

Chylothorax and Superior Vena Cava Syndrome as the Initial Presentation of Non-small Cell Lung Cancer, which was Successfully Resolved by Systemic Chemotherapy

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We describe a 58-year-old male who presented with chylothorax and superior vena cava syndrome (SVCS). A computed tomography (CT) scan of the chest revealed a long tumor and thrombi within the superior vena cava and bilateral brachiocephalic veins and a lobulated soft-tissue mass 10 cm in diameter in the right upper lung with chest wall involvement and massive pleural effusion. A white, milky fluid was drained from the pleural cavity by thoracentesis. Pathologic examination of a CT-guided biopsy confirmed the diagnosis of moderately differentiated squamous cell carcinoma (SCC). Therefore, SCC of the lung combined with SVCS and chylothorax was confirmed. Thereafter, he received cisplatin-based chemotherapy. The chylothorax resolved slowly and completely four months after chemotherapy.

Key words: Lung cancer; squamous cell carcinoma; chylothorax; superior vena cava syndrome

INTRODUCTION

Non-small cell lung cancer (NSCLC) accounts for 85-88% of all cases of lung cancer in Taiwan. Squamous cell carcinoma (SCC) accounts for 13.2% of all cases of NSCLC according to the cancer registry of the Tri-Service General Hospital¹. Chemotherapy plays a major role in improving the quality of life and survival of locally advanced NSCLC patients. Although pleural effusion is frequently a presenting symptom in NSCLC, an initial presentation of chylothorax is rare. There have been few reports on this condition in recent years². In lung cancer patients, chylothorax is mostly caused by complications associated with pulmonary resection. The incidence of chylothorax is 0.3-2.4%³⁻⁵. We present a case of SCC of the lung with an initial presentation of chylothorax and superior vena cava syndrome (SVCS), which resolved completely after treatment. Case reports were reviewed and clinical manifestations, risk factors and outcomes were analyzed.

Received: October 13, 2008; Revised: February 4, 2009;
Accepted: February 17, 2009

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CASE REPORT

A 58-year-old Chinese male presenting with shortness of breath was referred to our hospital in August, 2006. Progressive swelling of the neck, face and bilateral upper extremities, a dry cough and a painful sensation over the right anterior chest wall were noted for two weeks. He had been a heavy smoker for 20 years and denied a history of previous systemic disease. Vital signs were pulse rate, 102 beats/min; blood pressure, 128/70 mmHg; respiratory rate, 28 breaths/min; and oral temperature, 35.8 °C. Physical examination revealed prominent engorgement of the jugular vein and edema of the right side of the neck, the face and bilateral upper extremities. Breath sounds were absent over the right hemithorax and there were mild rhonchi over the left upper lung.

Blood biochemistry revealed the following: blood urea nitrogen, 11 mg/dl; creatinine, 0.6 mg/dl; albumin, 3.6 g/dl; total cholesterol, 185 mg/dl; triglyceride, 95 mg/dl; lactate dehydrogenase, 455 IU/l; and carcinoembryonic antigen, 1.01 ng/ml. Chest radiography revealed a consolidated lesion with massive pleural effusion in the right lower hemithorax. A computed tomography (CT) scan of the chest showed long thrombi within the superior vena cava and bilateral brachiocephalic veins (Figure 1A) and a 10 cm diameter soft-tissue mass in the right upper lung with chest wall involvement and surrounding bony destruction. Thoracentesis drained 600 ml of white, milky

