Pleural Effusion as the Initial Presentation of Gastric Adenocarcinoma: A Case Report

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Patient: Male, 73-year-old
Final Diagnosis: Gastric adenocarcinoma
Symptoms: Shortness of breath
Medication: —
Clinical Procedure: —
Specialty: Oncology

Objective: Unusual clinical course

Background:
Gastric adenocarcinoma is a common malignancy, representing the third most common cause of cancer-related death globally. Most patients are initially asymptomatic, but as the cancer progresses, patients typically present with vague gastrointestinal complaints, including early satiety, heart burn, vomiting, or abdominal pain. Metastatic gastric cancer is relatively uncommon, with ~26% of patients having metastasis to a single site and 13% having metastases to multiple sites. The most common site of metastasis is the liver, followed by peritoneum, lung, and bone.

Case Report:
In this case report we describe a 73-year-old man who presented with shortness of breath, found to have large hiatal hernia along with segmental branch pulmonary embolism, bilateral pleural effusion, and diffuse interlobular septal thickening. The pleural effusion was later found to be malignant in nature and the patient was diagnosed with metastatic stage IV infiltrative gastric adenocarcinoma with metastasis to the lung and bone. Notably, the patient had no hepatic involvement.

Conclusions:
This represents a unique case, as only 2% of malignant pleural effusions are attributable to gastric cancer. Furthermore, malignant pleural effusion is an extremely rare initial presentation of gastric adenocarcinoma, especially without liver involvement, with few existing cases documented in the literature. This case demonstrates that gastric cancer should be included on the differential diagnosis as a rare cause of pleural effusion.

Keywords: Adenocarcinoma • Pleural Effusion, Malignant • Positron-Emission Tomography

Abbreviations:
GERD – gastroesophageal reflux disease; ED – Emergency Department; CTA – computed tomography angiography; EGD – esophagogastroduodenoscopy; PET – positron emission tomography; ABG – arterial blood gas; ICU – Intensive Care Unit; ETT – endotracheal tube; DNR – do not resuscitate

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/935434
Background

Gastric cancer is the third most common cause of cancer-related deaths worldwide [1]. While incidence and mortality have been on a slow decline, gastric cancer still causes significant burden to patients and the healthcare system [2]. Between 90% and 95% of all diagnosed gastric cancer cases are gastric adenocarcinoma [3]. The initial presentation of gastric cancer typically includes broad gastrointestinal complaints (eg, dysphagia, gastrointestinal bleeding, vomiting, abdominal pain) [4]. Pulmonary metastasis is relatively uncommon, comprising only 15% of all gastric cancer metastases [3]. Pleural effusion is an even more rare initial presentation, as only 2% of malignant plural effusions are attributable to gastric cancer and the current literature contains fewer than 10 instances of pleural effusion as the presenting symptom of gastric cancer [5-8]. Pulmonary metastases from gastric carcinoma are typically a late manifestation of incurable disease at the time of presentation. The following is a case of pleural effusion as the presenting symptom of stage IV gastric adenocarcinoma from an academic hospital. Reporting for this manuscript is in line with the CARE Case Report Guidelines [9].

Case Report

A 73-year-old White man with history significant for hypertension, hyperlipidemia, atrial fibrillation, gastroesophageal reflux disease (GERD), and hiatal hernia presented to the emergency department (ED) for shortness of breath. The patient stated that 2 months prior he was cleaning a storage shed in the Great-Lakes region and was exposed to dust and animal droppings. Three weeks prior, the patient had seen his primary care physician who presumptively diagnosed hypersensitivity pneumonitis and prescribed a 5-day course of prednisone followed by 2 weeks of clarithromycin, without symptomatic improvement. The day prior to the ED visit, the patient underwent outpatient pulmonary function testing and went home in stable condition. In the ED, the patient reported a 12-hour history of significant cough and shortness preceded by 2 months of worsening exertional dyspnea with concurrent onset of solid food getting stuck in the epigastric area. Review of systems was significant for intermittent pleurisy, dry cough, solid food dysphagia, heartburn, and 10-pound weight loss. A physical exam revealed decreased right-sided breath sounds and tachycardia. Vital signs showed oxygen saturation of 88% on room air, which improved to 98% on 2L nasal cannula oxygen. A computed tomography angiography (CTA) was ordered, and the preliminary report noted acute pulmonary embolism. The patient was admitted for further workup and management of acute hypoxic respiratory failure due to acute pulmonary embolism.

