A rare mimic of interstitial pneumonia

USCAP, Boston

Sunday 22\textsuperscript{nd} March 2015

"It is interstitial, but not idiopathic."

Professor Andrew G Nicholson, DM, FRCPath
Consultant Histopathologist, Royal Brompton and Harefield NHS Foundation Trust
Professor of Respiratory Pathology National Heart and Lung Division Imperial College,
London, United Kingdom
Disclosure of Relevant Financial Relationships

The USCAP requires that anyone in a position to influence or control the content of all CME activities disclose any relevant relationship(s) which they or their spouse/partner have, or have had within the past 12 months with a commercial interest(s) [or the products or services of a commercial interest] that relate to the content of this educational activity and create a conflict of interest. Complete disclosure information is maintained in the USCAP office and has been reviewed by the CME Advisory Committee.

Dr. ANDREW NICHOLSON declares he/she has no conflict(s) of interest to disclose.
Case history

- 41F
- Referred to respiratory physician October 2011
- Patient had symptoms of shortness of breath, which were present for approx 4 years. This had been progressive over a period of time.
- At time of presentation, short of breath going upstairs or up an incline, but could walk one to two miles at her own rate on a good day.
- No wheezing, chest pain, cough or phlegm.

- PMH Asthma, depression, psoriatic arthropathy treated with methotrexate, breast implants (2004).
- Current smoker up to 15 roll ups per day for 30 years.
- Alcohol – occasional
- Not working at time of presentation, but previously worked as cleaner.
- No known asbestos exposure.
- Has a dog. 10 years ago, she used to transport her sister’s racing pigeons to the training ground everyday for about 18 months, but did not notice any shortness of breath.
- Allergic to penicillin.
CT chest - Patchy ground glass scattered throughout both lungs.

No reticulonodular pattern.

No significant airtrapping on the expiratory phase scan.

No significant bronchiectasis.

No significant abnormality on the limited slices through the upper abdomen.

? HP ? RBILD
Case history

• On examination – not cyanosed or clubbed. Oxygen saturations 93% on air.

• Bibasal fine crackles on respiratory examination.

• Lung function tests FEV1 1.96 (82% predicted) FVC 2.5 (92% predicted), FEV1/FVC ratio 77%, transfer factor and transfer coefficient reduced, 59% and 69%.

• Clinical differential diagnosis
  1. Hypersensitivity pneumonitis due to previously working with pigeons,
  2. Respiratory bronchiolitis associated interstitial lung disease secondary to smoking.
  3. IP in relation to psoriatic arthropathy/methotrexate

• Bronchoscopy and transbronchial biopsy undertaken – Reported as non – diagnostic – “no features of extrinsic allergic alveolitis, few Masson bodies, no fibrosis or fibroblastic foci.”

• Patient referred to thoracic surgeon for lung biopsy.
Open lung biopsy performed February 2012

If looks “near normal” at low power, always look at the airways and vessels

Summary of histology

• ALVEOLAR INTERSTITIUM
  • *Preserved alveolar architecture.*
  • *Focal hemosiderosis.*
  • *No fibrosis and minimal inflammatory changes.*

• ALWAYS LOOK AT ALL COMPARTMENTS OF THE LUNG (AIRWAYS, VASCULATURE (ARTERIES, CAPILLARIES, VEINS, LYMPHATICS), PLEURA
  • *Many variably sized clear globules which are not birefringent are seen within the intra-alveolar capillaries diffusely throughout the biopsy.*
  • *In a few areas these globules extend into the pulmonary interstitium and alveolar spaces where they are associated with a foreign-body type giant cell reaction*
  • *Morphologically similar to “silicone mastitis”*
Silicone embolism syndrome
Silicone embolism syndrome

- Liquid silicone (polydimethylsiloxane) is an inert material that is injected subcutaneously for medical or cosmetic purposes.

- Common injection sites include the breasts, trochanteric and gluteal region. In some cases parts of the injected material enter the venous system and finally reach the pulmonary arteries.

