Case and Review

Alpha-Fetoprotein-Producing Gastric Cancer with Nonbiliary Pancreatitis

Arda Yavuz^a Büşra Güleç^b Rabia Burçin Girgin^c İlyas Tuncer^a

^aGastroenterology Department, Göztepe Research and Training Hospital, Istanbul Medeniyet University, Istanbul, Turkey; ^bInternal Medicine Department, Göztepe Research and Training Hospital, Istanbul Medeniyet University, Istanbul, Turkey; ^cPathology Department, Göztepe Research and Training Hospital, Istanbul Medeniyet University, Istanbul, Turkey

Keywords

Pancreatitis · Alpha-fetoprotein · Metastasis · Gastric cancer

Abstract

Alpha-fetoprotein (AFP)-producing gastric cancer (AFPGC) is a rare, aggressive tumor. In the absence of metastasis in diagnosis, close observation and long-term follow-up is needed to monitor and slow its progress. We report a young patient who presented with nonbiliary pancreatitis. Upon finding Virchow's nodule, we conducted tests and observed multiple lymph nodes and liver and pancreatic metastasis. We subsequently made a diagnosis of AFPGC. This study describes the different presentations of this rare but aggressive subtype of gastric cancer with a review of the literature.

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Introduction

Alpha-fetoprotein (AFP) is an oncogenic marker mainly produced by the yolk sac and fetal liver tissue, but also, to a lesser extent, in the fetal gastrointestinal tract [1, 2]. AFP levels are highest between 12 and 15 weeks after birth and decrease to normal adult levels after 1 year. Higher AFP levels are also associated with hepatocellular carcinoma, yolk sac tumors, and noncancerous liver disease [3–6]. In some cancers, higher AFP levels can be detected in tumors of the stomach, lung, pancreas, colon, bladder, and ovary [7–13]. Bourreille et al. [14] reported the first AFP-producing gastric cancer (AFPGC) case in 1970. At present, we know that this subgroup of gastric tumors is highly aggressive.

Pancreatic metastases from malignancy are rare [15]. In autopsy series, the prevalence of pancreatic metastases ranges from 6 to 11% [16]. Renal cell carcinoma is the most common cause of pancreatic metastasis, followed by non-small-cell lung cancer, colon cancer, and sarcomas [17].

Herein, we report a patient who was initially admitted for nonbiliary pancreatitis, the underlying cause of which was subsequently found to be gastric cancer.

Case Report

A 33-year-old Turkish male patient was admitted to the emergency services for severe stomachache. His pains had started 1.5 months previously. One week before admission, he was treated at another clinic for pancreatitis. In BT scan there was lymphadenopathy in the supraclavicular, mediastinal, and abdominal regions. The color of stool samples had become increasingly darker. He had weighted 70 kg before the disease and had lost 3–4 kg in the last 3 months, and had used three packs of flurbiprofen. He had no systemic disease, and his family history was unremarkable. He smoked cigarettes for 10 pack-years. He did not drink alcohol or use herbal medicine. On physical examination, he had Troisier's sign (palpable left supraclavicular lymphadenopathy). His pain partially decreased with hydration.

Abdominal ultrasonography showed that the gallbladder had sludge, seemed sub-hydronic, was 38 mm in diameter, and was 2.5 mm thick. Blood tests showed amylase at 332 U/L and lipase at 414 U/L (Table 1). We admitted the patient to evaluate further for malignancy and nonbiliary pancreatitis.

Gastroscopy revealed a 15-mm-wide gastric ulcer on the posteroinferior wall of the gastric corpus (Fig. 1). The surrounding mucosa was hypertrophic. We performed multiple biopsies. In contrast-enhanced BT, edema was extensive in the pancreatic head and corpus. Multiple lymphadenopathies were observed in the para-aortic and paraceliac nodes and portal hilus. These findings were compatible with pancreatitis. Moreover, we performed magnetic resonance cholangiopancreatography, which revealed multiple metastases in the liver. The pancreatic head presented a soft tissue density mass measuring 80 × 60 mm, which was probably associated with metastasis.

Positron emission tomography-computed tomography scans revealed lymph nodes and lesions in several areas. There were conglomerate lymph nodes (maximum standardized

uptake value [SUV_{max}] = 13.0) in the left supraclavicular-lower jugular region. Multiple lymph nodes were found in the mediastinum, with the biggest one measuring 26 mm (SUV_{max} = 16.7). In the liver, segment 4B had an 18-mm hypodense lesion and both lobes showed multiple lesions (SUV_{max} = 11.3). The antrum of the stomach had heterogeneous lesions (SUV_{max} = 13.3), while the pancreatic head and corpus had low-density lesions (SUV_{max} = 12.3). Multiple lymph nodes were also observed in the abdomen, particularly the periportal, retrocaval, para-aortic, and common iliac regions (SUV_{max} = 12.2) (Fig. 2).