The patient was a former 19-pack-year smoker and endorsed occasional alcohol consumption. He was a retired Army veteran who worked for over 30 years in chemical manufacturing and was exposed to several solvents during that time. Past surgical history included appendectomy, prostate ablation, and retinal surgery. He had a non-anaphylactic allergy to latex and his home medications included omeprazole 20 mg tablet twice daily, atorvastatin 20 mg tablet once daily, losartan/hydrochlorothiazide 100/25 mg tablet once daily, and Motrin 200 mg tablet as needed. The patient had health insurance and experienced no barriers to health care access.

On admission, CTA showed a large hiatal hernia along with segmental branch pulmonary embolism, bilateral pleural effusion, and diffuse interlobular septal thickening, thus anti-coagulation with IV unfractionated heparin was initiated (Figure 1). Pleural fluid analysis from diagnostic thoracentesis was exudative (PH: 7.35, LDH: 1310 u/l), with cytology suggestive of metastatic adenocarcinoma. Due to the cytology being suggestive of adenocarcinoma, further studies were conducted to find the source. Microscopic examination of a cell block from the right pleural fluid revealed numerous tumor cells arranged in clusters with high n/c ratios, vacuolated cytoplasm, enlarged nuclei, irregular chromatin, and prominent nucleoli. Immunostaining of pleural fluid revealed expression of CDX2, CX7, and partially CK20, and negative TTF-1, suggesting adenocarcinoma of gastrointestinal origin. On day 5 of hospitalization,

Figure 1. CT angiogram of chest showing right lower lobe segmental branch pulmonary embolism demonstrated by the red arrow, diffuse interlobular septal thickening with associated ground glass, bilateral pleural effusion, and massive hiatal hernia causing compression of the left atrium and pulmonary veins.
esophagogastroduodenoscopy (EGD) demonstrated diffusely thickened, edematous, nodular gastric folds, and an erythematous nodular duodenal bulb at the posterior wall (Figure 2). Duodenal and stomach biopsy results confirmed the diagnosis of invasive, diffuse gastric adenocarcinoma. General surgery was consulted for possible hiatal hernia repair, but given the poor clinical picture and alternative reasons for the cough, the decision was made to forgo treatment until after further GI and pulmonary workup. On admission day 8, the patient’s pulmonary function was stable on supplemental oxygen and a chest X-ray showed the pleural effusion had resolved. The patient was discharged home on 2L nasal cannula oxygen and oral prednisone with management of gastric adenocarcinoma by outpatient Oncology and respiratory comprise by outpatient.

**Pulmonology**

Two weeks after discharge, an outpatient positron emission tomography (PET)/CT scan revealed increased activity in bilateral lung fields and diaphragmatic surfaces (Figure 3), along with bone metastases. Notably, there was no increased activity in the stomach or duodenum. The CT also revealed ground-glass opacities in the bilateral upper lung fields along with interlobular septal thickening. Due to the pulmonary imaging findings combined with reported worsening shortness of breath, the patient was sent to the ED.

From the ED the patient was admitted for acute hypoxic respiratory distress due to worsening malignant pleural effusion. He was placed on 5L NC after which arterial blood gas (ABG) returned pH of 7.37, PCO2 of 41 mmHg, PO2 of 49 mmHg (moderate hypoxemia), and HCO3 of 24 mmol/L. Pulmonary was consulted and the patient was transferred to the intensive care unit (ICU) for higher-level care. The patient stated that he had progressive worsening of his shortness of breath with increased anxiety over the past few days. He was unable to lay flat and woke up panicking shortly after falling asleep. Decreased dietary intake was also noted. Physical exam revealed decreased bibasilar breath sounds, widespread bilateral rales, and tachycardia.

