

## Left bronchial isomerism associated with bronchomalacia, presenting with intractable wheeze

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### Abstract

**The cause of the Williams Campbell syndrome (bronchomalacia with bronchiectasis) is controversial. A boy with bronchomalacia, bifid ribs, and left bronchial isomerism presented with intractable wheeze mimicking asthma. The combination of the abdominal, bronchial, and atrial anatomy seen in this child has been described only once previously. The coexistence of these congenital abnormalities in this boy supports a congenital cause for the Williams Campbell syndrome. The need to assess wheezy children critically is emphasised.**

In 1960 Williams and Campbell described five children with widespread bronchomalacia and bronchiectasis,<sup>1</sup> postulating that the primary defect was a developmental deficiency of bronchial wall cartilage.<sup>1,2</sup> Others believe that bronchiectasis secondary to pertussis, measles, or adenovirus infection is the main abnormality, causing secondary bronchomalacia.<sup>3</sup> All previous children with the Williams Campbell syndrome have had normal bronchial anatomy—that is, the morphologically right and left lung in the right and the left hemithorax respectively. The anatomical arrangement of the lungs may be of three other forms, however: situs inversus, right isomerism (two morphologically right lungs), and left isomerism (two morphologically left lungs). The morphology of the bronchial tree is variously defined on the basis of the length of the main bronchus before the takeoff of the upper lobe bronchus, the relation between the pulmonary artery and the upper lobe bronchus, and the number of lobes in the lung.<sup>4-7</sup> These anatomical arrangements are of clinical importance—right isomerism may be associated with asplenia (Ivemark's syndrome) and left isomerism with polysplenia.<sup>4</sup> Both left and right isomerism may be associated with malrotation of abdominal viscera and congenital heart disease.<sup>4,5</sup> Atrial situs and bronchial situs are normally identical,<sup>6</sup> an important consideration in the sequential description of cardiac anatomy in the setting of congenital

heart disease.<sup>7</sup> This report describes a boy who had had intractable wheezing from infancy as a result of widespread discrete areas of bronchomalacia without bronchiectasis, and who also had some minor congenital malformations and a rare combination of bronchial, atrial, and abdominal anatomical arrangements. We report this case because of the unusual anatomy and other congenital malformations, and to emphasise the care needed in assessing wheezy children.

### Case report

This 12 year old boy was referred as a case of steroid resistant asthma. He had had recurrent episodes of coughing and noisy breathing from the age of 5 months, usually precipitated by an upper respiratory infection. At 22 months a murmur was noted during an episode of right lower lobe pneumonia, and he subsequently underwent ligation of a patent arterial duct. He subsequently developed wheezing in the early morning, a chronic cough, and breathlessness on minimal exertion, despite inhaling salbutamol and beclomethasone. A trial of oral prednisolone, 30 mg daily for one week, failed to improve his symptoms. The only physical finding of note was widespread inspiratory and expiratory wheeze, more pronounced on the left. Investigations included a normal full blood count, an erythrocyte sedimentation rate of 5 mm in one hour, and normal immunoglobulins; no serological evidence of viral infection, and normal results from an auto-antibody screen. The chest radiograph showed bifid left first and fourth ribs, but was otherwise unremarkable. A barium swallow and a computed tomogram of the thorax were normal. Lung function test results, expressed as % predicted,<sup>8</sup> were: forced expiratory volume in one second (FEV<sub>1</sub>) 33%; forced vital capacity (FVC) 65% (FEV<sub>1</sub>/FVC ratio 43%); total lung capacity (TLC) 72%, residual volume 91%, and carbon monoxide transfer 89%. Specific airways conductance (sGaw) was 1.15 s<sup>-1</sup> kPa<sup>-1</sup> (normal > 1.3 s<sup>-1</sup> kPa<sup>-1</sup>). Ten second accessible lung volume was 87% of TLC, and carbon monoxide transfer/litre of accessible volume (Kco) was 135% predicted. The flow-volume loop showed (fig 1) substantially reduced expiratory flow, particularly at low lung volumes, with relatively well preserved inspiratory flows. Fiberoptic bronchoscopy with bronchography showed a normal trachea with left isomerism (fig 2). Localised areas in both main bronchi narrowed to slits on expiration, reopening on inspiration so that the bronchoscope could easily be passed through to the more normal bronchial tree beyond. Bronchography showed a single discrete proximal area of narrowing in the left sided bronchial tree, and multiple additional areas of variable narrowing in the subsegmental bronchi beyond the narrowing in the right sided main bronchus. There was no evidence of bronchiectasis. An echocardiogram was normal, showing the usual arrangement of atria. Abdominal ultrasound showed normal visceral positions with a single spleen.

