Tuberous sclerosis with pulmonary lymphangioleiomyomatosis and renal angiomyolipomas

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Abstract: The case report describes the presentation of a 19-year old female with tuberous sclerosis who presented with progressive dyspnoea over 2 days. Chest radiograph revealed bilateral pneumothorax. Computed tomography showed features of pulmonary lymphangioleiomyomatosis and bilateral renal angiomyolipomas. The coexistence of both conditions may cause devastating morbidity and mortality.

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Introduction

Tuberous sclerosis (TSC) is an inherited disorder associated with severe learning difficulties, epilepsy, behavioural problems, skin and renal pathology. Lymphangioleiomyomatosis (LAM), characterized by alveolar smooth muscle proliferation and cystic destruction of parenchyma, occurs as an infrequent symptomatic pulmonary complication in TSC. Considered a generalized and progressive cystic lung disease that is difficult to treat with a poor prognosis, it has been reported almost exclusively in women, most commonly presenting with dyspnoea and pneumothorax in those of childbearing age.

Case presentation

A 19-year old girl presented with sudden onset of dyspnoea in the morning on 8th April 2013. Her symptoms progressively worsened and she became more dyspnoeic at night. She arrived in casualty at Hospital Tuanku Jaafar, Seremban in the early morning of 9th April 2013. She was tachypnoeic, required nasal oxygen. Her BP was 118/62mmHg, pulse 108/min. She had reduced breath sounds bilaterally. Her chest X-ray showed bilateral pneumothorax. Her breath sounds improved with chest tube drainage. The patient has been an active teenager in school. She denied any respiratory symptom and did not smoke. Past medical history was characterized by the presence of skin lesions over her face since she was a child around 3 years old. She was not aware of the cause despite had dermatology review. Patient's mother passed away at forty years old due to bilateral pneumothorax. Patient was the only child.

Patient had features of sebaceous adenoma over her nasal bridge and cheeks. She has no cardiac murmur. Abdomen examination reveal a soft mass over her right lumbar region. Patient's white cell count was 9.5x 10^9/L, hemoglobin11.2g/dl and platelet 398x10^9 /L, serum creatinine was 48umol/l, liver function normal-albumin 31g/l and alanine transaminase 12U/L. ECHO showed normal valves and chamber size. Left ventricular function was good and there was no tumor or pericardial effusion. Ultrasound abdomen: multiple hyperechoic lesions seen in both lobes of liver and bilateral kidneys (Figures 1 and 2). There was a large heterogenous mass in the lower pole of right kidney. No significant Doppler signal within. CECT thorax, abdomen and pelvis: Features are in keeping with hepatic and renal angiomyolipomatosis complicated with malignant transformation in the right kidney and segment VII of the liver. There was evidence of lymphangioleiomyomatosis. The findings are consistent with tuberous sclerosis.

The patient was referred to a respiratory physician in Hospital Serdang for further evaluation and follow up. She had right pneumostat inserted. The patient was readmitted on 25th May 2013 to Hospital Tuanku Jaafar, Seremban with pus discharge from the pneumostat site. Pneumostat was removed at A&E but patient developed right pneumothorax subsequently (Figure 3). Chest tube was reinserted. Patient was intubated and ventilated. She had left pneumothorax on the next day and left chest drain was inserted. The patient progressively deteriorated. Her lungs were trapped. The lungs were not expanding despite high setting of ventilatory support and chest tube drainage. She passed away on 31st May 2013. Cause of death was recurrent bilateral pneumothorax with underlying tuberous sclerosis (Figure 4).

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Figure 1: Multiple hypoattenuating lesions of fat density scattered in both liver lobes. One lesion demonstrate enhancement in arterial phase and washout on portovenous and delayed phases suspicious of malignancy.

