
ESIM 2013
Case Presentation
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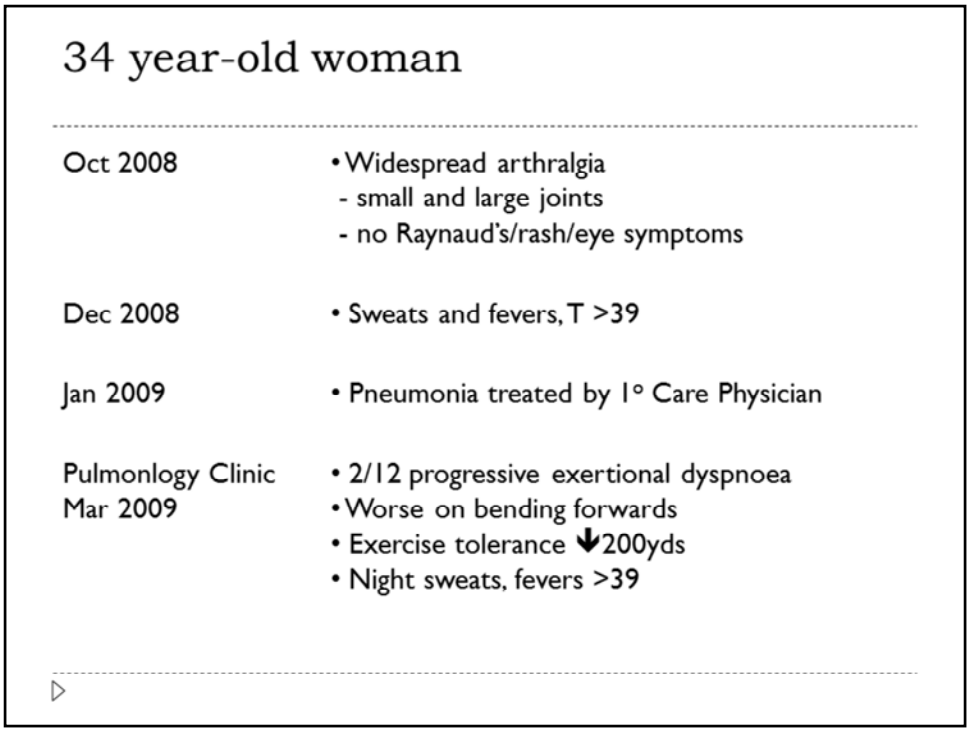
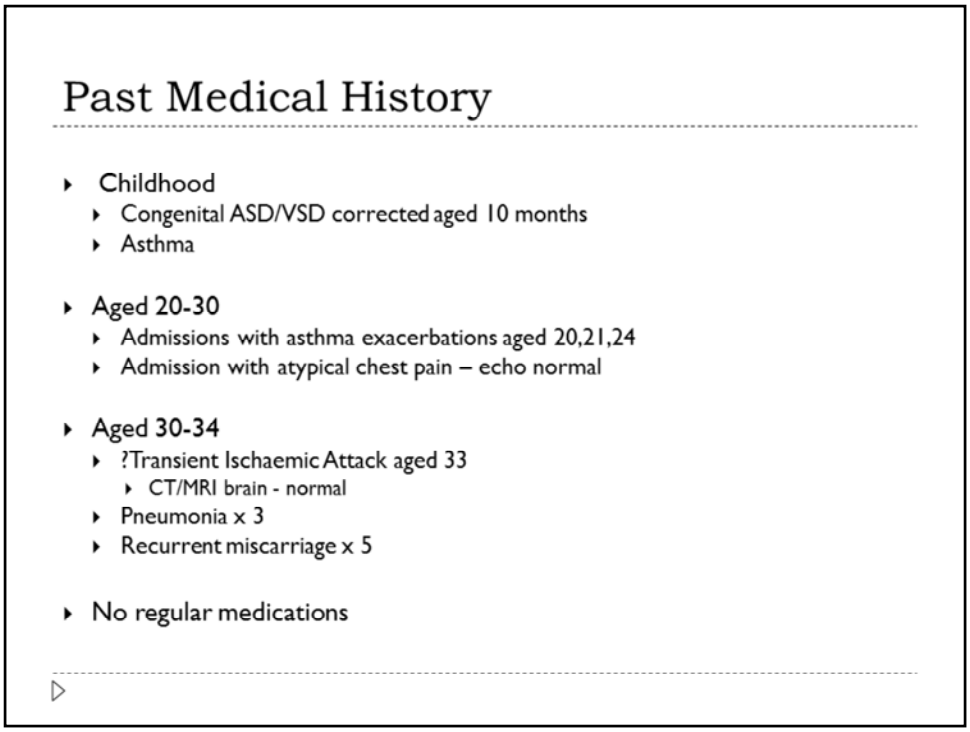
UK



