Case Report with Systematic Review

Chylothorax in gastric adenocarcinoma: A case report and systematic review of the English literature

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ABSTRACT

Background: Chylothorax is a rare complication of gastric adenocarcinoma and data on its identification, prevalence and outcomes are scant. Objectives: To enable identification of gastric carcinoma as a cause of chylothorax. Methods: A case report and a systematic review were conducted of all reported cases of gastric adenocarcinoma with chylothorax as the presenting complaint in the English literature. Results: Chylothorax is a rare presenting complaint of gastric adenocarcinoma. There are only 18 case reports in the world literature, of which six are in English. Chylothorax occurred variably in gastric adenocarcinoma, either as a presenting feature or as a complication of therapy. Here, we analyze the index case and six patients in whom gastric carcinoma presented with chylothorax as the initial symptom. Respiratory features of cough and dyspnea preempted any abdominal complaint. Bilateral chylothorax (66%) with associated chylosus ascites (50%) was common. Four of the six patients had skin lymphedema also as a prominent feature. The chylothoraces have been treated by therapeutic pleurocentesis, intercostal tube drainage and restriction of oral intake. Gastric adenocarcinoma was associated with high mortality (50%) and morbidity. Conclusions: Chylothorax can be the presenting feature of gastric adenocarcinoma. A thorough search for this life-threatening disease should be done before labeling the chylothorax as idiopathic.

KEY WORDS: Chylothorax, gastric adenocarcinoma, lymphedema

INTRODUCTION

Chylothorax is the accumulation of milky, lymphatic fluid in the pleural space. This can occur due to chyle leak from the thoracic duct secondary to tumor or trauma or as a post-surgical complication. Miscellaneous causes like superior vena cava obstruction and granulomatous diseases affecting the mediastinum also result in the formation of chylothorax. Rarely, the cause is unelicitable. Chylothorax is an unusual complication of gastric adenocarcinoma and data on its frequency, management and outcomes are scant.

We describe a classic case of chylothorax occurring in gastric adenocarcinoma and review all the reported cases of chylothorax as a presenting feature of gastric adenocarcinoma in the English literature.

CASE REPORT

A 23-year-old man presented with diffuse swelling in the left half of the neck and the left half of the chest of 4 weeks’ duration and gradual onset of breathlessness of 1 week duration. He also complained of early satiety and unquantified weight loss. He was a farmer by occupation, did not smoke or drink alcohol and did not have any significant past medical history. On examination, he was afebrile and normotensive, with respiratory rate of 26 breaths/min and a pulse rate of 98 beats/min. His neck swelling was a diffuse lymphedema, extending to the upper chest, up to the mammary area. The jugular venous pressure was not elevated and there was no erythema, tenderness or elevation of local temperature over the swelling. The respiratory system examination revealed findings consistent with left pleural effusion. The rest of the physical examination was unremarkable.

Investigations showed a hemoglobin count of 13.7 g/dL,
leukocyte count of 8000 cells/cm³ with 78% neutrophils and a platelet count of 2.1 × 10⁵/L. His liver function tests showed a total protein of 5.5 gms/dL, albumin of 2.7 gm/dL, normal transaminases and alkaline phosphatase of 1848 U/L. His serum creatinine was 0.8 mg/dL and lactic acid dehydrogenase (LDH) was 203 U/L (normal 140-280 U/L). Chest radiography showed a large left-sided pleural effusion. Diagnostic pleurocentesis revealed milky white pleural fluid, with a cell count of 708/cm³ and differential count of 98% lymphocytes and 2% neutrophils. The fluid was consistent with an exudative effusion (by Light’s criteria), with protein of 3.4 gm/dL, albumin of 2.4 gm/dL and LDH of 172 U/L. The other pleural fluid characteristics were glucose of 90 mg/dL, adenosine deaminase (ADA) of 5.8 U/L, amylase of 18 U/L, triglycerides of 274 mg/dL and cholesterol of 104 mg/dL. The pleural fluid analysis was suggestive of chylothorax. Cytology was negative for malignant cells in the pleural fluid and the gram stain revealed no microorganisms.