The patient was started on high-flow oxygen and Eliquis was held in anticipation of thoracentesis and/or chest tube placement. The patient developed acute urinary retention and left-sided hydronephrosis requiring foley placement. Oncology deemed chemotherapy was inappropriate due to the patient’s worsening clinical status, thus palliative care was consulted. The following morning on admission day 1, the patient required intubation. Subsequent renal failure and shock developed, requiring vasopressors and continuous renal replacement therapy.

On admission day 2, bilateral pigtail chest tubes were placed, which returned pleural fluid consistent with metastatic adenocarcinoma. Overnight, the patient’s endotracheal tube (ETT) cuff blew and had to be exchanged. The following morning, on admission day 3, the patient had high plateau pressures and bedside bronchoscopy showed significant mucous plugging. The patient had increased agitation requiring sedatives and paralytics to maintain ventilator compliance.

On admission day 4, the patient had worsening leukocytosis and appeared to be progressing into acute respiratory distress syndrome (ARDS). The antibiotic regimen was escalated to Vancomycin and Cefepime with a low tidal volume ventilator strategy. On admission day 5, an attempt to remove the

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**Figure 2.** Series of images from esophagogastroduodenoscopy showing in image A. An irregular Z-line and a 4 cm hiatal hernia, in image B. A 2-cm tongue of salmon-colored mucosa in the esophagus, and in image C. Diffusely thickened circumferential edematous nodular gastric folds.
The symptomatic presentation with metastatic adenocarcinoma of this case is unique. Metastatic gastric cancer is relatively uncommon, with ~26% of patients having metastasis to a single site and 13% having metastases to multiple sites [3]. A variety of testing and imaging showed multiple sites of metastasis for our patient, with stomach and duodenal biopsies consistent with invasive gastric adenocarcinoma and PET/CT imaging showing evidence of lung, pleural, diaphragmatic, and bony metastasis. Pleural and bony metastases are also quite unique, as the most frequent sites of gastric cancer metastasis are the liver (48%) and the peritoneum (32%), and more rarely the lung (15%) and bone (12%) [3]. Interestingly, the PET scan after the patient’s initial hospitalization did not demonstrate increased uptake in the stomach or duodenum despite biopsy-proven disease. While PET scan has significant utility for early detection of various PET-avid tumors, its utility with gastric carcinomas is widely debated due to varying sensitivities and current lack of guidelines for gastric carcinoma work-up [12]. Additionally, although PET scans may be used to complement anatomic imaging in gastric cancer, its utility in staging is not well understood and is not recommended by most international guidelines [13]. When surveilling for distant metastasis of gastric cancer, PET scans are less sensitive but significantly more specific than contrast-enhanced CT scans [14]. Therefore, PET scans should be used in concert with other modalities so as to not underestimate the degree of tumor spread.

Initial symptoms of gastric cancer include some mix of vague gastrointestinal symptoms. Symptoms of gastric cancer are typically defined as either ‘early stage’ or ‘alarm’ symptoms [2]. Identifying and diagnosing gastric cancer at an early stage is difficult for 3 main reasons: (1) many gastric cancers have long precancerous phases, (2) the early stages of most gastric cancers are asymptomatic, and (3) when patients experience ‘early stage’ symptoms they are often vague and mistaken for more benign gastrointestinal manifestations. ‘Alarm’ symptoms alert the patient to the underlying issue and bring the patient to receive a further workup. Common alarm symptoms include dysphagia, weight loss, and palpable abdominal mass. Alarm symptoms are typically insidious from the standpoint that when noticeable symptoms arise, the underlying cancer has typically progressed or metastasized, conferring a worse prognosis. About 62% of gastric cancers are diagnosed after metastasis has occurred, procuring a 5-year survival rate of 32% [15]. Our patient aligns with this concept, initially presenting with alarm symptoms of worsening shortness of breath, intermittent pleurisy, dry cough, dysphagia with solid food, and 10-pound weight loss, leading to the eventual discovery of malignant pleural effusion due to late-stage gastric adenocarcinoma. It is important to consider, in this case, that the dysphagia was at least in part due to the large hiatal hernia. It is also important to consider there were multiple compounding factors that contributed to the shortness of breath.