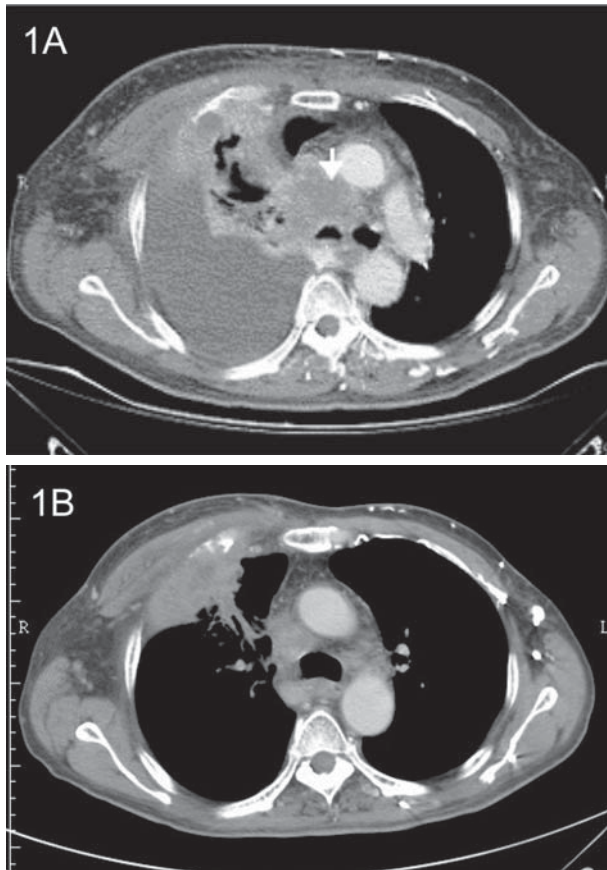


Fig. 1 (A)Tumor thrombi depicted within the superior vena cava (arrow) and massive pleural effusion of right hemithorax Figure. (B)Complete resolution of chylus pleural effusion after chemotherapy.

fluid (Figure 2), which had the following biochemical indices: pH, 8.24; triglyceride, 957 mg/dl; total cholesterol, 53 mg/dl; lactate dehydrogenase, 312 IU/l; protein, 4.34g/dl; glucose, 108 mg/dl; and carcinoembryonic antigen, 5.16 ng/ml. The fluid was negative for pathogens and cytological analysis revealed no malignant cells. An emergent pigtail catheter was inserted and the symptoms improved greatly. A CT-guided core needle biopsy was taken from the lobulated mass in the right upper lung and pathological analysis revealed moderately differentiated squamous cell carcinoma. The clinical stage of the carcinoma was T3N2M0 stage IIIb. Therefore, SCC of the lung complicated by chylothorax and SVCS was diagnosed. Chemotherapy with gemcitabine (1000 mg/m²) and cisplatin (75 mg/m²) was administered on days 1, 8 and 15 and on day 1, respectively of six 28-day cycles. The swelling of the right neck and bilateral upper extremities improved quickly and greatly after the first cycle of chemotherapy. He also



Fig. 2 Milk- like pleural fluid was drained out from pleural effusion.

received chest-tube drainage and a low-fat diet to control the chylothorax. The average amount of chyle effusion was 575 ml per day (300-1000 ml per day) before chemotherapy and it decreased to 410 ml per day (110-850 ml per day) after the first cycle of chemotherapy. Surgical treatment for chylothorax was considered but the patient refused. The patient was then discharged and received chemotherapy at outpatient clinics. After the fifth cycle of chemotherapy, the average chyle effusion had decreased to 220 ml per day (120-400 ml per day). The pigtail catheter was removed after the sixth cycle of chemotherapy was completed. A subsequent CT of the chest revealed complete resolution of pleural chyle effusion despite minimal resolution of the tumor thrombi in the superior vena cava (Figure 1B). Consequently, the patient underwent sequential chemotherapy with paclitaxel and pemetrexed, and underwent radiotherapy, but the tumor eventually progressed. The patient died in July, 2008 after having survived for 23 months.

