Mirror Image Man

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The Man

- Asian male age 52
- Married with 2 children
- Worked for many years as a “clicker” in a shoe factory
- Smoked until a few months ago
- Not a drinker
- Medically Boarded a year ago
- Referred from NDH for a physician’s report
The Problem

- Pain in the body, always tired
- Recent episode of pleurisy
- Dyspnoea of NYHA Class 3
- Chronic cough with white phlegm (sometimes yellow)
- Wheeze throughout chest
- Poor inhaler technique
- Clinically
  - COPD/Emphysema/Chronic Bronchitis
Investigations

- CXR – the wrong way round/emphysema
- ECG – meaningless
- Ultrasound abdomen – situs inversus
- Resp functions – insufficient effort
- Endoscopy
  - Oesophageal candidiasis
  - Gastritis with “heavy growth” of H pylori
Lab Tests

- FBC – Hgb 15.8; WBC 14.9; Plt 291
- U&E and creat – Normal
- LFT – TP 76; Alb 40; T bil 20 (0-17)
- Lipids – TG 2.98 (0.4-1.8); Chol 7.28 (3.89-6.48)
- ESR – 25
Treatment

- Omeprazole 20mg daily
- Amphogel 10ml tds
- Adalat XL 30mg daily
- Nuelin 1 bd
- Inflammide 200mcg 2 puffs bd
- Asthavent 2 puffs prn
- Fluconazole
The Diagnosis

Kartagener syndrome?
Kartagener

• Manus Kartagener – Swiss physician
• Described the syndrome that bears his name in 1933
• Beaten to it by Siewert – in 1904
• Kartagener described:
  – Situs inversus
  – Chronic sinusitis
  – Bronchiectasis
Kartagener Syndrome

• Primary features:
  – Situs inversus
  – Chronic sinusitis
  – Bronchiectasis

• Secondary features:
  – Infertility in males
  – Premature deafness

• Pathophysiology:
  – Dysmotile cilia
BUT!

• Not all subjects with situs inversus have chronic respiratory tract infections – it’s actually about 1 in 5

• Not all subjects with dysmotile cilia have situs inversus – it’s actually about 1 in 2
So!

• Situs inversus and primary ciliary dyskinesia (PCD) are both hereditary genetic disorders
• The number of genetic defects that can result in these phenotypes (that are compatible with life) is large
• So the phenotypic manifestations are quite varied
PCD

• A condition in which cilia don’t behave in their normal orderly and energetic fashion (and don’t produce enough nitrous oxide)
  – they beat too slowly
  – their amplitude is too low
  – they don’t all beat in the same direction
  – they are too stiff

• The result
  – chronic respiratory tract infections
  – male infertility
  – female subfertility
Cilia – why do they beat?

• Microtubules
  – Also have structural functions in cells
    • Neutrophils need them to form pseudopoda
    • They pull the chromosomes apart in cell replication
  – Intracellular elevators
    • Constantly being formed and degraded
    • Made of tubulin molecules
    • A helix with 13 molecules in each layer
    • Act as ladders for dynein molecules which walk along them
    • Dynein molecules act as porters in the cell – carrying things on their shoulders
Cilia and Flagella

• Flagella are long cilia
• Cilia have a very rigidly defined structure
  – Centriole at the base (basal body)
  – Triplets above this in the cell cytoplasm
  – Doublets outside the cell wall
    • Single central doublet in a sheath
    • Radial arms
    • 9 peripheral doublets separated and linked by
      – Dynein arms
      – Nexin links
So What Can Go Wrong?

• The dynein arms walk along the doublets, but they can’t deform the cilia completely because of the scaffolding provided by the radial arms and nexin links

• If there are structural problems in any of these places, the system doesn’t work properly

• Even the orientation of the basal bodies is important

• So there are lots of things that can go wrong
Situs Inversus

• The audience will be comforted to know that most of us suffer from situs solitus
• Situs solitus and situs inversus are perfect mirror images of each other (none of the texts mention the incidence of left handedness in situs inversus)
• But – as you guessed – it’s not as simple as that
What Else Can Go Wrong?

• Firstly there may be discordance between the thoracic contents and the abdominal contents
  – This is much more likely to be associated with serious cardiac anomalies
  – Dextrocardia without situs inversus is much more common than situs inversus with levocardia
And That’s Not All

• Secondly there may be situs ambiguous or heterotaxy
  – There may be right isomerism (asplenia syndrome with double right atria)
  – There may be left isomerism (polysplenia syndrome with double left atria)
  – There may be variants in between
  – These are also very likely to have serious cardiac anomalies
Imaging and Malrotation

• Be very careful not to attribute an apparently wrongly labelled imaging study to the carelessness of the radiographer or radiologist.

• Always examine the patient before making up your mind which side you are going to do the thoracotomy on.
So Why The Association?

• The first organ system to start functioning in the embryo is the cardiovascular system
• Major organogenesis occurs from the 4th to the 8th week of gestation
• Microtubules must play a part
What About Our Patient?

- Definitely has a full house of dextrocardia and situs inversus

- Probably has a mild form of primary ciliary dyskinesia
The Take Home Puzzle

Why has situs solitus held sway for the last couple of hundred million years?