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Case study

Primary squamous cell carcinoma of the stomach with paraneoplastic leukocytosis: a case report and review of literature

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Summary Apparently pure, primary squamous cell carcinoma of the stomach is exceedingly rare. To date, less than 100 cases have been reported. Here, we describe a case of primary squamous cell carcinoma arising in the gastric antrum of an 83-year-old man with persistent leukocytosis, which resolved on resection of the tumor. No foci of squamous metaplasia or gland-forming elements were identified in the resection specimen, although there was marked chronic gastritis with intestinal metaplasia. There was no evidence of *Helicobacter*, fungal, or parasitic infection. Immunohistochemical and in situ hybridization studies for human papillomavirus and Epstein-Barr virus were negative. This case suggests that gastric squamous cell carcinoma likely arises in the setting of long-standing, chronic inflammation, and like squamous cell carcinoma in other organ systems, may be associated with paraneoplastic leukocytosis.
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1. Introduction

Primary gastric squamous cell carcinoma (SCC) is an exceedingly rare disease, which accounts for less than 0.5% of all primary neoplasms of the stomach [1]. Since the first report in 1895, there have been fewer than 100 cases published in the world literature [2]. The pathogenesis of this neoplasm when it occurs at this site is unclear, and the prognosis is controversial [3]. Gastric SCC occurs mostly in males, with a male-to-female ratio of 5:1 [4]. The peak incidence is in the sixth decade of life, but a patient as young as 17 years has been reported [5]. We report a case of primary SCC of the stomach with persistent leukocytosis, which resolved after gastrectomy in a patient with coexistent stage II prostate adenocarcinoma.

2. Case report

An 83-year-old man was admitted to the Guillermo Almenara Irigoyen National Hospital emergency department with upper abdominal pain, asthenia, vomiting, hyporexia, and weight loss for 2 months. His medical history included

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hypertension treated with hydrochlorothiazide and nifedipine, diet-controlled non–insulin-dependent diabetes, and suprapubic prostatic adenomectomy. Physical examination revealed a cachectic, elderly male with a distended abdomen secondary to a palpable mass between the epigastric and umbilical region. Respiratory, heart, and bowel sounds were normal. A digital rectal examination disclosed a swollen and enlarged prostate gland of stony-hard consistency.

Laboratory tests on admission showed the following: 35.2 × 10^3/mm^3 white blood cells with 90% mature neutrophils, 3.05 × 10^3/mm^3 red blood cells, 7.5 g/dL hemoglobin, 571 × 10^3/mm^3 platelet count, 108 mg/dL blood urea nitrogen, 2.1 mg/dL serum creatinine, 18 U/L alanine aminotransferase, 32 U/L aspartate aminotransferase, 0.7 mg/dL total bilirubin, and 3.2 g/dL serum albumin. Serum CEA, AFP, and CA 19.9 were normal. However, serum CYFRA 21-1 and PSA were 17.1 and 10.3 ng/mL, respectively. An abdominal computer tomography (CT) scan showed a large polypoid lesion in the gastric antrum extending to the first portion of the duodenum. Upper gastrointestinal endoscopy revealed an infiltrative and stenosing large, ulcerated lesion located in the antrum and pyloric region (Borrmann III). A biopsy indicated the presence of SCC. Extensive evaluation, including bronchofibroscopy, bronchoalveolar lavage with bronchial brushing, and skin biopsy of a benign keratotic lesion (pigmented seborrheic keratosis), revealed no other possible primary site (s) of involvement. Prostate biopsy revealed prostatic adenocarcinoma (Gleason score 4 + 4 = 8). All blood and urine cultures were negative. A bone marrow aspiration was performed because of persistent leukocytosis (>20.0 × 10^3/mm^3) in absence of infection. The results showed a hypercellular marrow with myeloid hyperplasia but no dysplasia. The CT scan of the thorax, abdomen, and pelvis revealed no evidence of metastasis. Three weeks after admission, a radical subtotal gastrectomy with Roux-en-Y reconstruction and D2 lymphadenectomy was performed.