- Clinical findings are very similar to those observed in fat embolism syndrome
  - Dyspnoea,
  - hypoxemia,
  - hemoptysis,
  - alveolar hemorrhage,
  - petechiae and altered consciousness are observed in a high percentage of these patients

- Similar to fat embolism syndrome, silicone embolism rather causes “simple” mechanical obstruction and includes inflammatory reactions.

- Given the high number of legal and illicit injections of silicone worldwide and the relatively small number of reported cases it is not far to speculate that silicone embolism is a serious but rare occurrence

- A mortality of up to 24% has been reported.
Last week in UK press.....
• Most cases have a more acute course

• This case was associated with a more chronic course and there are no reports in the literature of silicone embolism associated with a leaking/ruptured breast implant. The patient had her implants removed in April 2012. These were PIP (Poly Implant Prothese) implants, with industrial grade silicone.
Silicone pulmonary embolism: report of 10 cases and review of the literature.


- 8 male (6 male-to-female transsexuals) and 2 female subjects. Average age was 29 years.
- Most common injection sites were gluteal and trochanteric.
- Respiratory symptoms developed between 15 minutes and 2 days after silicone injection.
- 6 developed ARDS and 2 subsequently died.
- Alveolar hemorrhage was demonstrated on pathological examination in 6, with silicone vacuoles in the lung parenchyma in 3.
- CT demonstrated peripheral ground glass opacities with interlobular septal thickening in all and peripheral airspace disease in 7 cases.
- The imaging findings are very similar to eosinophilic lung diseases, drug-induced eosinophilic pneumonia and fat embolism syndrome.
A 29-year-old man who required mechanical ventilation.
Severe respiratory difficulties after bilateral gluteal injection of liquid silicone.

Peripherally distributed, bilateral ground-glass opacities and reticular interstitial opacities with interlobular septal thickening.)

Imaging of nonthrombotic pulmonary embolism: biological materials, nonbiological materials, and foreign bodies.
History of previous silicone breast implants
Recent pain in surrounding soft tissues

Not within the alveolar spaces but actually within the pulmonary capillaries

SILICONE EMBOLISM

Slides courtesy of Drs Jeffrey R. Galvin and Teri J. Franks, AFIP, Washington
Transbronchial biopsy performed October 2011.
Most common causes of different forms of nonthrombotic pulmonary embolism.

<table>
<thead>
<tr>
<th>Iatrogenic*</th>
<th>Traumatic</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>*Includes direct and long-term effects of legal and illicit medical procedures.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Bone and tissue embolism (also traumatic)</td>
<td>• fat embolism</td>
<td>• peripartal: amniotic fluid embolism</td>
</tr>
<tr>
<td>• Iodinated oil and glue embolism</td>
<td>• bone and tissue embolism (also iatrogenic)</td>
<td>• oncologic: tumor embolism</td>
</tr>
<tr>
<td>• Radiotracer embolism</td>
<td>• gas embolism (also iatrogenic)</td>
<td>• infectious: septic embolism&lt;comma&gt; hydatid embolism</td>
</tr>
<tr>
<td>• Radioactive seed embolism</td>
<td>• bullet embolism</td>
<td>• suicidal: mercury embolism</td>
</tr>
<tr>
<td>• Cement embolism</td>
<td></td>
<td>• drug abuse: talc/cotton embolism</td>
</tr>
<tr>
<td>• Gas embolism (also traumatic)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Pacemaker lead embolism</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Lost intravascular objects</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Ventriculoperitoneal shunt embolism</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Intraoperative material embolism</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Catheter embolism</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Silicone embolism</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Hyaluronic acid embolism</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Fat and other tissues
Amniotic fluid
Trophoblast
Tumour
Foreign body
Air
Talc embolism

- Most patients with talc granulomatosis are drug addicts or chronically ill.
- Drugs intended for oral administration are dissolved in water and injected intravenously
- Particles contain additives like talc (hydrous magnesium silicate), starch, microcrystalline cellulose, crospovidone, or magnesium trisilicate and/or cotton.
- Particles cause mechanical obstruction, inflammation and giant cell reaction known as talc/cellulose/foreign body granulomatosis.
- Slowly progressive dyspnea that may be responsive to corticosteroid treatment.
- Continued injection may cause pulmonary hypertension and death.

