The patient showed some features common to C2 deficiency related nephropathy, but lacked the usual histological features. PAPS criteria were fulfilled by our patient; he had a history of thrombosis and a moderate level of anticardiolipin antibodies without a primary cause. The association of antiphospholipid antibodies with thromboembolic disorders is well established. In accordance with these reports, we believe that the existence of these antibodies in our patient increased the risk of cerebral ischaemic events, evidence of which was already present in the grossly dilated vertebral arterial anomaly. Here, renal disease seemed not to be directly related to antiphospholipid antibodies because thrombotic microangiopathy was not demonstrated.

Antiphospholipid antibodies have already been related to the presence of null alleles of C4 in patients with systemic lupus erythematosus, but not in PAPS patients.

The basis for the variation between inherited complement deficiency of early components and autoimmune disease is not understood. It is thought to involve the absence of microbial (or non-infectious antigens (such as cardioliaphospholipid) which may stimulate autoantibodies. In our patients, because of the pauciarticular juvenile C2 deficiency, it is likely that this condition was caused related to the antiphospholipid syndrome.

Might patients with HLA-B27 related diseases benefit from antiandrogenic treatment?

There are several rheumatic diseases which may be suspected of sharing the curious feature that both probands and their unaffected sibs have sex ratio biases that are in the same direction. For instance, rheumatoid arthritis (RA), early onset pauciarticular juvenile rheumatoid arthritis, and coxarthrosis are all conditions in which probands and their unaffected sibs seem to contain excesses of females, while ankylosing spondylitis (AS), juvenile rheumatoid arthritis and late onset pauciarticular juvenile rheumatoid arthritis are all conditions in which probands and their unaffected sibs seem to contain excesses of males. Thus the reasoning is approximate, because many of the data underlying these conclusions were gathered for other purposes and were therefore subject to possible volunteer bias or survivorship bias (both of which would be expected to lead to female excesses). However, these qualifications do not apply to the data on juvenile rheumatoid arthritis and they do not apply to recent reports of data explicitly gathered to test the sex ratio biases of sibs of RA and AS probands.1,4,5 Tables 1 and 2 summarise these data; they suggest that the biases are real.

What may be inferred from this? One may propose that the same agent causes both the disease in probands and the unusual sex ratios in their unaffected sibs.

There is very substantial evidence that parental hormone levels at the time of conception partially control the sexes of human offspring.8,9 We suggest that low testosterone levels are a cause of RA and of RA patients' excess of sisters, and that high testosterone levels are a cause of AS and of these probands' excess of brothers.1 However, the suspicion in regard to RA was strengthened by the subsequent demonstration that RA patients may benefit from androgen treatment.6-8 So the question arises if patients with HLA-B27 related diseases might, analogously, benefit from antiandrogen treatment.

This resolves into the question: what evidence is there that HLA-B27 related diseases are partially caused by high levels of androgens?

For illustrative purposes, I consider AS (because there are more published data on this condition), but the following speculations may also apply to the other B27 related diseases. It is suggested that patients with AS have high testosterone levels, on average.2-11 Moreover, there is evidence that B27 is associated with high testosterone levels in healthy controls also.10 Thus the high testosterone levels in AS patients may reasonably be interpreted as a genetically determined precursor of the disease, rather than its consequence. This conclusion is supported by the observation that disease, in general, causes men's testosterone levels to decrease, not increase.12

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Recently published data on the sex of sibs of probands with ankylosing spondylitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Source</td>
<td>Brokers</td>
</tr>
<tr>
<td>Calin et al</td>
<td>232</td>
</tr>
<tr>
<td>Ploski et al</td>
<td>34</td>
</tr>
<tr>
<td>Totals</td>
<td>266</td>
</tr>
</tbody>
</table>

Tested against an expected white birth sex ratio of 0.514, the pooled data here yield a χ² value of 3.2 (p < 0.05, one way).

So there seem to be good grounds for supposing that some of the sex related rheumatic diseases are caused by unusual hormone levels which are in turn (possibly) controlled by their associated HLA antigens. Accordingly, it seems reasonable to wonder if AS patients might benefit from antiandrogenic treatment.