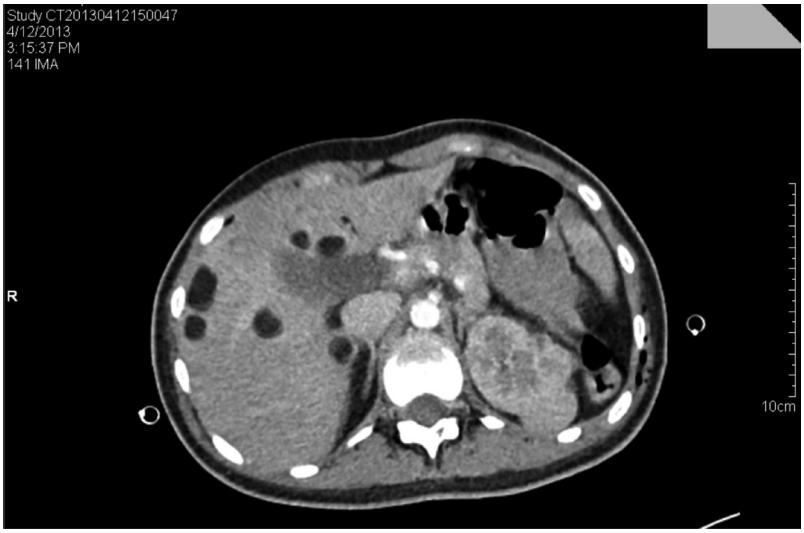


Figure 2: Right renal mass with soft tissue, angiomatous and fat components measuring 9.4x19.3 (APxWxL). Smaller nodules seen the rest of right and also the left kidney. There is poor plane of demarcation with the inferior margin of the liver and pancreas.