Talc embolism
Helminths: Trematodes
Schistosomiasis

- Arrive via pulmonary vasculature, but adult flukes may produce ova locally.
- Cause thrombosis, necrotising angiitis, angiomatoid lesions, eosinophilia, granulomatous inflammation.
- Can develop cor pulmonale.
- May rarely involve airways.
Pulmonary Carcinomatous Microangiopathy

- Severe obliterative fibrointimal hyperplasia.
- Response to presence of malignant cells in the pulmonary arterial system
- 3% of carcinoma patients
- 27% adenocarcinoma stomach
Veno-occlusive disease

Capillary haemangiomatosis
Other emboli…

• 37 year old male with a history of suspected alcoholic cardiomyopathy. Raised rheumatoid factor in March 2014. Gout in 2014 which was treated with allopurinol and colchicine

• September 2014 - ? Pneumonia, ? TB, ? sarcoidosis, ?? lymphoma and ?? mucinous ADC

• CT changes reported as longstanding so sent for surgical lung biopsy
“The thoracic surgeon on the other side of the telephone sounded somewhat bewildered; but then he called be back on the Monday morning to confirm that, whilst in hospital, the patient had "the mother of all" gout attacks.”

PMH: his urate levels was elevated 6 months ago and further studies showed his urate levels was still very high.
Embolic gouty tophus
Most common causes of different forms of nonthrombotic pulmonary embolism.

<table>
<thead>
<tr>
<th>Iatrogenic*</th>
<th>Traumatic</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Bone and tissue embolism (also traumatic)</td>
<td>• fat embolism</td>
<td>• peripartal: amniotic fluid embolism</td>
</tr>
<tr>
<td>• Iodinated oil and glue embolism</td>
<td>• bone and tissue embolism (also iatrogenic)</td>
<td>• oncologic: tumor embolism</td>
</tr>
<tr>
<td>• Radiotracer embolism</td>
<td>• gas embolism (also iatrogenic)</td>
<td>• infectious: septic embolism, hydatid embolism</td>
</tr>
<tr>
<td>• Radioactive seed embolism</td>
<td>• bullet embolism</td>
<td>• suicidal: mercury embolism</td>
</tr>
<tr>
<td>• Cement embolism</td>
<td></td>
<td>• drug abuse: talc/cotton embolism</td>
</tr>
<tr>
<td>• Gas embolism (also traumatic)</td>
<td></td>
<td><strong>Gout</strong></td>
</tr>
<tr>
<td>• Pacemaker lead embolism</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Lost intravascular objects</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Ventriculoperitoneal shunt embolism</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Intraoperative material embolism</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Catheter embolism</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Silicone embolism</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Hyaluronic acid embolism</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Includes direct and long-term effects of legal and illicit medical procedures.

Larger emboli
50 year old female post-surgery for varicose veins.....
The patient recovered from a shot into the left face in World War 2. Since then he did not have any severe physical complaints. Non-contrast CT demonstrated the position of the bullet in the middle lobe artery. Furthermore, massive fibrosis of the middle lobe was present, most likely due to reduced perfusion.

Conclusion

- If a biopsy looks “near normal”, always look closely at other anatomic compartments
- Use of silicone in injections/implants is increasing, so embolic disease should be considered when there is appropriate clinical history
- Clinical history is key when assessing patients with suspected interstitial lung disease
Acknowledgements:

• Dr Ahsan Ali and colleagues, Norforlk and Norwich Hospital.
• Dr Piet Swanepoel, Ampath Laboratories, East London, South Africa.

Important Information Regarding CME/SAMs

The Online CME/Evaluations/SAM claim process will only be available on the USCAP website until October 2, 2015.

No claims can be processed after that date!

After October 2, 2015 you will NOT be able to obtain any CME or SAMs credits for attending this meeting.
Thank You!

Please go to the USCAP website to complete your Evaluation of the course and claim CME and/or SAMs Credits.