'Trickling-dwindling'

Drs. Yuk-Wo TSUI, Wing-Kin LAI

Department of Medicine and Geriatrics, Tuen Mun Hospital

History

A 24 years old lady, who was a lifelong non-smoker, presented to us because of dyspnea and abdominal distension.

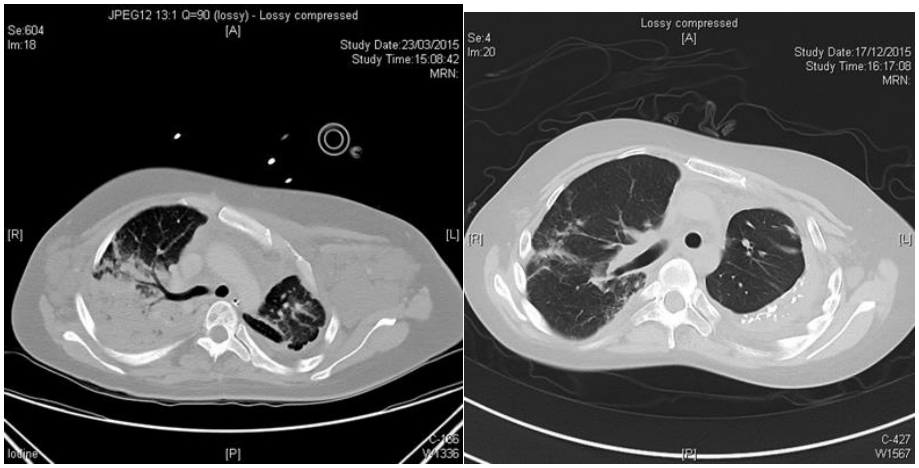
She had a past history of Wolff-Parkinson-White syndrome, bilateral pleural effusion since age of 5 and small bowel perforation with haemoperitoneum 4 years ago.

On physical examination she was having respiratory distress, with tachycardia and tachypnea. She also got low grade fever as well. On auscultation there were bilateral diffuse crackles over the chest. Abdomen was distended without focal tenderness.

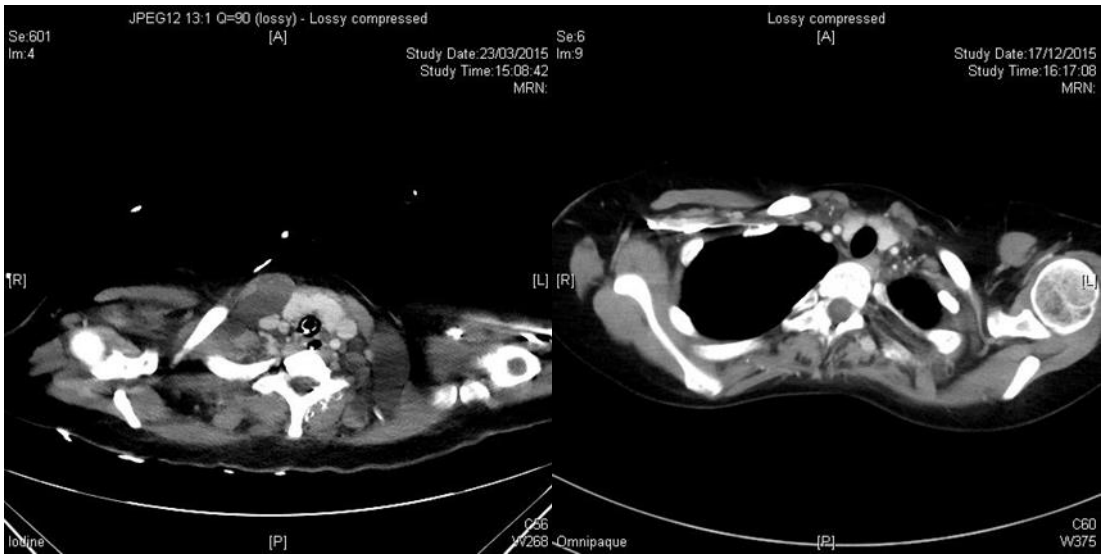
Her condition rapidly deteriorated and subsequently required intubation and subsequently intensive care. Broad spectrum antibiotics were started. Blood test showed WBC 18 x 10^9 /L. Both liver and renal function was normal at that time. However arterial blood gas showed decompensated type 2 respiratory failure. CXR showed bilateral middle zones and lower zones opacity. Microbiological workup including tracheal aspirate, blood, urine, stool and peritoneal fluid couldn't yield any causative organisms.