Stomach pathology revealed widespread signet ring cell carcinoma (Fig. 3). Together with the high AFP levels obtained and other findings, the patient was diagnosed with AFP-producing nonhepatoid carcinoma, and we referred him to oncology and surgery. Biliary drainage was subsequently performed because of hyperbilirubinemia. He died after 1 month.

Discussion

Our patient was admitted to the hospital for nonbiliary pancreatitis, which did not present an immediate etiology. However, the finding of Virchow's nodule was revealing, leading us to uncover the underlying gastric cancer. Considering that AFPGC is an aggressive subtype of gastric cancer, the patient was already metastatic at diagnosis. Hydration decreased pancreatic pain and enzymatic action.

AFP-producing gastric tumors belong to an aggressive subtype of gastric cancer. Two different histological groups were identified by Nagai et al. [18] in 1993: AFP-producing nonhepatoid adenocarcinoma and hepatoid carcinoma. AFP gastric cancer has mostly only been diagnosed in the advanced stage. According to a 2014 study in Taiwan [19], the 1-, 3-, 5-, and 10-year survival rates of AFPGC patient with AFP levels of 20–300 ng/mL were 46.7, 28.9, 17.8, and 13.3%, respectively. In comparison, the survival rates of AFPGC patients with AFP levels >300 ng/mL at 1-, 3-, and 5-year follow-up were 15.4, 7.7, and 0%, respectively. In that study, 2.2% had papillary adenocarcinoma, 41.3% had tubular adenocarcinoma, 43.5% had poorly differentiated adenocarcinoma, 6.5% had signet ring cell carcinoma, and 2.2% had adenosquamous carcinoma, while 2.2% were undifferentiated and 2.2% miscellaneous. The liver and lymph nodes were often involved.

Tumor stage, depth of invasion, degree of lymph node metastasis, AFP expression, and p21 expression are important predictors of prognosis [20]. Increased mitosis, cell movement, proliferative activity, tumor progression, hepatocyte and receptor growth factor, c-Met, VEGF, and VEGF-C isoform expression as well as the presence of p-glycoprotein are related to AFPGC and poor prognosis [21–24]. Hirashima et al. [25] reported AFPGC to be sensitive to cisplatin, but fluoropyrimidine prodrugs (e.g., capecitabine) are ineffective [26]. Due to the aggressiveness of AFPGC, early management and aggressive treatment options are important.

Statement of Ethics

The research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. The authors wish to thank the family member who kindly gave written informed consent for this case to be presented in this report, including images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Dr. A. Yavuz wrote the manuscript and is the article guarantor. Dr. B. Güleç and Dr. R.B. Girgin revised the manuscript. Dr. İ. Tuncer revised the manuscript and approved the final version.

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Fig. 1. a Virchow's nodule. b Malignant gastric ulcer in the gastric corpus.

Fig. 2. Imaging of pancreatic metastasis. a Pancreatic metastasis in computed tomography. b Extensive involvement of the pancreatic head and corpus. c Pancreatic metastasis in magnetic resonance imaging. d Diffusion restriction in stomach tumor (upper arrow) and pancreatic metastasis (lower arrow).

Fig. 3. Biopsy of the stomach corpus. **a** Widespread signet ring cell in the lamina propria (H&E, ×200). **b** Intracellular mucin in signet ring cell (PAS-AB, ×400).

Table 1. Blood test results at hospital admission

Test	Normal value	Hospital admission
AST	0–37 U/L	33
ALT	0–42 U/L	20
ALP	40–150 U/L	73
GGT	0–55 U/L	54
T.bil	0–1.2 mg/dL	0.36
D.bil	0–0.5 mg/dL	0.14
WBC	4,000–10,000/μL	6,900
Hb	13.5–17.0 g/dL	10.4
MCV	80–100 fL	90.9
Amylase	0–125 U/L	332
Lipase	<78 U/L	414
AFP	<9 ng/mL	191.63
CA125	<35 U/mL	21.4
CA19-9	<37 U/mL	35.41
CA15-3	<30 U/mL	9.6
Triglycerides	<150 mg/dL	104