DISCUSSION

The association between chylothorax and malignancy may occur as follows. Firstly, direct invasion or extrinsic compression of the thoracic duct by the tumor may increase pressure in the thoracic duct and result in its rupture⁶. Secondly, chylothorax has been identified as a complication of obstruction or high pressure in the superior vena

Table 1 Six patients of non-small cell lung cancer presented with Chylothorax

Case	Age/gender	Histology	Primary tumor site	SVCS	Previous RT	Treatment	Chylothorax remission	Reference
1	M/42	SCC	RUL	Yes	Yes	Pleurodesis with OK-432	Yes	14
2	M/66	SCC	RUL	No	Yes	Pleurodesis with OK-432	Yes	15
3	M/62	SCC	Right	No	Yes	NA	NA	16
4	M/68	Adenoca.	Right	No	No	Low fat diet, tube drainage, pleurodesis with streptokinase and C/T	No	2
5	F/79	LCC	RUL	No	Yes	Low fat diet, tube drainage, pleurodesis with streptokinase	No	10
6	M/58	SCC	RUL	Yes	No	Low fat diet, tube drainage and C/T	Yes	Our case

Abbreviations:

SCC=squamous cell carcinoma; Adenoca.=adenocarcinoma; LCC=large cell carcinoma; RUL=right upper lung; RT= radiotherapy; C/T=chemotherapy; NA=not available

cava⁷⁻⁹. In humans with an obstruction of the superior vena cava, venous pressure may increase to 20-40 mm Hg, at which point pressure in the venous system will exceed that in the thoracic duct (10-25 cm H₂O). The consequent leakage of chyle from the pleural lymphatic ducts into the pleural space may cause rupture of the duct or its collaterals. Thirdly, chylothorax is considered a late-onset complication of radiotherapy¹⁰⁻¹³, possibly because of impairment of lymph flow by radiotherapy-induced mediastinal fibrosis and narrowing of lymph vessels. This complication has been observed after treatment of soft tissue sarcoma¹¹, Hodgkin's lymphoma¹², SCC of the esophagus¹³ and SCC of the lung¹⁰.

Lung cancer chylothorax rarely occurs in the absence of lung surgery. In recent years, there have been five case reports of lung cancer-induced chylothorax^{2,10,14-16}. Table 1 shows the clinical manifestations and outcomes of the five reported cases and those of our case.

The five reported cases consisted of four males and one female. The median age of all six cases was 64 years. There were four cases of SCC, one of adenocarcinoma and one of large cell carcinoma. Dählback et al.¹⁷ studied the thoracic duct lymph fluids of seven patients with SCC of the lung and nodular metastases. Malignant cells were detected in the lymph fluid of five of seven cases. A high level of micrometastasis within the thoracic duct in patients with SCC of the lung may be mechanistically related to chylothorax. All of the cases of primary lung cancer were located on the right lung, mostly on the right upper lung. Chylothorax was predominantly located in the right pleural space and only one case was affected bilaterally. Simul-

taneous SVCS and chylothorax was observed in two cases. Of the cases reviewed, four received radiotherapy.

Management of chylothorax includes treatment of the underlying disease, repeated thoracenteses, a low-fat diet with a medium-chain triglyceride supplement, chest tube drainage and chemical pleurodesis^{6,18}. Surgical interventions such as thoracic duct ligation or a pleuroperitoneal shunt are considered when the amount of chyle effused exceeds 500 ml per day or when chylothorax persists for more than two weeks. In the cases reviewed, treatment of two cases with chemical pleurodesis was successful. In the two unsuccessful cases, surgical intervention was considered but not performed because of the poor general condition of the patients, who expired after several weeks. Chylothorax induced by obstruction or thrombi of the superior vena cava, subclavian vein or brachiocephalic vein can be improved by removal of a clotted central venous catheter and anticoagulant or thrombolytic therapy. Beghetti et al.⁸ reported that most cases of refractory chylothorax are caused by SVC obstruction. SVC-associated tumor obstruction should be treated by cytoreductive means. Our case received more than four months of aggressive chemotherapy and the chylothorax resolved completely. Treatment of the underlying cancer may have resolved the tumor thrombi of the SVC and bilateral brachiocephalic veins, which would have resulted in resolution of the obstruction and chylothorax. A rapid improvement of the symptoms of SVC syndrome after the first cycle of chemotherapy may be indicative of a favorable potential response to chemotherapy.

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