Case Report

"The not-so pretty pearl in an Oyster" - A case report of primary gastric squamous cell carcinoma with brief literature review

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ABSTRACT

Primary gastric squamous cell carcinoma (PGSCC) is an extremely rare histological subtype of gastric carcinoma with an incidence of 0.04–0.07% of all gastric cancers. It has a male preponderance and is common between 55 and 80 years of age. Here, we present the occurrence of this rare tumor in a 33-year-old male, a chronic smoker and alcoholic. Imaging revealed a large heterogeneously enhancing mass in the body of the stomach. The patient underwent total gastrectomy with perigastric lymph node dissection. Histopathological examination of the tumor proved to be a squamous cell carcinoma with positivity for CK5/6, P63, and p16 and negative for CK7 and CK20. The tumor was staged pT2N0. Whole-body positron emission tomography computed tomography failed to identify an alternative primary squamous malignancy. PGSCC is a rare gastric malignancy that poses significant diagnostic and therapeutic challenges. The present case is notable for its occurrence in a relatively young patient and for diffuse p16 expression, which raises the possibility of human papillomavirus-related pathogenesis. Increased reporting of such cases may improve the understanding of the clinicopathological features and pathogenesis of this uncommon entity.

Key words: Gastric, Primary, Squamous cell carcinoma

Primary gastric squamous cell carcinoma (SCC) is an extremely rare malignancy accounting for 0.04–0.07% of all gastric cancers [1]. They are aggressive tumors, often presenting at an advanced stage and associated with a poor prognosis as compared to gastric adenocarcinomas. It has a male preponderance and is common between 55 and 80 years of age.

Here, we present the occurrence of this rare tumor in a 33-year-old male, a chronic smoker and alcoholic.

CASE REPORT

A 33-year-old male, an alcoholic and a smoker, presented with complaints of abdominal pain and vomiting for 1 week. He had a history of loss of weight and appetite for 2 months.

On examination, the patient was emaciated and had severe pallor. Computed tomography (CT) of the abdomen revealed a large, irregular, heterogeneously enhancing mass within the body of the stomach measuring 10 × 5 cm. Upper gastrointestinal endoscopy was performed, and a biopsy was done, which was positive for malignancy.

The patient underwent laparotomy and total gastrectomy with perigastric lymph node dissection. Macroscopic examination showed a large gray-white proliferative friable tumor, measuring 10 × 8 × 5 cm in the body of the stomach. The tumor was 3 cm away from the cardia and 12 cm from the distal resected margin (Fig. 1). Thirteen perigastric lymph nodes were identified.

Microscopy showed a tumor composed of nests and sheets of polygonal tumor cells with intercellular bridges and exhibiting nuclear atypia with keratin pearl formation (Fig. 2a and b). The tumor infiltrated into the underlying muscularis propria. Serosa was free of tumor infiltration. Proximal and distal resection margins were free of tumor involvement. No lymphovascular or perineural invasion was identified. All 13 lymph nodes were free of metastasis. A panel of immunohistochemical markers was performed, which showed positivity for CK5/6 and p63, confirming squamous origin (Fig. 3a and b). In addition, there was also diffuse nuclear and cytoplasmic positivity for p16 (Fig. 3c).

Postoperatively, the patient was evaluated for other possible primary sites of squamous malignancy, including whole-body positron emission tomography computed tomography, which was negative. Bronchoscopy and ear, nose, and throat examination were normal. Thus, a diagnosis of primary SCC of the stomach (pT2N0M0) was made. The post-operative period was complicated

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by sepsis, resulting in progressive clinical deterioration and death approximately 1 month after surgery, before initiation of chemotherapy.

DISCUSSION

Primary gastric SCC is an extremely rare malignancy and is characterized by aggressive behavior and poorer prognosis when compared to gastric adenocarcinoma. Its incidence varies between 0.04% and 0.07% of all gastric malignancies. It has a male preponderance and is more prevalent in the sixth decade of life.

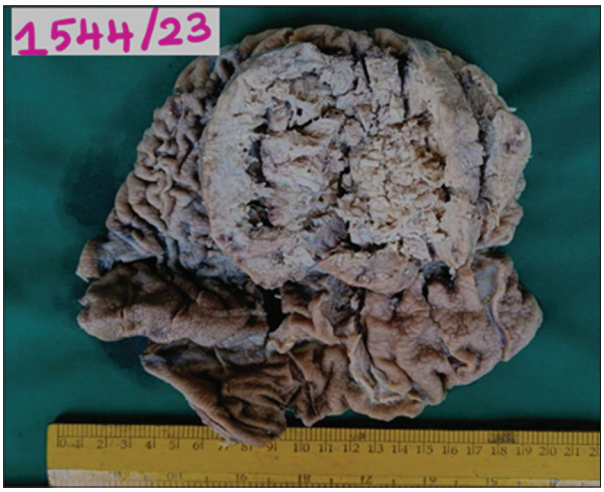

Figure 1: Gross image showing cut section of stomach with a large exophytic friable tumor situated 3 cm from the cardia