The case is that of a 34 year-old woman whom I saw as a new referral to the respiratory clinic in March 2009. She gave a 2/12 hx of progressive exertional dyspnoea that had started following a chest infection. She had previously been very active but the dyspnoea now limited her exercise tolerance to 200yds and was particularly noticeable when she bent forwards. The cough had resolved but she described ongoing night sweats and had recorded fevers higher than 39 degrees.

However, on closer questioning, it was clear that she had not been well for some time and had a complex past and more recent medical history:

She first became unwell after moving to Australia in 2007 but before settling there she had travelled to Thailand, Fiji, NZ and Singapore. She was admitted in Oz with a pneumonia that was slow to resolve. In 2008 she spent several days in hospital having fainted on 3 occasions; on the last occasion she woke up with weakness/numbness affecting the left side of her body that continued for 6hrs. A CT and MRI were normal. She returned to UK in Sept 2008 and shortly after developed widespread arthralgia affecting both large and small joints. By Dec of that year she was having drenching sweats and spiking fevers higher than 39 degrees. In January 2009 she visited her general practitioner for an unrelated matter and was noted to be tachypnoeic and have focal chest signs for which she was treated with antibiotics. However, breathlessness and fevers persisted, hence she was referred to the respiratory clinic



Her past medical history was not entirely straightforward either: she had had a congenital Atrioseptal defect, ventriculoseptal defect and anomalous pulmonary drainage corrected at the age of 10 months. She had been followed up at Addenbrookes Hospital until the age of 16 but had an admission at the age of 28 with atypical chest pain and was told that an echo at that time was essentially normal. She had had asthma since childhood with 3 admissions in early adulthood, at least 3 documented pneumonias and a pulmonary embolus at the age of 22. She had also suffered recurrent miscarriages. Despite this extensive history she was not on any regular medications.

She was a current smoker, had a history of previous excess alcohol (although she didn't admit this at the time) and currently worked as a healthcare assistant, although she had previously been a dive instructor and had been very active.

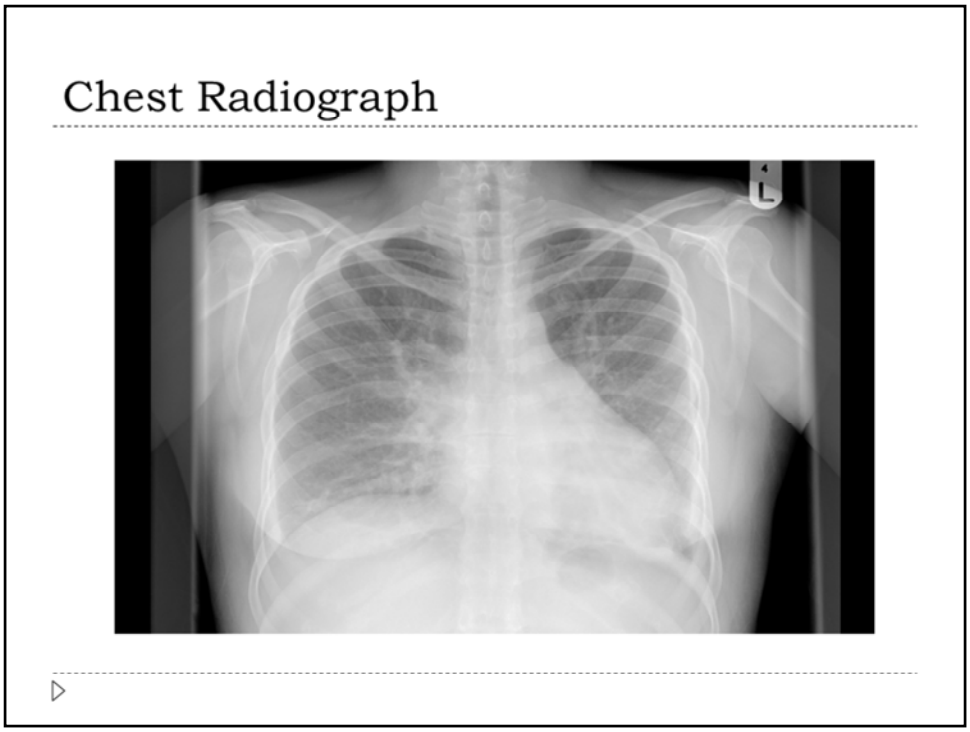
She was clearly very frustrated by the time she saw me and felt that the various healthcare professionals she had seen were not taking her symptomatology very seriously.