An appropriate low-fat diet for chylothorax was initiated, with most fats in the form of medium-chain triglycerides. He was also started on octreotide to reduce chyle formation. Intercostal tube (ICD) insertion and drainage was performed to relieve his grade IV breathlessness. Three hundred milliliters to 400 mL of fluid was drained per day during the first 6 days of hospitalization. A search for the cause of chylothorax was undertaken. The patient denied any history of recent trauma or abdominothoracic surgery. There was no history of any febrile illness suggestive of tuberculosis. A computed tomogram (CT scan) of the chest showed moderate lymphangitis in the left lung, left-sided pleural effusion, minimal right-sided pleural effusion and minimal ascites [Figure 1]. A CT scan of the neck region revealed multiple enlarged left submandibular, posterior triangle and supraclavicular lymph nodes, the largest measuring 2.2 cm × 1.3 cm [Figure 2]. The left internal jugular vein was narrowed by 80% as compared with the right jugular vein. This, along with the lymphangitis, was concluded as the cause of chylothorax.

Ultrasound-guided fine needle aspiration of the neck lymph node was suggestive of adenocarcinoma [Figure 3]. As part of the work-up for malignancy, his carcinoembryonic antigen was elevated with a level of 11.91 ng/mL (normal 0.2-3.8).

Upper gastrointestinal endoscopy showed an ulcerated growth with everted margins measuring 2 cm × 2 cm in the posterior part of the stomach [Figure 4]. Biopsy of the ulcer confirmed it to be signet ring cell adenocarcinoma [Figure 5]. A diagnosis of gastric adenocarcinoma with metastasis to neck nodes was made. The chylous drain reduced to 100 mL/day after the first week. He was offered chemotherapy, which he wished to receive in his home town. The patient was discharged home at his request after ICD removal. On further telephonic follow-up, it was revealed that the patient expired 4 months after diagnosis after receiving alternative medicines.

![Figure 1: CT Chest: Bilateral effusion, left more than right. Note diffuse soft tissue edema in the anterior aspect of left hemithorax](image1)

![Figure 2: CT Neck: Diffuse soft tissue edema and multiple enlarged lymph nodes on the left side. The jugular veins are shown by the thick arrows](image2)

![Figure 3: FNAC of cervical lymph node: Smear shows cluster of cells with irregular nucleus exhibiting moderate pleomorphism and moderate amount of vacuolated cytoplasm - consistent with metastatic adenocarcinoma](image3)
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MATERIALS AND METHODS

Literature search and study selection
Two of the authors (UD and PR) conducted a systematic search of the literature independently in the MEDLINE, OVID and Cochrane library databases using the terms “Gastric carcinoma”/AND “chylothorax.”

A second search was then performed using the terms “stomach cancer” AND “pleural effusion,” “stomach cancer” AND “chylothorax” and “gastric adenocarcinoma” AND “chylothorax.” In addition, another search was performed using the term “chylothorax” and abstracts were searched for possible cases of chylothorax secondary to gastric carcinoma. Only those articles that were reported in the English literature and included patients with diagnosed chylothorax fulfilling the criteria of a triglyceride level of more than 110 mg/dL or presence of chylomicrons were included for this analysis. The study was approved by the institution’s ethical review board.

Data extraction
A data extraction form was pre-designed with regard to the age, sex, clinical features, etiology of chylothorax, mode of diagnosis of chylothorax in relation to gastric carcinoma, comorbidities, treatment of chylothorax and gastric carcinoma and outcomes. Abstracts and full text articles, both or either, when available, were reviewed. Data are expressed in a descriptive manner (mean, range).

RESULTS

Our search yielded 2904 references [Figure 6]. This included 18 cases of chylothorax in gastric adenocarcinoma. Six case reports[1-5] were in the English language and full text or abstracts were available for all the 18 cases.[6-17]

Two other cases that reported chyloous effusion and signet cell adenocarcinoma are not included in this analysis as the primary cause was unknown.[18,19] One case with lymphedema, pleural effusion and gastric adenocarcinoma was also excluded as the pleural fluid characteristics confirming chylothorax were not available.[20] An additional 2883 references were excluded due to reasons such as (1) chylothorax not associated with gastric carcinoma, (2) studies in the pediatric population, (3) chylothorax was a post-operative complication and (4) published in languages other than English.