3. Materials and methods

Multiple sections of the tumor mass including adjacent (n = 12) and distant (n = 4) gastric mucosa were obtained. The tissue specimens were routinely fixed in 10% buffered formalin, embedded in paraffin, and serially sectioned into 4-μm-thick sections. Routine staining with hematoxylin and eosin was performed. Additional immunohistochemical staining with high molecular weight cytokeratin 5/6 (clone D5/16B4, Zymed, San Francisco, CA; 1:200), p63 (clone 4A4, Dako, Carpenteria, CA; 1:200), and p53 (clone DO-7, Dako; 1:10,000) was performed with parallel positive and negative controls. Immunohistochemical stain for p16INK4A was performed with the DakoCytomation Autostainer (DakoCytomation, Glostrup, Denmark) on 4-mm-thick sections with the DakoCytomation CINtec p16INK4A histology kit using a primary mouse antihuman monoclonal antibody (clone E6H4, DakoCytomation; predilute). Staining with ProEx C, a mouse antihuman monoclonal antibody directed at minichromosome maintenance protein 2 (MCM2) and DNA topoisomerase II alpha (TOP2A) (Tripath Imaging Inc, Burlington, NC; predilute), was performed according to manufacturer's instructions. In situ hybridization staining for HPV was conducted with GenPoint HPV DNA Probe Cocktail according to the manufacturer's instructions (Dako). Cervical biopsy tissue previously shown to be positive for HR-HPV by polymerase chain reaction (PCR) was used as a positive control for p16INK4A and ProEx C. In situ hybridization staining for EBV RNA was done using the Ventana oligonucleotide probe (Ventana Systems, Tucson, AZ), also using positive and negative controls.

4. Results

4.1. Pathology

The surgical specimen contained an ulcerated, exophytic polypoid growth arising from the anterior gastric wall of the lesser curvature of the antrum, measuring 15 × 8.3 × 2.5 cm (Fig. 1). Microscopic examination revealed a moderate to well-differentiated, keratinizing SCC with invasion to the subserosal layer (Fig. 2). There was no squamous metaplastic or glandular component. No lymphatic space invasion was identified. The intervening and adjacent nonneoplastic stomach showed intestinal metaplasia, but no dysplasia (Fig. 2). No *Helicobacter*, fungal, or parasitic organisms were identified on routine, Grocott's methenamine silver

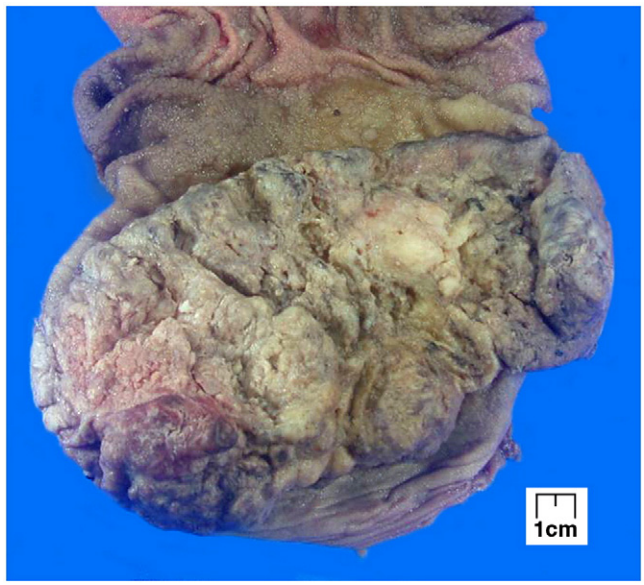

Fig. 1 Resected SCC in the gastric antrum. The surgical specimen shows an ulcerated, exophytic tumor mass arising from the anterior gastric wall of the lesser curvature.

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