Social history

- Current smoker
- No illicit drug use
- Healthcare assistant
  - no occupational exposures
- No sexual risk factors
- No known TB contacts,
  - previous BCG vaccination

Examination

- No clubbing/splinter haemorrhages/lymphadenopathy
- Respiratory:
  - Oxygen saturations 96% room, no desaturation on exercise
  - Bibasal crackles, no wheeze
- Cardiovascular
  - BP 122/84
  - Normal heart sounds
  - JVP +2cms, no peripheral oedema
- Abdominal
  - Distended, soft
  - Mild right upper quadrant tenderness, no organomegaly



Would anyone like to comment on the radiographic appearances?

Well, it shows increased opacification at the right heart borderand mediastinal shift to the left but this was in fact stable over a series of films and is the classic appearance of pectus excavatum secondary to her previous cardiac surgery

Initial differential diagnosis?

Differential diagnosis

	Differential Diagnosis
Respiratory	Poorly controlled asthma
	Diaphragmatic weakness
	Pulmonary embolus
	Interstitial lung disease
	Sarcoid
Cardiac	Endocarditis
	Septal defect and shunt
	Myocarditis
Infectious	TB
	Pneumonia ?immunodeficiency ?bronchiectasis
Inflammatory	Rheumatoid arthritis
	SLE
	Antiphospholipid syndrome

So there was a lot of information to process but the initial differential diagnosis I came up with is outlined in this table.

I felt that her dyspnoea was probably respiratory in origin and given her previous history of asthma and lack of inhaled therapies wondered if her breathlessness was simply due to poorly controlled asthma. Going against this was the fact that she did not have any wheeze and she felt that this episode was very different to previous exacerbations.

I thought that she may have diaphragmatic weakness as suggested by increased symptoms on bending over.

Could her breathlessness be due to a PE?....– but she didn't have any chest pain and had normal oxygen saturations…although neither of these factors of course rules it out.

Could the bibasal crackles, and dyspnoea be due to interstitial lung disease, perhaps connective tissue-related in view of the arthralgia?

Could this be sarcoid – well just about anything could be sarcoid

In terms of cardiac aetiologies – she had this history of congenital heart disease so was it possible that she had developed endocarditis, she didn't have any peripheral stigmata and could she have developed a further septal defect and shunt?...but there was no audible murmur

Could she have heart failure, perhaps due to myocarditis in view of her young age?...but she denied CP and myocarditis is often accompanied by at least an element of pericarditis. In addition, she did not have any signs of RV failure.

Infection obviously needed to be excluded in view of the high fevers. She had an extensive travel history so TB was obviously a consideration. She had also suffered recurrent pneumonias so could this be due to underlying immunodeficiency? Could she have bronchiectasis

Lastly, was the aetiology inflammatory?

What investigations would you request?

Baseline Blood Tests

T	
Full blood count	Normal
Renal function	Normal
Liver function	Normal
C-reactive protein	4.6mg/L (<10)
Erthyrocyte Sedimentation Rate	44 (<20)
TSH	3.5 (0.4-4.5)
Corrected calcium	2.10 mmol/L (2.05-2.60)
Serum ACE	38 U/ml (8-52)
HIV	Negative
Thrombophilia screen	Negative

Immunological Tests

Protein electrophoresis	Chronic inflammatory pattern
ANCA	Negative
Latex RF	Negative
Anti-cyclic citrullinated peptide (CCP) Abs	Negative
Anti-nuclear Abs (ANA)	Negative x 2
Extractable Nuclear Antigens (ENA)	Negative
Anti-dsDNA	Negative
Anticardiolipin Abs	Negative x 4
Lupus anticoagulant	Negative x 2 Weakly positive x 1