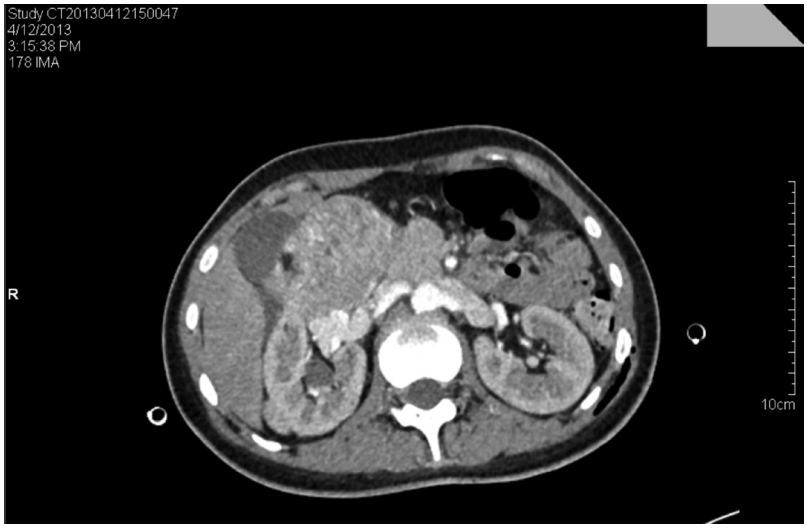


Figure 3: Right pneumothorax

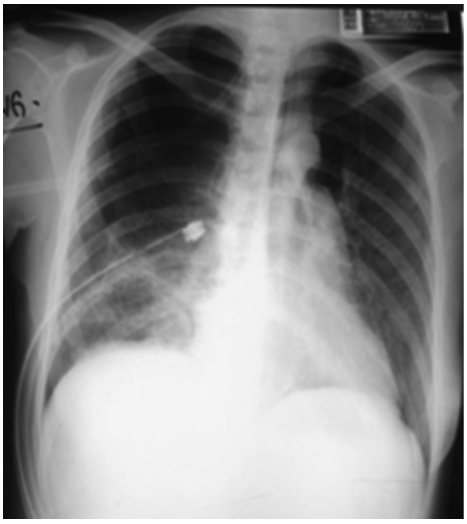


Figure 4: Bilateral pneumothorax

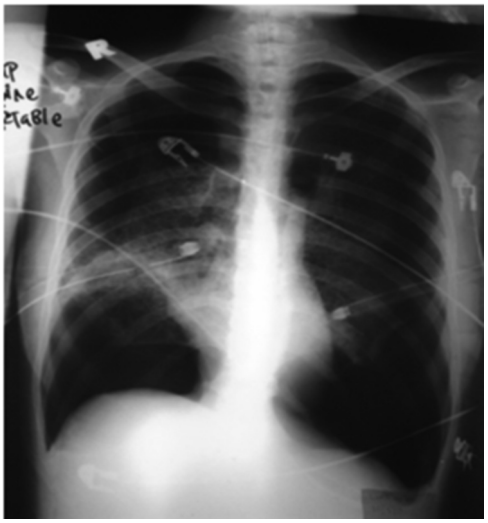
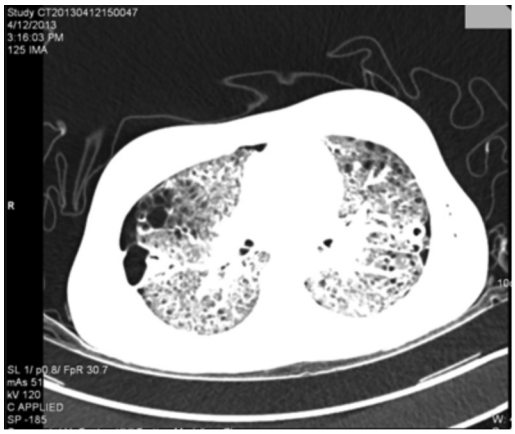


Figure 5: Multiple small thin walled cysts throughout both lungs. There are also bilateral subpleural blebs (right more than left)



Discussion

Tuberous sclerosis complex (TSC) is a rare, multi-system genetic disease that causes benign tumors to grow in the brain and on other vital organs such as the kidneys, heart, eyes, lungs, and skin. TSC is caused by defects, or mutations, on two genes-TSC1 and TSC2. TSC can affect many different systems of the body causing a variety of signs and symptoms. Signs of the disorder vary depending on which system and which organs are involved. The natural course of TSC varies from individual to individual, with symptoms ranging from very mild to quite severe. In addition to the benign tumors that frequently occur in TSC, other common symptoms include seizures, mental retardation, behavioural problems and skin abnormalities. Tumors can grow in nearly any organ, but they most commonly occur in the brain, kidneys, heart, lungs, and skin. Malignant tumors are rare in TSC. Those that do occur primarily affect the kidneys.

Lung lesions are present in about one-third of adult women with TSC and are much less commonly seen in men. Lung lesions include lymphangioleiomyomatosis (LAM) and multinodular multifocal pneumocyte hyperplasia (MMPH). Lymphangioleiomyomatosis is a rare disease of unknown aetiology, which mostly affects female.[1,2] Hormonal factors appear to play a part in both the initiation and progression of lymphangioleiomyomatosis as evidenced by the female predilection for the disease, the finding of hormone receptors on some LAM cells, and the suggestion that exogenous oestrogens[3] and pregnancy may exacerbate the disease whilst progesterone treatment may reduce its progression.

The mean age of onset for TSC in these patients was 16 years whereas the onset of lung disease was 33 years, similar to that seen in isolated lymphangioleiomyomatosis. The present patient was 19 years old. TSC is characterized by progressive dyspnoea, haemoptysis, pneumothorax, and chylous pleural effusions. Lymph nodes in the abdomen and pelvis may be involved and up to half the patients have renal angiomyolipomas.[1,2]

The lung in lymphangioleiomyomatosis contains numerous cysts, ranging in diameter from millimetres to centimetres[1], and these are responsible for the

pneumothoraces and the striking appearance of blebs over the lung surface (Figure 5). The natural history of lymphangioleiomyomatosis is of progressive airflow obstruction leading to respiratory failure and cor pulmonale. The rate of progression is highly variable between patients. The current subject deteriorated rapidly with recurrent bilateral pneumothorax complicated with trapped lungs and respiratory failure. Pneumothorax should be managed conventionally but, as it is more likely to be recurrent, bilateral, and less responsive to conservative measures, surgeons should be involved at an early stage. Recurrent pneumothorax will require pleural abrasion, talc or chemical pleurodesis, or pleurectomy. Lung transplant could be considered.

The diagnosis of tuberous sclerosis is generally made clinically and criteria have been described by Gomez[4] and the National Tuberous Sclerosis Association (NTSA). The presence of one primary feature, two secondary features, or one secondary and two tertiary features are required for a definite diagnosis of TSC. The presented subject had facial angiofibromas, affected first degree relative, renal angiomyolipoma and pulmonary lymphangioleiomyomatosis.

The overall prognosis of LAM is not good, due to the lack of effective treatment, other than lung transplantation, and death usually occurs from respiratory failure.

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