This raises a moral problem which is illustrated in the predicament of the television playwright, the late Dennis Potter. His suffering from psoriatic arthritis (a B27 related condition) was dramatised in _The Singing Detective_. One may suppose that Potter's creativity and persuasive interest in sex may both have had a hormonal basis. Practitioners offering antiandrogen treatment should advise patients of their possible psychological side effects. Men who want relief from their B27 related diseases may nevertheless not be keen to risk compromising their masculinity in the process; so it might be preferable to consider treating female patients first...
Asymmetric rheumatoid vasculitis in a hemiplegic patient

In 1962, Thomson and Bywaters described the phenomenon of unilateral rheumatoid arthritis occurring in a hemiplegic patient; 1 Oblick subsequently described a similar sparing in a patient in whom the limbs had been paralysed as a result of poliomyelitis. 2 This protection was initially explained by lack of use of the hemiplegic limb, sparing the joints. More recently, a neurogenic mechanism has been proposed. 3

The case to be described is of rheumatoid vasculitis which largely spared the hemiplegic side—a phenomenon not described previously. It is suggested that the asymmetric distribution supports a neurogenic mechanism.

The patient, who suffered from an arteriopathy, had his first myocardial infarction at the age of 37. A second infarct one year later was followed rapidly by a cerebrovascular accident, thought to arise from embolism of a left ventricular wall thrombus, seen on the echocardiogram. This resulted in a dense left hemiplegia. In 1988, at the age of 48, he developed seropositive rheumatoid arthritis and presented with a predominance of right sided synovitis, involving the right hand, knee and ankle, although there was mild involvement of the left hemiplegic side. He was treated with Voltarol retard, sulphasalazine 1 g twice daily and chloroquine 250 mg three times a week, which produced good disease control and a decrease in the erythrocyte sedimentation rate from 50 to 25 mm/1st h. Radiographs of the hands, taken two years later, showed bilateral erosions; joint space loss was considerably greater on the right side.

In April 1994, at the age of 51, the patient presented with a predominantly right sided vasculitic rash involving his hand, arm, foot, thigh, and buttock, with vasculitic ulcers on his right thigh and buttock (figure). He had nail fold infarcts of the right fingers and toes. Peripheral pulses were present and equal; joints were not active. There was no evidence of peripheral neuropathy, and no fever. There had been no recent change in medication to suggest a drug induced aetiology. Urine analysis was negative. Immunological studies showed him to be negative to antinuclear factor, antineutrophil cytoplasmatic antibodies, and lupus anticoagulant, but positive to La(SS-B) antibody. A skin biopsy demonstrated a leucocytoclastic vasculitis. He was treated with intermittent pulsed intravenous cyclophosphamide 15 mg/kg and prednisolone. The rash faded and healed over the first two weeks of treatment, and he made a good subsequent recovery.

Whilst one could explain the unilateral rheumatoid joint involvement in this hemiplegic patient in terms of joint sparing in the paralysed limb, this mechanism could not be evoked to explain the predominantly unilateral distribution of the vasculitis to the non-hemiplegic side as described in this patient. This may provide further support for a neurogenic mechanism.

Evidence for sensory nerve involvement in chronic arthritis comes from animal studies in which sectioning of the sciatic nerve seven days before the induction of adjuvant arthritis delayed the onset and severity of disease in the operated limb. 4 Levine has suggested that neuromechanisms may also explain why rheumatoid arthritis is bilaterally symmetric. 5 Evidence is growing that these effects are mediated through substance P in the sympathetic nervous system. 6

The vasculitis in rheumatoid arthritis is predominantly small vessel and is caused by a precipitate of immune complex with subsequent postcapillary leukocyte infiltration. 7 Why the vasculitis should have occurred asymmetrically in this patient is unknown. There was no recent change in his medication to suggest a drug induced aetiology. The cerebrovascular accident predated the vasculitis by 10 years and was embolic; it was thus unlikely to have been the result of a single vascular process such as Sneddon’s syndrome. One could speculate that alteration in vascular sympathetic tone in the hemiplegic limb 8 could decrease the local precipitation of immune complexes and thus explain the unilateral rheumatoid vasculitis described here.
Might patients with HLA-B27 related diseases benefit from antiandrogenic treatment?

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