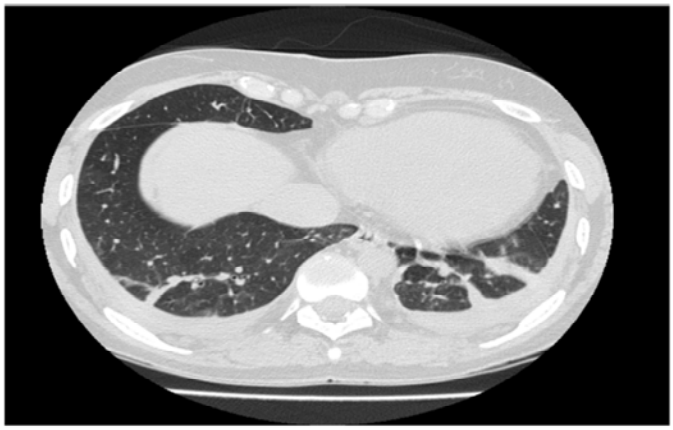
Respiratory Investigations

- Arterial Blood Gas
  - P02 9.6kpa (11-13) C02 4.6kpa (4.5-6.0)
- Lung function tests
  - FEV1 1.03 (40%), FVC 1.32 (44%), Ratio 78% = restrictive defect

	Mar 2009	May 2009	Jan 2010
FVC	1.32	1.11	0.92

  - TLCO 35% KCO 77%
- Bronchoscopy
  - Normal appearances
  - Lavage negative for acid-fast bacilli and pneumocystis jirovecii
- CT Pulmonary angiogram
  - No pulmonary embolus

High Resolution CT



Small pleural effusions, atelectasis at the bases, no interstitial lung disease

Other Investigations

- Multiple blood cultures negative
- Transthoracic echo
  - Normal valves and biventricular function
  - No evidence of pulmonary hypertension
- Transoesophageal echo
  - No vegetations
- Cardiopulmonary Exercise Test
  - Ventilatory limitation with a degree of V/Q mismatch
  - No features of cardiac dysfunction

Rheumatology Consult

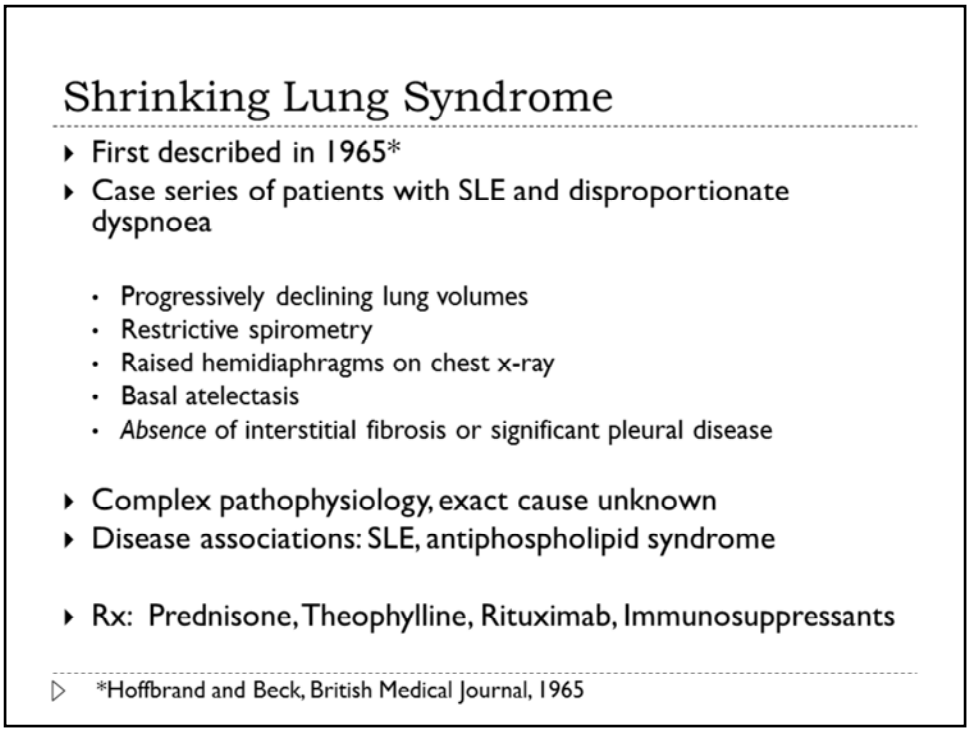
Summary

- 34 year-old woman
- Progressive dyspnoea, fevers, arthralgia
- Elevated ESR and weakly +ve lupus anticoagulant
- History of recurrent miscarriage
- Now developed livedo reticularis

Undifferentiated Connective Tissue Disease

But what is the cause of the dyspnoea?