The age of the patients with chylothorax in gastric adenocarcinoma ranged from 28 to 69 years Table 1. Four of the six patients were above 50 years at diagnosis. Our patient is the youngest to be diagnosed at the age of 23 years.

Male and female patients were equally affected (M: F: 1:1). All the reported patients presented with cough, dyspnea or pleuritic chest pain of short duration except one, reported by Shibata et al.,[3] who developed chylous effusion 4 years after the initial symptom of lymphedema. The chylous effusion was bilateral in all except one case. The level of triglyceride in the pleural fluid was above 200 in all the case reports except one, and crossed 3000 in the patient reported by Majoor et al.[4] Three patients had chylous ascites and one patient had pericardial effusion associated with the chylothorax. The pleural fluid cytology was positive in four of the reported cases, although not diagnostic.

Lymphedema of the skin was another major finding in these cases, with four of the six patients and the index case presenting with the same.

Only one patient at presentation had gastrointestinal complaints in the form of abdominal pain and nausea.
DISCUSSION

Chylothorax occurs when disruption to normal lymphatic flow through the thoracic duct results in accumulation of chylous fluid in the pleural space. Less than 50% of the cases have the characteristic milky-white, opalescent nature of the chyle.[22] When the turbidity or milkiness clears after centrifugation, or when the pleural fluid cholesterol is >200 mg/dL, it is a pseudochylothorax.[23] Chylothorax is confirmed when the pleural fluid triglyceride levels exceed 110 mg/dL or in the presence of chylomicrons. The etiology of chylothorax is presented in Table 2.

The occurrence of chylothorax in gastric adenocarcinoma is rare, and several large series of patients with chylothorax, both in children[24,25] and in adults,[26‑28] have not reported any case of gastric adenocarcinoma.

The involvement of the lymphatics by the malignancy or chylous ascites leaking into the pleural space has been implicated in the causation of chylothorax in previously reported cases.[2‑4] The constriction of the left internal jugular vein causing impediment of thoracic duct drainage and the left lung lymphangitis was the purported cause of chylothorax in our patient.

Chylothorax is a late manifestation of occult gastric adenocarcinoma, as evidenced by the fulminant course and death within months in the reported patients.

Management of chylothorax depends on the underlying etiology. It ranges from careful observation without intervention and somatostatin or its analogue (octreotide), to more invasive procedures like intercostal drainage and pleurodesis, percutaneous embolization of the thoracic duct, thoracoscopic ligation of the thoracic duct or insertion of a pleuroperitoneal shunt.

Signet cell adenocarcinoma is a diffuse, mucinous type of adenocarcinoma. Large pools of mucus are produced and delivered in the interstitium by tumor cells. It is termed “signet cell” when the mucus remains inside the tumor cell, pushing the nucleus to the periphery.

Signet cell adenocarcinoma occurs more often in males and in young patients (as is the index patient), and is associated with a worse prognosis. The major risk factors are *Helicobacter pylori* infection, smoking and some dietary factors such as smoked foods. Our patient was not a smoker and was not investigated for *Helicobacter pylori* infection. Systemic chemotherapy is the treatment modality of choice in patients with metastatic disease. Palliative surgery, radiation and/or endoscopic procedures are the other treatment modalities available.

The index case is unique in that chylothorax occurred as an early presenting feature of unsuspected asymptomatic abdominal malignancy. The chylothorax was secondary to a non-lymphomatous malignancy in a young person.

Her initial endoscopy was consistent with antral gastritis. Two patients[4,21] developed gastrointestinal bleed, which led to endoscopy and diagnosis of malignant gastric ulcer. Most often, the diagnosis was established from the distant metastatic site.

