Case reports

Commentary: bronchiectasis and inflammatory bowel disease

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In 1861 Paul Broca and Louis Pierre Gratiolet spent more than six months arguing over the relevance of skull size to intelligence. Broca argued that "study of the brains of human races would lose most of its interest and utility if variation in size counted for nothing. Why had anthropologists spent so much time measuring heads if the results had no bearing upon the relative worth of different peoples?"

Unfortunately time has proved that Broca and his followers contributed little by their studies. With this in mind, how are we to view the continuing appearance of case reports in medical journals? Surely if they are being written and published, they must be of some benefit, or do they in reality provide no more than an interesting anecdote that has no long term contribution to medicine?

The current issue of *Thorax* contains two cases of bowel disease and a relationship to bronchiectasis.[1 2] Are these two reports yet further chance associations or do they provide some insight that may direct our thinking into the pathogenic processes involved in the lung condition?

Bronchiectasis, although often considered clinically, is based on a pathological definition. For many years the bronchogram had been the gold standard, although now high resolution CT scanning is being used with increasing frequency. There is some concern as to whether the use of such sensitive tests is, in a more widespread epidemiological way, detecting the same or a different disease condition from that which we have understood it to be in the past. For instance, one of the cardinal features of the disease on the CT scan is bronchial wall thickening and this may occur in other conditions where oedema of the airway wall is present. Clearly, classical bronchial dilatation or cystic change would be accepted by most as features of what was, in the past, recognised as bronchiectasis. However, tracking cylindrical changes through a scan is often difficult and the more subtle changes may indicate a different clinical condition from that recognised previously.

The pathogenesis of bronchiectasis has been extensively studied and many associations have been identified. Inflammation in the bronchial tree is thought to predate inflammatory damage leading to colonisation by bacteria and persistent inflammation and continuing tissue destruction (the much quoted vicious circle). With that as a background, inflammatory bowel disease has been well recognised as an association (although rare) with bronchiectasis. In particular, this is true of ulcerative colitis. This provides yet another tantalising epidemiological link between the bowel and the lung. For instance, the positive correlation of smoking with exacerbations of Crohn's disease and the negative influence of smoking in ulcerative colitis are well documented but difficult to explain. Might the associations of bowel and lung disease be related to a common immunity between both systems, the fact that the epithelial lining of both organs is exposed to common antigens in the environment, or that epithelial antigens share similarities at both sites? Discussions as to whether bronchial associated lymphoid tissue and gut associated lymphoid tissue are distinct or partly interrelated immune systems have yet to be resolved, but both IgA producing B cells and T cells are believed to migrate from the gut to the lung. Thus, if Crohn's disease is related to an excessive immune response to a bacterial antigen, the immune cells may well be represented in the lung. Reactions against self antigens or the same bacterial antigen being inhaled may lead to inflammatory damage at both sites.

Of the current cases, Crohn's disease has a less well recognised association with bronchiectasis than ulcerative colitis, although clearly from a clinical point of view (and even from a pathological point of view) there is some overlap with ulcerative colitis. With that as a background, one must question why removal of bowel would be associated with a precipitation of symptoms that led to the recognition of bronchiectasis. It could be the effect of surgery with intubation and postoperative atelectasis due to pain with or without infection (we are given no details).

However, the likelihood is that this in some way reflects the severity of the condition. Resection would only be undertaken in the presence of severe disease or of adhesions or fistulae and these, particularly the latter, could also be associated with pus. Such changes would lead to, or be due to, a heightened immune response as is often seen in idiopathic bronchiectasis. Whether these changes alone lead to a perversion of the immune system, such that activity against self antigens in the lung becomes a problem, remains an interesting but unproven concept. However, certainly neutrophil infiltration has often been implicated in the pathogenesis of the tissue destruction of both ulcerative colitis and Crohn's disease and, of course, the same has been true in bronchiectasis. It remains possible therefore that primary defects in neutrophils may play a

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part in some of the pathogenic changes that take place at both epithelial surfaces.

Of more interest, perhaps, might be the association with coeliac disease. The concepts of coeliac disease have changed in recent years as the immune mechanism has started to be dissected. In the past the diagnosis was based upon clinical evidence of malabsorption, the presence of a flat biopsy section on histological examination, and the fact that both symptoms and the biopsy changes resolved with diet.

It now becomes clear that many cases of coeliac disease are subclinical. There is a clear genetic predisposition and biopsy changes can be found in first degree relatives in the absence of symptoms.[3] In addition, the hallmark of the diagnosis now rests on the detection of antigliadin antibodies which can also be found in subjects who have a normal mucosal profile. However, histological examination has shown an increase in T cell infiltration, particularly of cells expressing the γδ T cell receptor.[4] Studies have shown that a decrease in the gluten content of the diet results in a decrease in cells of this phenotype in the biopsy specimens. In addition, rectal challenge with gluten has shown an increase in the CD3 γδ positive T cells within four hours.[5] This does suggest that, in some way, γδ T cells play an early and important role in coeliac disease. Mucosal derived T cells have been shown to respond to gluten in a DQ w2 restricted manner.

Our understanding of lymphocytic infiltration in bronchiectasis is relatively superficial although elegant studies by Lapa E Silva *et al*[6] did indicate a major lymphocytic infiltration in patients with bronchiectasis with the T cells being predominantly of the CD8 (suppressor) subtype. T cell receptor restriction, however, has yet to be analysed. It would therefore be of importance to determine whether a similar expansion in the γδ T cell population also occurs in bronchiectasis. These cells are found in the lung and have been associated with tuberculosis, sarcoidosis, and asthma. In particular, in patients with asthma these cells have been shown to respond to steroids. However, it must be pointed out that, although the T cell infiltrate is clearly present in coeliac disease, the same cannot be said of other inflammatory cell infiltration such as the neutrophil as seen in bronchiectasis.

It is to be hoped that these two case reports may prompt some further thinking and research in the field of the pathogenesis of bronchiectasis. However, one important lesson that does arise from both of these case reports is that there was a significant response to steroids. Again, although this may suggest an immunological basis, the response clearly indicates that reversible airflow obstruction or inflammation is often a feature of bronchiectasis. It should therefore be clearly looked for and treated appropriately in patients with less rare associations. Of interest, however, would be whether such a response changes the appearance of bronchiectasis seen on CT scanning.

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Bronchiectasis in association with coeliac disease

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Abstract

A 48 year old woman presented with a history of fatigue, regular sputum production, and wheeze. High resolution computed tomographic scanning of the thorax demonstrated widespread bronchiectasis. Coeliac disease was diagnosed on the basis of an iron deficiency anaemia, subtotal villous atrophy on small bowel biopsy, and raised anti-gliadin and anti-endomysial antibodies. The temporal relationship of her bronchiectasis and coeliac disease, and the subsequent stabilisation of her clinical symptoms and improvement in pulmonary physiology following treatment with inhaled corticosteroids, suggests a relationship between the two conditions which may be due to immunological mechanisms.

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Case history

A 48 year old woman presented with a history of fatigue, episodes of winter bronchitis over six years, and daily sputum production and intermittent wheeze for 18 months. There was no history of pneumonia, whooping cough, measles, or tuberculosis and she had never smoked. As a child she had episodes of wheezy bronchitis which had resolved while a teenager. Examination revealed conjunctival pallor, no finger clubbing, and bilateral basal expiratory wheezes and coarse crackles. Pulmonary