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Accepted 15 February 1991

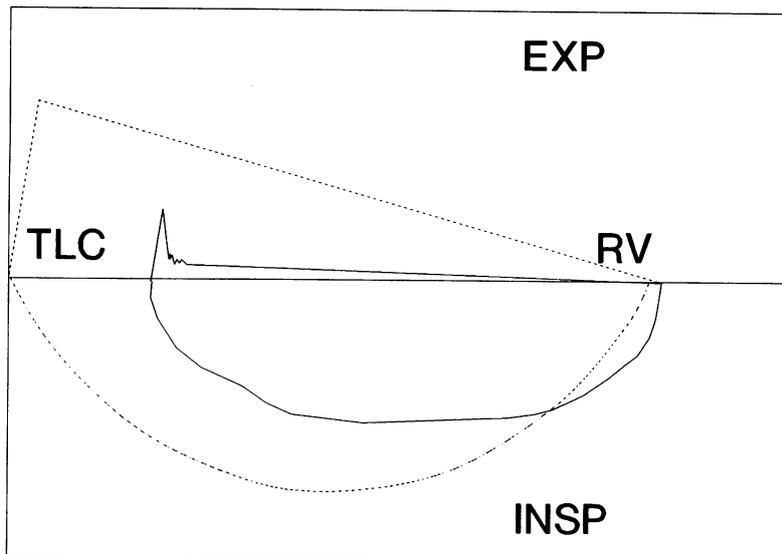


Figure 1 The flow-volume loop. The predicted loop is given by the dotted line, and is based on the work of Denison *et al.*<sup>11</sup> There is disproportionate reduction in expiratory flow rates, with a normal residual volume (RV) and slightly reduced total lung capacity (TLC). INSP—inspiration; EXP—expiration.

### Discussion

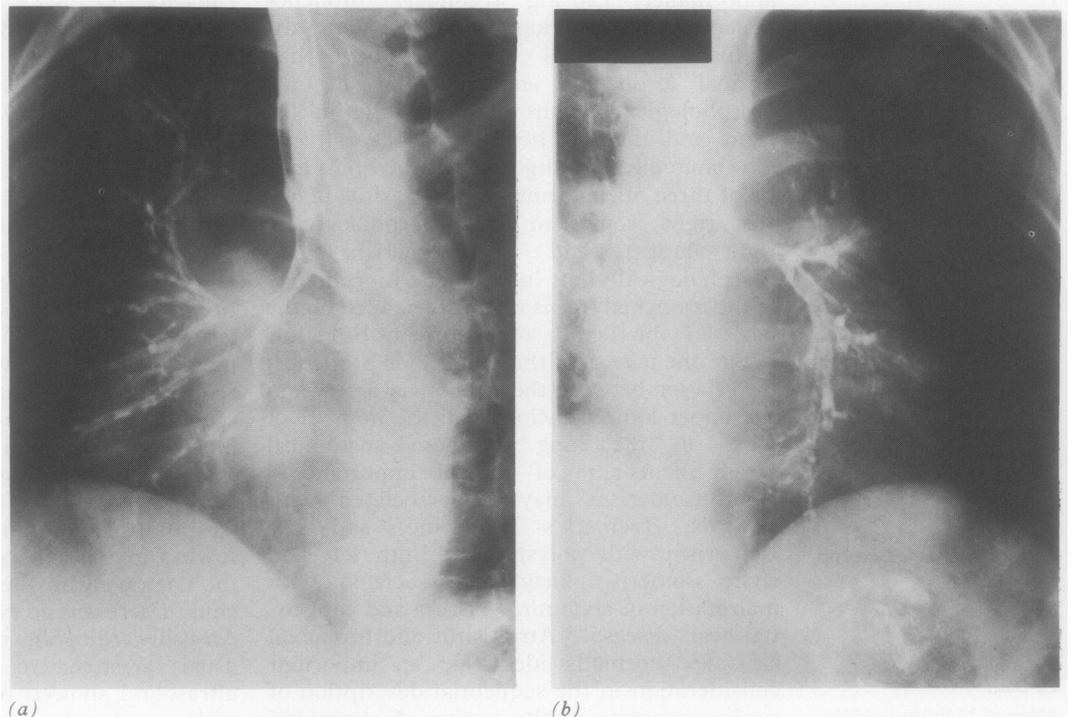
There has been disagreement in published reports about whether the Williams Campbell syndrome is truly congenital or acquired secondary to a viral infection.<sup>2,3</sup> In favour of a congenital cause is its occurrence in two siblings<sup>9</sup> and the report of a four month old baby with symptoms from birth and generalised bronchomalacia without bronchiectasis.<sup>10</sup> The negative serological results in this child and other patients<sup>1,2</sup> suggest that a viral cause is unlikely, but infection cannot be excluded as an aetiological factor in some cases. Our patient had had symptoms from 5 months of age, which