Gastric adenocarcinoma is the most common type of gastric cancer and commonly arises in the distal stomach with a long precancerous phase [1,10]. The leading risk factor for gastric adenocarcinoma is H. pylori infection. Other known risk factors include gastroesophageal reflux disease (GERD), tobacco smoking, alcohol consumption, dietary consumption of salt and nitrosamines, obesity, radiation, and gastric surgery. This patient had a history of GERD, which affects ~30% of the U.S. population, and has an association with increased risk for esophageal, esophagogastric, and proximal gastric cancer [1,11,12].

Discussion

Gastric adenocarcinoma is the most common type of gastric cancer and commonly arises in the distal stomach with a long precancerous phase [1,10]. The leading risk factor for gastric adenocarcinoma is H. pylori infection. Other known risk factors include gastroesophageal reflux disease (GERD), tobacco smoking, alcohol consumption, dietary consumption of salt and nitrosamines, obesity, radiation, and gastric surgery. This patient had a history of GERD, which affects ~30% of the U.S. population, and has an association with increased risk for esophageal, esophagogastric, and proximal gastric cancer [1,11,12].

patient from sedation was unsuccessful due to worsening tachypnea. Life-support measures were withdrawn and the patient was terminally extubated.

Figure 3. PET/CT scan with increased activity along the right posterior pleural surface, bilateral diaphragmatic surfaces, left posterior acetabular bone, right SI joint, S2 segment of the sacrum, and the spine between T11 and L5. Notably, no increased activity is seen in the stomach or duodenum.
in this case. While the malignant pleural effusion may have led in part to the shortness of breath experienced by this patient, it may also have been caused or exacerbated by the segmental branch pulmonary embolism or the diffuse interlobular septal thickening consistent with congestive heart failure. Nonetheless, the shortness of breath prompted workup for pulmonary disease, leading to the discovery of pleural effusion, which diagnostic thoracentesis confirmed to be caused by gastric adenocarcinoma.

The segmental branch pulmonary embolism in itself is an interesting component of this case, as it may have also been caused by the hypercoagulable state induced by stage VI gastric adenocarcinoma. While in this case report we consider pleural effusion to be the ‘initial presentation’ due to specific cytology and histology demonstrating its direct malignant cause from the gastric adenocarcinoma, it is completely plausible that the pulmonary embolism was also caused by the gastric adenocarcinoma. The hematology/oncology consult on the patient’s second admission noted the likely cause of the pulmonary embolism to be hypercoagulable state due to adenocarcinoma. This well-studied phenomenon of hypercoagulation during malignancy is due, in large part, to increased secretion of procoagulant substances and inflammatory cytokines into the bloodstream, and thromboembolism occurs in around 13% of patients with gastric cancer [16].

The initial presentation of pulmonary disease due to gastric adenocarcinoma-related malignant pleural effusion is incredibly rare, and to our knowledge only 6 such cases have been documented in the literature [6-8]. While adenocarcinomas of the stomach are the most common cause of malignant pleural effusions out of all gastrointestinal tract cancers, rarely is this the initial manifestation of the carcinoma, as the gastric cancer is typically already diagnosed by the stage lung metastasis would occur [11]. The present case report is limited in that it only represents 1 patient; furthermore, it is difficult to condense the complexity of this patient’s case within a single report. The case report holds value because it demonstrates the potential for occult gastric adenocarcinoma to present overtly though pulmonary symptoms.

Conclusions

This case demonstrates a rare initial presentation of gastric adenocarcinoma-related malignant pleural effusion and highlights that gastric adenocarcinoma should be included on the differential diagnosis as a rare cause of malignant pleural effusion.

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