MATTERS ARISING

Treatment of a case with pooled intravenous immunoglobulin as an alternative to immunosuppression

Enevoldson and Wiles¹ describe a patient with systemic lupus erythematosus (SLE) who developed a severe corticosteroid-resistant vasculitic neuropathy subsequently responsive to cyclophosphamide. They note the rarity of vasculitic neuropathy due to SLE, and the need to exhibit immunosuppressant therapy similar to that used in other systemic vasculitides, rather than steroids alone, in this context. We describe a further patient with an unusual pattern of central and peripheral neurological SLE, compatible with underlying vasculitis, who was successfully treated with pooled intravenous immunoglobulin (IVIg), having reacted adversely to cyclophosphamide.

The patient originally presented at the age of 20 years with generalised convulsions following her first pregnancy. Eight years later, she developed arthralgia, Raynaud's phenomenon, an urticarial rash and absence seizures. She presented again aged 40 years with a photosensitive rash and synovitis. Investigation then revealed positive ANA with a homogeneous pattern and elevated DNA binding at 942 units (normal <50). Skin vasculitis was subsequently controlled with prednisolone and azathioprine. Two years later she developed a severe and acute right ulnar neuropathy. Despite high dose oral prednisolone, a right median neuropathy supervened within two months. Treatment with pulsed intravenous cyclophosphamide (15 mg/kg) and methylprednisolone (10 mg/kg) was complicated by lymphopenia, alopecia, lingual ulceration, staphylococcal dactylitis and candidiasis. DNA binding remained high (242 units), anti-cardiolipin antibody was 42% (normal <25%), platelet count and coagulation screen were normal. She progressed over the next month to diffuse brain-stem/cerebellar involvement characterised by a one-and-a-half syndrome, consistent with a lesion of the right paramedian pontine reticular formation, ataxia and a left lower motor neuron facial palsy. MRI brain scan appearances were compatible with pontine micro-infarcts. She then received IVIg ("Sandoglobulin", Sandoz, Basle, Switzerland, infused at 400 mg/kg per day for five days), after which no new neurological deficit accrued over a follow up period exceeding nine months.

The evidence for vasculitis as the cause of the neurological deterioration in our patient was indirect. But this pathological basis seems likely in view of the stepwise presentation, particularly the multifocal peripheral nerve involvement, MRI appearances, associated serological abnormalities (including a marked and persistent elevation of the ESR), and previous demonstration of cutaneous vasculitis. Corticosteroids did not arrest the development of new neurological lesions when used alone and the addition of cyclophosphamide was associated with largely infective complications. The brainstem syndrome developed after her first pulse of

cyclophosphamide. Disease progression was apparently only halted when IVIg was exhibited, suggesting that this treatment may be added to existing therapeutic strategies for vasculitic neurological manifestations of SLE. Although IVIg has been used with benefit in other systemic vasculitides,² and for non-neurological complications of SLE,³ we are not aware of previous reports of its efficacy in cases of SLE dominated by nervous system involvement.

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Spontaneous intracerebral haemorrhage

The excellent review by David Mendelow omitted to mention one important cause of intracerebral haemorrhage (ICH).¹ Cerebral amyloid angiopathy (CAA) accounts for 5-10% of all cases of ICH² and its frequency increases with age.³ The association with dementia in non familial cases is well recognised.^{4,5}

The clinical and radiological diagnosis of CAA have important management implications.⁶ Surgical evacuation is not only difficult but dangerous.⁷ Recent reports on ICH in patients with CAA during tPA therapy for acute myocardial infarction⁸ should lead to caution in its use in elderly or demented patients. Cerebral amyloid angiopathy has already been shown to be a cause of ICH during anticoagulant therapy.⁹

With the increasing availability of CT scanning in this country¹⁰ and its possible use for elderly patients with stroke, one can expect increased recognition of CAA as a cause of ICH. Any lobar or multiple ICH at a site perhaps not typical of hypertensive bleeding in an elderly or a demented patient should alert the clinician to the possibility of CAA.

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Internuclear ophthalmoplegia in giant cell arteritis

Recently, Trend and Graham reported two patients with unilateral internuclear ophthalmoplegia (INO) in association with giant cell arteritis (GCA).¹ These authors stated that the INO caused diplopia in their patients and resulted from embolism to brainstem perforators from thrombosed extradural segments of the vertebral arteries. They also claimed that these are the first such cases reported in the literature.

We would like to draw your attention to an article entitled "Internuclear ophthalmoplegia in giant cell arteritis" published in the *Journal of Rheumatology* in 1989.² In this article, we described two patients with INO and biopsy-proven giant cell arteritis. We proposed that the most likely cause of the INO in our patients was brainstem ischaemia from embolism to midline perforating vessels supplying the medial longitudinal fasciculus. However, direct arteritic involvement of these perforators could not be entirely excluded, as inflammation of the basilar artery has been shown in at least three cases.^{3,5}

Contrary to what Trend and Graham¹ suggest, diplopia is not a common complaint of patients with INO⁶ and may be explained by other ocular misalignments, such as a skew deviation.

We would agree with the authors' conclusions that giant cell arteritis should be considered as a cause of internuclear ophthalmoplegia and that corticosteroid therapy be instituted promptly to prevent further brainstem ischaemia.

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Chronic fatigue syndrome

As neurologists in a country where the chronic fatigue syndrome (CFS) has almost no recognized official existence, we often feel bewildered by the papers on the subject we read in the Anglo-Saxon literature. We wonder whether the clinical experience of some of their authors is so different from ours that they do not consider that their approach may result in a disservice to their patients. The JNNP has followed a sensitive line culminating in Wessely's excellent editorial.¹ We still, however, feel that his kid-glove handling of the subject reflects the controversy that surrounds it in the UK.