"Shrinking Lung Syndrome"



Well, it was thought that her dypsnoea was probably due to shrinking lung syndrome, a phenomenon first described in the BMJ in 1965 by Hoffbrand & Beck. They noted that a proportion of their patients with lupus had "unexplained" dypsnoea in that there was no clinical or radiological cause found and alternative diagnoses such as heart failure had been excluded.

It is characterised by reduced lung volumes with restrictive spirometry. Raised hemidiaphragms and basal atelectasis (which is a common finding) but no evidence of interstitial fibrosis or significant pleural disease on CT.

The cause is unknown but the pathophysiology appears to be multifactorial – it has been postulated that it is due to diaphragmatic weakness or phrenic nerve palsies but diaphragmatic and phrenic nerve studies have proven inconclusive.

Various treatments have been successfully tried including steroids, theophylline, Rituximab and immunosuppressants.

There is only one case report of shrinking lung syndrome in antiphospholipid syndrome which raises the question of whether this patient was extremely rare or whether she in fact had ANA-negative lupus which is again extremely uncommon (although had been previously reported in associated with APS)?

Clinical — Vascular thrombosis (A or V) or pregnancy mortality

Laboratory Presence of aPL on 2 or more occasions at least 12 weeks apart (IgG and/or IgM

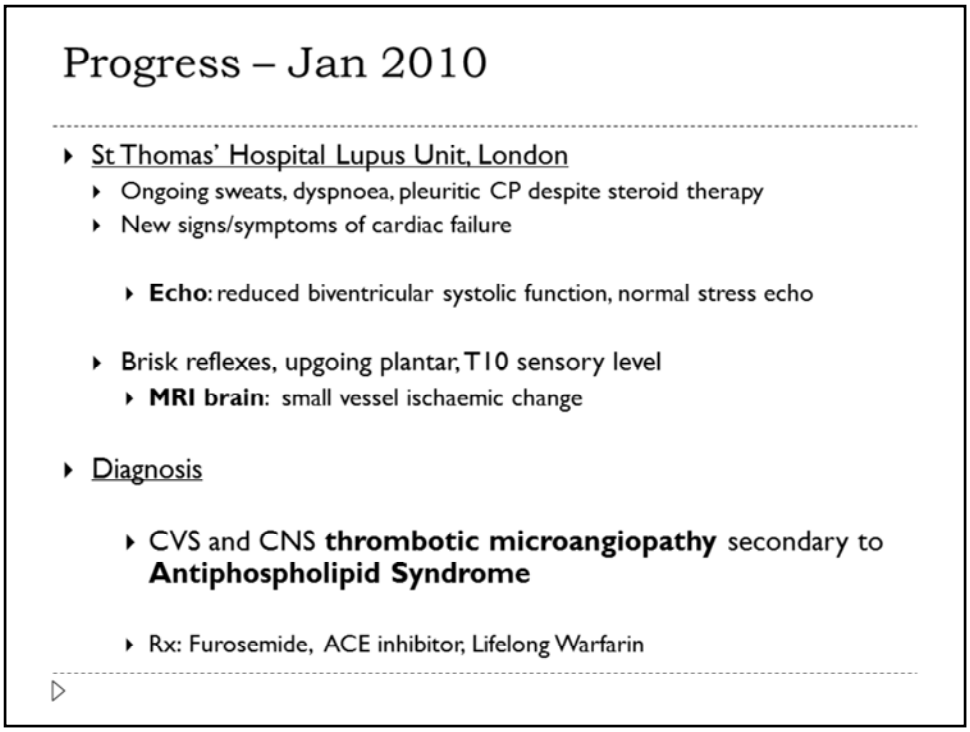
anticardiolipin antibodies

Learning Point

- In patients with:

Connective tissue disease (especially SLE)
+
Unexplained dyspnoea…

…THINK SHRINKING LUNGS!!



She was seen by the rheumatologists at her local hospital who started her on a reducing dose of prednisolone and aspirin in view of the positive lupus anticoagulant. They were still uncertain of the diagnosis and referred her to the specialist Lupus Unit at St. Thomas's Hospital in London.

Thank you

Any Questions?