J R Coll Physicians Edinb 2012; 42:116–8
http://dx.doi.org/10.4997/JRCPE.2012.205
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CLINICAL

Right-sided bronchial isomerism diagnosed in adulthood

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ABSTRACT This case report describes a diagnosis of right-sided isomerism and specifically right-sided bronchial isomerism in a patient who was being investigated for deteriorating bronchiectasis. Right-sided bronchial isomerism is a variation of the normal bronchial anatomy (situs solitus) consisting of a left lung that is identically configured at the bronchial and lobar level to the right. It is sometimes referred to as bilateral right lung and is usually associated with congenital asplenia and therefore impaired immunity with susceptibility to pneumococcal sepsis and cardiac abnormalities which may be severe and result in a high mortality in infancy.[1] Ivemark syndrome (also known as right atrial isomerism) combines these associations with malrotation of the gut and a midline liver.[2] Interestingly, left-sided isomerism is associated with polysplenia as well as midline liver, malrotation of the gut, partially anomalous pulmonary venous drainage and cardiac septal defects.[3] To the best of our knowledge cases of right-sided isomerism are sufficiently rare in adulthood that there are only two other reports in the literature and only one of the patients had bronchial isomerism.[4,5]

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KEYWORDS Right-sided bronchial isomerism, bronchiectasis, respiratory

DECLARATION OF INTERESTS No conflicts of interest declared.

CASE REPORT

A 55-year-old woman was frequently reviewed in the respiratory clinic because of deteriorating health, due to repeated exacerbations of bronchiectasis. She had a complex medical history, having previously been diagnosed with ulcerative colitis, asthma and Churg-Strauss syndrome. Her family history showed that her father had died of leukaemia and that her twin sister was in good health. The patient had smoked 20 cigarettes per day but had quit eight years previously. She currently held a clerical job. It was also noted that she had tried unsuccessfully to conceive throughout her reproductive life. Churg-Strauss syndrome was diagnosed in 1995 on the basis of a strongly positive peri-nuclear (protoplasmic-staining) antineutrophil cytoplasmic antibodies (p-ANCA), rhinitis, asthma, peripheral blood eosinophilia and eosinophils in bronchoalveolar lavage. No tissue diagnosis was made and an extended course of steroids achieved resolution. It is possible that this had in fact been chronic eosinophilic pneumonia in relation to her long-term treatment with sulphasalazine for ulcerative colitis. Bronchiectasis had been diagnosed by computed tomography (CT) scan in September 2000 following an episode of lobar collapse in association with a presumed pneumonia. Since then the patient had experienced recurrent exacerbations of bronchiectasis usually precipitated by *Haemophilus influenzae* or *Streptococcus pneumoniae*. In 2004 *Pseudomonas aeruginosa* was isolated from sputum and it was aggressively treated by arranged inpatient admission for eradication therapy with intravenous gentamicin and piperacillin/tazobactam. Recent sputum cultures were negative and mycobacterial cultures subsequently proved to be negative. Chest radiography was normal. Blood tests including full blood count, urea and electrolytes, liver function, immunoglobulins (A, G [including subsets], M and total IgE), aspergillus precipitins, aspergillus specific IgE and ANCAs were unremarkable. A repeat high-resolution CT scan demonstrated bilateral right lung morphology and asplenia with evidence of worsening basal bronchiectasis (Figure 1). Functional antibodies were normal (the patient was regularly vaccinated) but ciliary motility studies revealed no demonstrable motility. Detailed ultrastructural cilial studies subsequently showed structurally normal cilia. Importantly, echocardiogram suggested no cardiac abnormality. After the patient's intercurrent exacerbation of bronchiectasis had responded to a prolonged course of macrolide antibiotic she began long-term macrolide therapy. She continues her daily physiotherapy regime to aid sputum expectoration and is regularly reviewed in the bronchiectasis clinic. The patient continues to have difficult-to-control bronchiectasis. This case raises interesting questions about the aetiology of the patient's bronchiectasis and the associations of right-sided isomerism.

