Unusual cases of Wegener's granulomatosis

Sir,

We read with interest the article by Watts (Vol 61(4), 2000, p. 250) describing unusual presentations of Wegener's granulomatosis (WG) including renal, gastrointestinal, cardiac and neurological problems. We feel skin manifestations should have been described in more detail as this has been a feature in up to 50% of WG patients described in some series as stated in the above paper. However, we would also like to highlight persistent skin problems. These may be the sole presenting feature of WG, particularly in unusual sites, before any other definite diagnostic clues are found.

We have recently described presentation of WG with recurrent panniculitis of the breast before confirmation of the diagnosis (Chowdhury and Natarajan, 2000). This lady initially had no other problems but 7 years later developed other features of the disease and positive antineutrophil cytoplasmic antibodies (ANCA).

Skin lesions may also occur simultaneously with or after the appearance of lesions in other organs. Patten et al (1993) described skin signs in WG which can manifest as urticarial, ulcerative, plaque-like, bullous and petechial lesions. Subcutaneous nodules, panniculitis, necrotic papules, gingival hyperplasia, splinter haemorrhages, pustules, xanthoma, livedo reticularis and necrotizing vasculitis may all also occur as the presenting feature.

We would urge all clinicians including dermatologists to be vigilant for the skin manifestations of this multi-system disease which can be a diagnostic challenge. Early diagnosis would hopefully avoid long delays before appropriate management is instigated.

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Sir,

Further to Dr Watts's excellent article on unusual presentations of Wegener's granulomatosis (WG), I like to add two more rare but important presentations of WG to the list: polymyalgia rheumatica (PMR) and temporal arteritis.

Limited forms of WG (without renal involvement) can present in a similar manner to PMR, as shown by Herrero-Beaumont et al (1991). The initial response to steroids would be dramatic with this presentation, although later on the response will be variable and inadequate even with high doses of steroids. Therefore careful clinical evaluation and long-term follow up are necessary before diagnosing idiopathic PMR. There have also been case reports of patients with WG who initially presented with clinical features typical of temporal arteritis (Nishino et al, 1993). Temporal artery biopsies in all but one of those patients showed non-giant cell arteritis. They subsequently developed typical pulmonary and renal manifestations of WG with positive tissue diagnosis.

Therefore it is important to consider WG as a possible underlying diagnosis in patients with PMR and temporal arteritis requiring high doses of steroids, with fluctuating responses and/or with other systemic involvement. WG has an excellent prognosis with early diagnosis and immunosuppressive treatment. Steroid treatment for PMR and temporal arteritis may mask the underlying systemic vasculitis and delay the clinical manifestations and thus treatment for WG.

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Aetiology of rheumatoid arthritis

Sir,

Dr Griffiths' editorial (Vol 61(6), 2000, p. 378) succinctly summarizes many of the issues relating to the longstanding debate as to whether a viral aetiology exists for rheumatoid arthritis (RA). He cites new and potentially important studies implicating a role for a newly described retrovirus in RA. However, RA is a complicated disease and we should not try and explain everything we do not yet understand as being caused by a virus.

The genetic component in RA is estimated to contribute 50–60% of the total disease susceptibility. This is accounted for by multiple genes (perhaps six or more) and partly explains why RA does not 'breed true' in a Mendelian sense. Major studies are presently underway to identify these individual RA susceptibility genes.

The environment also makes a significant contribution to RA susceptibility and the key issue will be understanding how genes and the environment interact to both trigger and perpetuate a chronic disease state. It is important to remember that both infectious and non-infectious environmental factors are likely to be important in RA. More women than men develop RA, suggesting that sex hormones have a role to play. Other risk factors appear to be pregnancy, contraceptive pill usage, breastfeeding and smoking.

The relatively similar prevalence of RA worldwide, the apparent lack of epidemics and seasonal variation in onset and the considerable age range observed for disease onset, have all been interpreted as evidence against an infectious trigger in RA.

However, an important consideration is the underlying genetic and clinical heterogeneity that exists within the condition broadly and phenotypically defined as RA. At present we may feel uncomfortable about considering sero-positive/erosive RA, sero-negative/non-erosive RA, late-onset seronegative RA and Type II collagen autoantibody positive RA as being different aetiologically-based diseases. However, if such phenocopies have different genetic bases, it is likely that earlier epidemiological data will have to be re-examined. Ultimately this may support the case for a viral aetiology in some forms of RA, help us understand gene–environment interactions and show us how best to treat our patients.

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Sir,

'We don't know the cause, so it must be a virus'. This statement, frequently made by the puzzled clinician, is also the refuge of scientists faced with a pathological phenomenon which defies explanation.

In rheumatoid arthritis (RA), much is known about the process but nothing about the cause. The process is a massive uncontrolled proliferation of the synovial membrane with the production of pro-inflammatory cytokines and metalloproteinases which eventually erode through cartilage, bone and surrounding joint structures. 'So it must be a virus' is also a negative statement. RA is not apparently caused by a simple bacterial infection. Nor is it purely genetic, although the genetic contribution may be as high as 30% from at least six independent genes. The virus answer is therefore, at best, a hypothesis.

Having made the hypothesis, the next question is 'which virus?'. This has to be a guess as well. In his editorial, Dr Griffiths suggests that the best candidate is a common persistent infection in the joint giving rise to chronic inflammation in genetically predisposed individuals. He makes the very important point that merely detecting the virus in the tissue is no proof of causality: a point which is apparently not appreciated by many high ranking scientific journals, resulting in a quite reasonable scepticism among its more critical readers. Those of us who are chasing viruses have to rely on two linked guesses (that it is caused by a virus, and that it is the one that we are interested in). Some may call this a fishing expedition, which is likely to fail to make the right catch. We would argue that finding a viral aetiology for RA is so important that it is worth pursuing, even if we often return with empty nets.

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