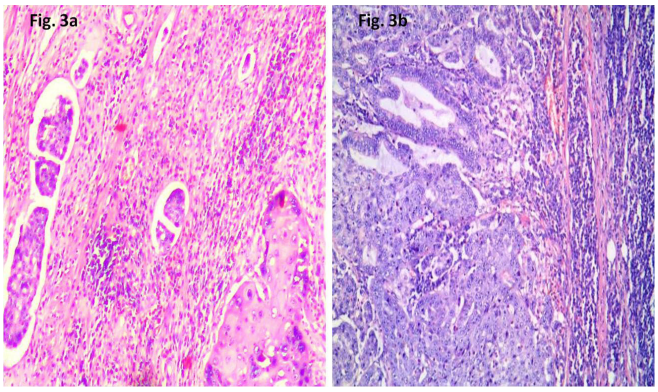

Figure 3. (A) Microscopy showing lymphovascular invasion [H and E×10]. **(B)** Squamous and adenocarcinoma components in the lymph node [H and E×10].

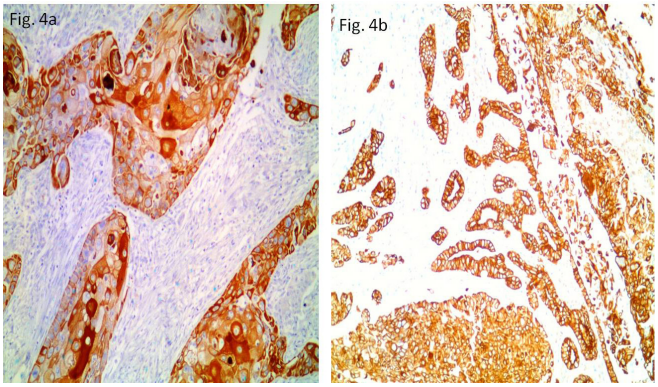

Figure 4. (A) Strong cytoplasmic positivity for CK5/6 in the squamous component [H and E×10]. **(B)** Strong cytoplasmic positivity for CK7 in the adenocarcinoma component [H and E×10].

Histogenesis of a neoplastic squamous component in primary gastric carcinoma has not been clearly defined. There are five possible hypotheses: 1) squamous differentiation in a pre-existing adenocarcinoma; 2) cancerization of metaplastic squamous cells; 3) cancerization of ectopic squamous epithelium; 4) the endothelial cells of the gastric vessel differentiate toward both lines; and 5) stem cells differentiate toward both lines [2,5,8,9]. Mori et al., in their histogenetic and ultrastructural study of ASC of the stomach, identified three types of cells - adenomatous, squamous and intermediate. The intermediate cells had both large electron-dense vacuoles and tonofibrils in the cytoplasm. Clear identification of a cell containing two different characteristics supports the multipotential stem cell origin of ASC [10].

Lee et al. investigated the expression of p53, p16 and RB proteins in 15 cases of primary ASC and two of SCC of the stomach. The expression of p53 in the adenocarcinoma and squamous cell components was exactly the same in all the cases. The expression patterns of p16 and RB were also identical in most cases. The fact that the alteration of the three tumor suppressor gene products shared the same pattern suggested that squamous and adenocarcinoma components in the stomach originate from the same or a genetically-related clone [11].

Upon immunohistochemical analysis, both the adenocarcinoma and squamous cell components exhibited carcinoembryonic antigen (CEA) immunoreactivity in comparison to cytokeratin which was detected only in squamous areas. The findings of CEA reactivity in both components along with the presence of microscopic transitional zones support the hypothesis of squamous metaplasia taking place in an already existing adenocarcinoma in the development of adenosquamous carcinoma of the stomach [12].

Kim et al. evaluated eight cases of primary SCC (1) and ASC (7) of the stomach without early gastric cancer. Overexpression of p53 was seen in five cases (62.5%) and their survival was poor when compared to the p53-negative group. The mean ki67 labeling index was 70.0 +/-20.8%. Hence, it was concluded that p53 protein overexpression and high ki67 labeling index might be the predictors of poor prognosis [13].

ASCs usually invade deep into the muscular layer, present with venous and lymphatic invasion and tend to be diagnosed late in more advanced stages. Its biological behavior is usually determined by the adenocarcinoma component [8,11,13]. In our patient, the tumor was also extended into the serosa, with nodal metastasis and extensive lymphatic and venous invasion.

Differential diagnosis includes gastric adenocarcinoma of intestinal or poorly differentiated type with squamous differentiation, collision tumors, pure squamous cell carcinoma of the stomach, mucoepidermoid carcinoma and metastatic tumors. Focal squamous differentiation in the intestinal type of adenocarcinoma is relatively common. Therefore, for a confirmatory diagnosis of ASC, the squamous component account for more than 25% of the tumor. ASC can be differentiated from collision tumors by gradual transition from the adenocarinoma component to a squamous component [14,15].

ASC is a more aggressive neoplasm. The median survival time for gastric ASC ranges from 12-22 months. The five-year survival rate is 10%. Several factors affect the prognosis of tumors, such as size, site, margins and TNM staging. Surgical resection is the opted line of treatment. Adjuvant therapy (chemo + radio) may prolong survival time [4].

Conclusion

Primary ASC of the stomach is a rare type of malignancy with an aggressive course. Patients are usually diagnosed at a late stage. Both adenocarinoma and squamous components have metastatic potential.

Conflict of interest statement

The authors have no conflicts of interest to declare.

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