in retrospect were attributable to bronchomalacia. The lung function tests showed relatively well preserved inspiratory flows and sGaw despite severe expiratory obstruction. The close agreement between accessible lung volume and TLC suggests that there was no substantial small airways disease, and the Kco was not reduced, suggesting that the lung parenchyma was probably not severely diseased. Bilateral bronchography and computed tomography of the thorax showed no evidence of bronchiectasis, but did show large airway disease—namely, discrete areas of narrowing of both main bronchi and numerous localised subsegmental areas of bronchomalacia on the right side, similar to those in the original description of the syndrome.<sup>1</sup> The areas of malacia were very localised and separated by regions of normal bronchi, suggesting that they were merely secondary to raised intrapleural pressure from another cause. The boy also had other congenital anomalies (left bronchial isomerism, bifid ribs, and a patent arterial duct), all of which strongly support a congenital origin.

Also of interest is the discrepancy between the abdominal and thoracic anatomy in this boy. All previous patients with the Williams Campbell syndrome have had a normal atrial and bronchial arrangement. Our patient had normal abdominal viscera with a single normally placed spleen, normal atria, but left bronchial isomerism. These anatomical features have been described only once before.<sup>6</sup>

We were in doubt about how to manage this child. There are no published reports of bronchial stenting in children, other than in the setting of heart-lung transplantation. It was felt that consideration of this procedure should if possible be postponed until adulthood. He is therefore having regular chest physiotherapy

Figure 2 Appearance of the bronchoscopic bronchogram: (a) right sided lung; (b) left sided lung. There is left bronchial isomerism and narrowed regions in both main bronchi, with more widespread narrowing of the segmental bronchi of the right sided lung. Contrast remains in the normally placed stomach from a previous barium swallow.



with aggressive treatment of any infection in an attempt to prevent progression to bronchiectasis.

In summary, this child had bronchomalacia of the pattern seen in the Williams Campbell syndrome and other congenital abnormalities, previously not encountered together, which supports a congenital cause for this syndrome. The case also emphasises the need critically to assess all wheezy children. For many years this boy was thought to have asthma, and was even treated with systemic corticosteroids. Flow-volume loops can show large airway disease and, as in this child, may alert the clinician to the possibility of another diagnosis.

- 1 Williams H, Campbell P. Generalised bronchiectasis associated with deficiency of cartilage in the bronchial tree. *Arch Dis Child* 1960;35:182-91.
- 2 Williams HI, Landau LI, Phelan PD. Generalised bronchi-