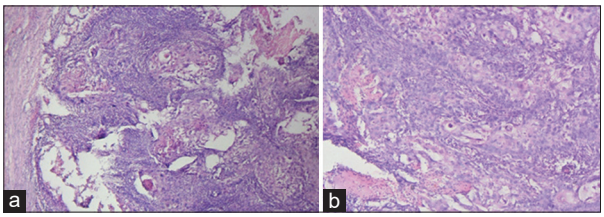

Figure 2: Microscopic appearance of the tumor composed of sheets and nests of (a) dysplastic squamous cells and foci of necrosis. (b) Tumor cells with intercellular bridging (Hematoxylin and Eosin, ×20)

The etiopathogenesis of primary gastric SCC remains poorly understood [2]. The various pathophysiological hypotheses include differentiation of totipotent stem cells, the transformation of existing ectopic squamous tissue, squamous metaplasia resulting from chronic inflammation, a squamous transformation of pre-existing adenocarcinoma, and infection with Epstein–Barr virus or human papillomavirus (HPV) [3-5]. The clinical presentation is non-specific and overlaps considerably with that of gastric adenocarcinoma.

Definitive diagnosis of primary gastric SCC can be made based on the following criteria proposed by Boswell and Helwig and Parks. The criteria to confirm squamous cell origin, of which at least one must be present to make a diagnosis, are: (a) Keratinized cell masses with pearl formation; (b) mosaic pattern of cell arrangement; (c) presence of intercellular bridges; (d) high concentration of sulfhydryl and/or disulfide groups indicating presence of keratin or prekeratin [6]. In our case, the presence of dysplastic squamous cells with dyskeratosis and keratin pearl formation was evident. The criteria to confirm gastric primary malignancy are: (a) Tumor not located in the cardia and 2 cm away from the cardia; (b) no esophageal extension of the tumor; and (c) no evidence of SCC in other parts of the body [7]. Our case satisfied all the above-mentioned criteria.

An IHC panel testing for CK5, CK7, CK20, TTF1, p63, chromogranin, synaptophysin, CEA, and CA 19-9 is required to complement the diagnosis of primary gastric SCC. CYFRA 21-1 is a reliable tumor marker for gastric cancer in predicting very advanced cases, recurrence of the disease, and overall poor prognosis [8]. Our case

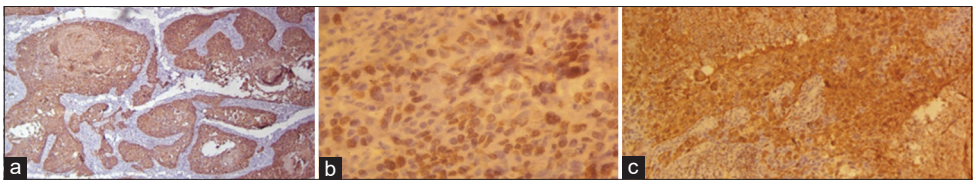

Figure 3: The tumor cells are immunoreactive for (a) CK5/6 (cytoplasmic and membranous) (immunohistochemistry [IHC], ×40); (b) p63(nuclear), proving squamous differentiation (IHC, ×40), and (c) diffuse nuclear and cytoplasmic expression of p16 favoring human papillomavirus association (IHC, ×40)

Table 1: Comparison of previous cases with the present case

Authors (year)	Age and sex of the patient	Tumor location	Tumor size	Stage	HPV testing	Outcome
Hwang *et al*. (2014)	61/Male	Cardia	7×6.7×4.5 cm	T4AN1M0	Negative	Death after 6 months
Gao *et al*.	50/Male	Antrum	12×8 × 6	T4bN3aM0	Not done	Alive with tumor in ascending coon
Vailas *et al*. (2019)	66/Male	Antrum	4.7×3 × 2.5	T3N3MO	Not done	Patient alive
Fernandez *et al.*	22/Male	Body and antrum	9×8	T4aN0M0	Not done	Not described
Wakabayashi *et al.*	61/Male	Cardia	4×4	T3N1M0	Not done	Alive without recurrence
Present case	33/Male	Body	10×8 × 5	T2N0M0	P16 diffuse positive	Died 1 month after surgery

HPV: Human papillomavirus

had coexpression of CK5/6 and p63, P16 positive, and ck7/20 negative.

At this juncture, we would like to highlight that compared with the previously reported cases, our patient had a younger age of presentation (33 years) and diffuse p16 expression (Table 1). The diffuse p16 expression in our case raises an interesting hypothesis regarding the possible role of HPV in the pathogenesis of a subset of primary gastric SCC [9]. However, HPV infection was not confirmed in the present case due to limited resources, and further molecular studies are required for its causal association. If a reproducible association between HPV infection and primary gastric SCC is established in future studies, targeted surveillance strategies may merit evaluation.

Gastric SCC frequently presents at an advanced stage, hence associated with poor outcome. The most common sites of metastasis are the liver, peritoneum, lung, and bones [10]. Hence, an intensive follow-up is necessary in these patients due to their aggressive behavior.

CONCLUSION

This is an extremely rare case of primary gastric SCC with a younger age of presentation. Literature has scarcely reported such cases so far, and the exact pathogenesis remains elusive, making treatment difficult. The present case highlights diffuse p16 expression in a young patient with primary GSCC and raises interesting questions regarding its pathogenesis, thereby prompting screening of all adults for HPV presenting similarly. This case will serve as a pilot for further studies.

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