Most of the patients were on parenteral nutrition and either nil oral intake or diet restriction of fats as medium-chain triglycerides to reduce formation of chylous effusion. Dyspnea was relieved by recurrent thoracentesis or intercostal tube drainage. Therapy for the primary cause, gastric carcinoma, was unsatisfactory and fatal in three of the six patients. The outcome is unknown in the rest of the cases. The index patient died 4 months after diagnosis.
Table 1: Summary of findings in patients with gastric adenocarcinoma presenting with chylothorax

| References       | Segal et al | Bautz et al | Shibata et al | Majoor et al | Altinoz et al | Kayacan et al | Our study |
|------------------|-------------|-------------|---------------|--------------|---------------|---------------|-----------|
| Year of publication | 1986        | 1991        | 1998          | 2007         | 2007          | 2008          | 2013      |
| Age/Sex          | 69/M        | 38/M        | 58/F          | 64/M         | 63/F          | 28/F          | 23/M      |
| Gl symptoms at presentation | NA          | Y           | Y             | Y            | Y             | Y             | N         |
| Weight loss      | NA          | Y           | N             | Y            | N             | N             | N         |
| Chylothorax      | NA          | Y           | Y             | Y            | N             | N             | N         |
| Pericardial effusion | N           | N           | N             | N            | N             | Y             | Y         |
| Primary tumor    | Gastro      | Probable    | Gastro        | Gastric      | Gastric       | Gastric       | Gastric    |
| Diagnosis        | established by | Open lung biopsy | Skin biopsy | Endoscopic biopsy | Endoscopic biopsy | Bronchial biopsy | lymph node FNAC |
| Pleural fluid cytology | NA          | Y           | Y             | Y            | Y             | Y             | N         |
| Endoscopy        | NA          | Ulcer on second endoscopy | Erosion in gastric body | Gastric ulcer | Large bleeding ulcer | Gastric carcinoma | Gastric ulcer |
| Time to diagnosis | 2.5 months  | Chylothorax on followup | 4 months     | 2 months     | 7 months      | 1.5 months    |           |
| Lymphedema       | NA          | N           | Y             | Y            | 673           | 3383.5        |           |
| Triglyceride level (mg/dl) | NA          | 238         | Y             | Y            | 3383.5        | 600           | 121       |
| Outcome          | NA          | Expired at 2 months | Expired at 4 months | Expired at 6 months | Referred to oncologist | Oral anticoagulants for deep vein thrombosis other treatment not mentioned | Expired at 4 months |
| Treatment received | NA          | B/L ICD, NPO, ligation of thoracic duct, pleurodesis | Repeated thoracentesis, Failed pleurodesis, NPO | Medium chain TGL, repeated thoracentesis, palliative therapy | Referred to oncologist | NPO, pig tail drainage, medium chain TGL, referred to oncologist |

Y: Yes, NA: Not available, N: No, B/L ICD: Bilateral intercostal drainage, NPO: Nil per oral, TGL: Triglycerides

Table 2: Causes of chylothorax

| Malignancy | Lymphomas | Bronchogenic carcinoma | Other solid tumors |
|------------|-----------|-------------------------|-------------------|
| Trauma     | Surgical (especially thoracic surgery) | Non surgical trauma |
| Idiopathic | Congenital | Other unidentifiable causes |
| Miscellaneous | Sarcoidosis | Congestive cardiac failure | Lymphangioleiomatosis (LAM) | Yellow nail syndrome | Gorham’s syndrome | Castleman’s disease | Superior vena cava obstruction | Kaposis sarcoma in acquired immunodeficiency syndrome (AIDS) | Radiation therapy to the mediastinum |
| Infections | Tuberculosis, histoplasmosis, or filariasis |

Lymphedema is another common finding in patients with chylothorax and occult gastric adenocarcinoma. This case highlights the importance of a thorough search for an occult malignancy when faced with a non-traumatic chylothorax in the young.

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How to cite this article: Devaraj U, Ramachandran P, Correa M, De Sozsa GA. Chylothorax in gastric adenocarcinoma: A case report and systematic review of the English literature. Lung India 2014;31:47-52.

Source of Support: Nil, Conflict of Interest: None declared.