Avoiding the futile organic versus functional debate, in our neurology department we refer to many of the problems we see in our practice as the "chronic vigilance syndromes": specific patterns of enhanced attention centred on particular bodily structures and functions. Naturally, the commonest in a neurologist's outpatient clinic are the "cephalic vigilance syndromes" in their two main forms: the painful, with its several varieties of chronic headaches, and the operational one with its subjective unsteadiness, concentration problems and various odd turns. "Thoracic vigilance" patients are often referred to cardiologists or pneumologists but a fair number also come to us, especially if they have hyperventilation symptoms such as dizziness and paraesthesiae. Among the different types of patients with fatigue we are also familiar with the occasional "neuro-muscular vigilance" patient whose symptoms parallel your CFS cases. We have the non-controlled impression that in our environment such patients often have a premonitory preoccupation with their locomotor system.

We believe that an important element in all these syndromes consists of the patients' misconceptions about the causes, mechanisms and prognosis of their symptoms derived from popular health concepts and also not infrequently from counterproductive health education campaigns and doctors' remarks. In fact, we find it remarkable that the influence of the public and medical interest in CFS on its proliferation does not figure prominently in any discussion. That is why our approach to these syndromes consists mainly of a kind of "cognitive therapy" which tries to bring to the fore the patient's ideas on the problem and to demolish misconceptions, together with a sparing use of drugs. Our experience tells us that whereas some of these syndromes can be dealt with reasonably well, others are much more resistant. Such is the case for example with the "facial vigilance syndrome", better known as atypical facial pain, and the "neuromuscular vigilance syn-

drome". Fortunately the latter is not common in our environment.

But not for long. Our compatriots are starting to be taught about this "new" disease. The widely read Madrid newspaper *El Pais* ran a full page story on the CFS as "the disease of the nineties". A highly-reputed private teaching hospital has also given press releases on this "impending epidemic" and even a local newspaper has informed our neighbourhood about the shape of things to come. Some months ago a chat-show on Spanish television hosted the "first" Spanish patient with CFS.

So now we are bracing ourselves. Wessely quotes an article on "the role of culture in making a diagnosis".² There is also a role for culture in developing and expressing illness. Our colleagues are being educated in this new pattern of self-vigilance, and the successful incorporation of Spain into the Western democracies will be enriched by this new cultural acquisition. They will also be taught that this disease is chronic, long-lasting, makes inactivity advisable and has no treatment: a self-fulfilling recipe for chronicity. They will learn to mistrust doctors who suggest that their symptoms, real, disabling and worthy of treatment as they are recognised to be, may not be due to a testable specific organ disease: a mistrust that will deny them the first step towards improvement. And presumably we Spanish doctors will soon start publishing papers on CFS.

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Wessely replies:

Dr Digon and colleagues believe that cultural factors play a vital role in the aetiology of CFS, a view I can only share. There is a considerable degree of iatrogenesis in the rise of these conditions, and if one is to understand their sudden rise, and occasional fall, it is essential to understand cultural attitudes towards health and illness, and in particular prejudice against conditions which, whether fairly or not, are frequently seen as psychological in origin.¹² We have previously concluded that such prejudices and unhelpful polarisation between "physical or psychological", which all too often means "real or unreal", may be more virulent than any virus.³

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BOOK REVIEWS

All titles reviewed here are available from the BMJ Bookshop, PO Box 295, London WC1H 9TE. Prices include postage in the United Kingdom and for members of the British Forces Overseas, but overseas customers should add £2 per item for postage and packing. Payment can be made by cheque in sterling drawn on a United Kingdom bank, or by credit card (Mastercard, Visa or American Express) stating card number, expiry date, and your full name.

Post-Viral Fatigue Syndrome. Edited by R JENKINS AND J MOWBRAY. (Pp 463; Price £60.00). Chichester, John Wiley & Sons Ltd, 1991. ISBN 0 471 928461.

What is regarded as increasing enlightenment, or perhaps an increased journalistic interest in medical matters, has led to much more "self-diagnosis" in the Neurology Clinics. One of the more popular diagnostic labels attached to the patient by himself or his informed friends, is myalgic encephalomyelitis or ME.

Many patients attending the clinic, convinced of the correctness of the diagnosis will bring evidence of confirmation from specialist practitioners and organised groups and will not be persuaded otherwise. They will not accept that there is an alternative explanation for their problems to "post-viral fatigue" or whatever. These patients pose a considerable problem. It is not surprising that an attempt has been made to rationalise this "syndrome", to give it an identity as a nosological entity, consider the pathogenesis, importance, and implications and to define the diagnostic criteria.

This book is edited by a principal medical officer at the department of health, a psychiatrist by training and a professor of immunopathology. They have invited contributors from diverse backgrounds to discuss their involvement in ME and to resolve the "particularly challenging problem for contemporary medicine . . . those puzzling clinical entities which are defined purely in terms of symptoms, which are accompanied by little in the way of consistent physical signs, which affect quite large numbers of patients for which no specific treatment appears effective".

Thirty-five contributors address the problem in a book of 275 pages. It is stated unequivocally on page 167 . . . "it is however beyond any doubt that muscles are involved in this syndrome with both metabolic and ultrastructural abnormalities" and yet on page 237 the more orthodox neurological view is expressed . . . "our management of patients . . . is based on our belief that the condition forms part of the spectrum of a depressive illness, triggered by a viral infection". The psychologist, recognising that it has "attracted much controversy" concludes that it is not clear whether we are dealing with a single syndrome or with a heterogeneous group of disorders which share some common characteristics.