CT was then performed, showing bilateral pleural effusion, bilateral parenchymal changes of lung and ascites. Multiple cystic lesions at neck, mediastinal area, spine and spleen were noted. Ascitic drainage was done days later. Most significant finding was the presence of chyle inside. We then looked back years ago, found that the patient had done a laparotomy 18 years ago. Cystic lesions were obtained during that operation and results came back to be lymphangiomatosis.

The patient was then put on propranolol. However it was stopped later because of patient developed hypotension afterwards. Sirolimus was the next drug that we used. Her drain output reduced significantly with around 1-2 litres daily, compared with 3-4 litres before the use of sirolimus. Another set of CT scan was done 6 months after taking sirolimus, showing the regression of cystic lesions in the neck and reduced pleural effusion.



CT imaging of pre-treatment (left) and post-treatment (right), showing reduction in pleural effusion



CT imaging of pre-treatment (left) and post-treatment (right), showing reduction in cystic lesions at the neck region.

Discussion

Lymphangiomatosis is a very rare congenital disease which leads to abnormal dilatation and connection of lymphatic vessels. Major affected sites are lungs, bones, heart, liver, spleen and gastrointestinal tract. It mainly affects children, with a mortality as high as 40%.

It may be easily confused with another disease, lymphangioleimyomatosis (LAM). This table shows the major difference between them.

Histology is gold standard to make the diagnosis. Other supportive investigations including:

1. Imaging scans like X-ray or CT scan, to look for cystic bone lesions, pleural

effusion and diffuse ground glass opacity lung field.

2. Biochemistry, with chyle can be found in pleural effusion or ascitic fluid
3. Lymphoscintigraphy, to look for abnormal lymphatic drainage in cases of chyuria, chylothorax and chyloperitoneum.

There are no standardized treatments yet. Thoracocentesis and paracentesis can provide immediate symptomatic relief. Medium chain triglyceride are suggested but usually failed due to poor compliance.

Several drugs were proposed to be useful.

1. Propranolol can down regulate vascular endothelial growth factor (VEGF) level and hence may reduce the cystic lesion and lymphatic proliferation
2. Sirolimus, proven to be useful in treating LAM, is a specific inhibitor of mammalian target of rapamycin (mTOR). It inhibits cell proliferation by the VEGF pathway and hence induces regression of the cystic lesions. Current suggestion is to give 0.8mg per metre square per dose twice daily to maintain level of 10-15ng/mL.
3. Bevacizumab, a cancer drug, also shows disease regression in case reports.

For surgical treatment, if we can identify the affected lymphatic vessels, ligation could be done to stop the chylous fluid accumulation. Shunting can provide symptomatic relief in patients with chylous ascites by draining from peritoneal cavity back to right atrium. Lung transplant is the last resort for patients with significant lung involvement.

Lymphangioleiomyomatosis	Lymphangiomatosis
CT showed typical cystic lesions	Proliferation, dilatation, and thickening of lymphatic vessels
Smooth muscle cells of LAM react with HMB45	Spindle cells is HMB 45 ve-
Proliferating lesions composed of smooth muscle cells and epithelioid cells	Proliferating lymphatic channels and spindle cells with spaces filled up by chylous material
Female predominant	No sex predominant
Mixed obstructive and restrictive pattern in lung function test with hyperinflation and air-trapping	Mixed obstructive and restrictive pattern in lung function test without hyperinflation and air-trapping

Reference

1. Hong Kong Med J Vol 14 No. 5, October 2008
2. Bone 2010 Mar; 46(3):873-6
3. N Eng J Med 364;14, April 7, 2011
4. Laryngoscope, 121:1051-1054, 2011
5. Mayo Clin Proc, December 2014: 89(12):e129
6. Pediatr Pulomonol 2000 Apr:29(4); 321-4
7. Annals of Oncology Vol 21; No. 8; August 2010