- ectasis due to extensive deficiency of bronchial cartilage. *Arch Dis Child* 1972;47:423-8.
- 3 Capitanio MA. Commentary. *J Pediatr* 1975;87:233-4.
- 4 Landing BH, Lawrence TK, Payne CV, Wells TR. Bronchial anatomy in syndromes with abnormal visceral situs, abnormal spleen and congenital heart disease. *Am J Cardiol* 1971;28:456-62.
- 5 Deanfield JE, Leanage R, Stroobant J, Chrispin AR, Taylor JFN, Macartney FJ. Use of high kilovoltage filtered beam radiographs for detection of bronchial situs in infants and young children. *Br Heart J* 1980;44:577-83.
- 6 Caruso G, Becker AE. How to determine atrial situs? Considerations initiated by 3 cases of absent spleen with discordant anatomy between bronchi and atria. *Br Heart J* 1979;41:559-67.
- 7 Shinebourne EA, Macartney FJ, Anderson RH. Sequential chamber localisation: the logical approach to diagnosis in congenital heart disease. *Br Heart J* 1976;38:327-40.
- 8 Cotes JE. *Lung function: assessment and application in medicine*. 4th ed. Oxford: Blackwell, 1979.
- 9 Wayne KS, Taussig LM. Probable familial congenital bronchiectasis due to cartilage deficiency (Williams Campbell syndrome). *Am Rev Respir Dis* 1976;114:15-22.
- 10 Agosti E, de Filippi G, Fior R, Chiussi F. Generalised familial bronchomalacia. *Acta Paediatr Scand* 1974;63:616-8.
- 11 Denison DM, Du Bois R, Sawicka E. Pictures in the mind. *Br J Dis Chest* 1983;77:35-50.

*Thorax* 1991;46:461-2

## Malignant pleural effusion in chronic myelomonocytic leukaemia

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### Abstract

**A case of malignant pleural effusion due to chronic myelomonocytic leukaemia is reported.**

Malignant pleural effusions are extremely rare in patients with chronic myelomonocytic leukaemia, a haemopoietic stem cell disorder with myeloproliferative and myelodysplastic features.<sup>1,2</sup>

### Case report

A 52 year old woman presented with a three week history of lethargy, weakness, and progressive dyspnoea. Examination disclosed bilateral pleural effusions, greater on the left than the right side, minimal generalised lymphadenopathy, and splenomegaly of 7 cm. Chest radiography and computed tomography showed mediastinal lymphadenopathy and bilateral pleural effusions. Abdominal computed tomography showed hepatosplenomegaly and para-aortic lymphadenopathy. A full blood count showed: haemoglobin 12.8 g/dl, white blood cells  $87 \times 10^9/l$  (neutrophils 52%, monocytes 27%, blasts 4%, promyelocytes 1%, myelocytes 4%, metamyelocytes 4%, and band forms 8%), and platelets

$205 \times 10^9/l$ ; some neutrophils were hypogranular and some platelets were noted to be large on the blood film. Bone marrow examination showed hypercellularity, active erythropoiesis, active myelopoiesis with 28% monocytes or monocytoid cells and an increased number of megakaryocytes with abnormal forms, including micronuclear and mononuclear forms. Cytogenetic studies showed an abnormal chromosome constitution: 46,XX,del(7)(q22), del(20)(q11). Clotting studies gave normal results, arterial blood gas analysis showed hypoxaemia (oxygen tension 5.7 kPa), and results of liver function tests were abnormal. Pleural fluid biochemical investigations showed: protein 38 g/l, glucose 3.7 mmol/l, and lactic dehydrogenase 482 (normal 55-120) U/30 l. Cytological examination of pleural fluid (figure) showed features of chronic myelomonocytic leukaemia. A pleural biopsy was not done. Excision biopsy of an axillary lymph node showed diffuse monocytoid leukaemic infiltration, with frequent mitotic figures.

During the four days when investigations were in progress, repeated left sided thoracenteses were required for symptomatic relief, and her white blood cell count increased from 87 to  $130 \times 10^9/l$ . She was started on treatment with low doses of cytarabine (10 mg/m<sup>2</sup> every 12 hours subcutaneously), 6-thioguanine (40 mg every 12 hours orally), and etoposide (100 mg a day orally) for 10 days, with good results. Six weeks later she was clinically well with reduced splenomegaly (4 cm); her chest radiograph showed a small opacity at the left base posteriorly. Her haemoglobin (11.5 g/dl), white blood count ( $32 \times 10^9/l$ ), and platelets ( $60 \times 10^9/l$ ) had also improved. Further treatment, at the patient's request, consisted only of intermittent low dose single agent therapy with 6-thioguanine or hydroxyurea.

In March 1989 four months after her initial

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Accepted 11 January 1991