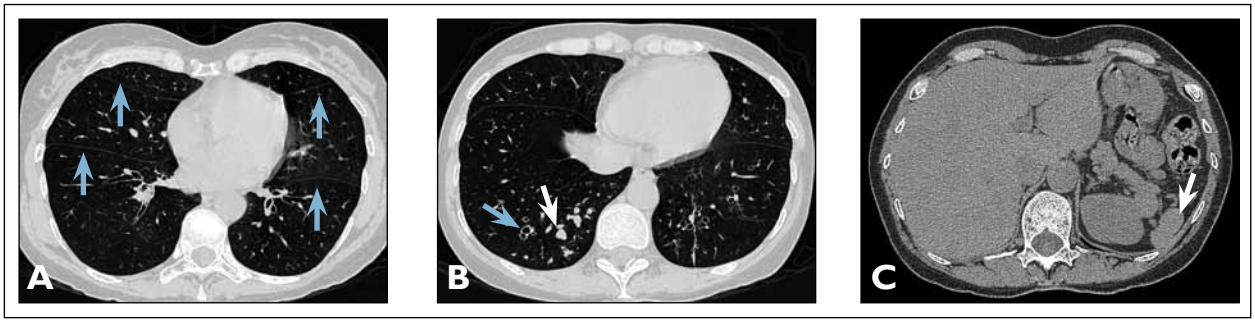

FIGURE 1A Lung image from thin section computed tomography (CT) study showing bilateral oblique and 'horizontal' fissures (marked with blue arrows). **FIGURE 1B** Lower zone lung CT section showing basal bronchiectasis (example marked with blue arrow) and nearby dilated bronchi plugged with mucus (example marked with white arrow). **FIGURE 1C** Upper abdominal CT section showing small splenunculus (marked with white arrow).

DISCUSSION

Our patient has a complex constellation of conditions, pathologies and problems. These may have arisen independently but one could postulate a common origin for some of them. The aetiology of bronchiectasis in this case is difficult to assign but could be idiopathic, inflammatory bowel disease, post-pneumonic, primary ciliary dyskinesia or a new association of bronchiectasis with right-sided isomerism.

Bronchiectasis is the most common pulmonary manifestation of inflammatory bowel disease,[6] asthma may also be associated,[7] while Churg-Strauss syndrome can cause bronchial wall thickening and non-specific radiographic infiltrates. The diagnosis was made following a presumed pneumonia, complicated by lobar collapse, however a post-pneumonic cause seems unlikely from a temporal perspective as a longer, non-resolving, suppurative illness would be a more classical presentation. It is possible that our patient has a variant of primary ciliary dyskinesia (PCD). Among PCD patients 50% suffer from *situs inversus totalis* and *situs* anomalies are said to be variable (even between identical twins). One could speculate that right-sided bronchial isomerism may have arisen in association with PCD. This theory would also explain the patient's struggle with infertility as sub-fertility secondary to ciliary dysfunction in the fallopian tubes is described in PCD.[8] However, although there are many described cases of left-sided isomerism in PCD patients there is only one of right-sided isomerism in a patient who had a normal arrangement of left and right lungs (i.e. no right-sided bronchial isomerism). Additionally, a rare long-lived patient with cardiac abnormalities associated with right-sided isomerism was found to have abnormal cilia at post-mortem.[4] The aetiology of right-sided isomerism has been thought to be different from PCD, a diagnosis which is dependent on immotile cilia and usually cilial abnormalities.[9] Furthermore, there are no other descriptions of bronchiectasis in cases of right-sided isomerism, though it is possible that, as right sided-isomerism frequently results in early mortality from cardiac anomalies, bronchiectasis may not have had time to develop.

Random assignment of lateralisation is rare, occurring in less than 1% of the population.[1] Bush et al. described an association of left-sided isomerism with bronchomalacia and normal atrial arrangement in 1999 and speculated that this might represent a new syndrome, extending the spectrum of left-sided isomerism.[3] The patient described here may represent a similar extension of the spectrum of right-sided isomerism.

The rarity of right-sided bronchial isomerism means that specific screening (were it available) could not be recommended. However, cases would be likely to be diagnosed during the routine, appropriate investigation of bronchiectatic patients which should include CT and screening for ciliary abnormalities. Definitive diagnosis of PCD is obtained by performing a nasal biopsy or brushing/curettage from the inferior surface of the nasal turbinates. This specimen is then assessed for abnormal ciliary motility and ultrastructure. Ciliary ultrastructural studies can only be carried out in specialist laboratories with transmission electron microscopy, as ultrastructurally normal cilia may have defective motility.[10] The gold standard for measurement of ciliary motility is high speed video microscopy with a normal range of ciliary beat frequency of 11–16 hertz (Hz), although exhaled nitric oxide is emerging as a valuable screening tool in the identification of potential PCD patients. Clearly, given the intracardiac abnormalities associated with right-sided isomerism, it is important to obtain a good quality echocardiogram and similarly to assess immune function by measurement of functional antibodies and immunoglobulin subclasses.[11]

The management of PCD and by extension right-sided isomerism must be extrapolated from cystic fibrosis (CF) and non-CF bronchiectasis as there are no specific therapies for ciliary dysfunction. It should include

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vaccination, physiotherapy to aid sputum expectoration, early identification and prompt treatment of respiratory infections and consideration of long-term nebulised or oral antibiotics.

Future research will focus on developing reliable genetic screening tests to detect situs and ciliary anomalies. Gene therapy may potentially have a role in addressing pulmonary ciliary dysfunction while advances in surgical techniques and technology may influence cardiac mortality. The specialist bronchiectasis clinic plays an important role in the proper investigation and management of these patients and may potentially offer invaluable insight into the aetiology of this challenging pathology.

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