as the immunomodulatory drugs typically used for MS will be ineffective for relapse prevention in NMO and severe refractory attacks in NMO usually necessitate plasma phaspheresis or more effective immunosuppressive therapies [3].

In the management of this suspected case of NMO, the authors made use of investigatory tools such as cerebrospinal fluid analysis and MRI of the brain/spinal cord in diagnosis. However, as indicated by de Seze et al. [2], even when all these investigatory arguments are summoned there is still the pitfall of misdiagnosis and the inability to distinguish the two. Recently, using the technique of dual immunostaining, Lennon et al. [4] have demonstrated that a serum autoantibody marker, NMO-IgG, is highly specific for neuromyelitis optica and can significantly curtail the diagnostic ambiguity.

Perhaps, with the aid of a specific autoantibody marker, the management of this patient might have been more streamlined.

The authors have declared no conflicts of interest.

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Devic’s syndrome in systemic lupus erythematosus and probable antiphospholipid syndrome: reply

We thank Drs Chan and Liu for their interest in our case report. We entirely agree that it is fundamental to distinguish between neuromyelitis optica caused by an inflammatory/demyelinating process and a genuine case of multiple sclerosis. In fact, this was our main concern.

Our patient had clear evidence of lupus with multisystem involvement and had several clinical and laboratory signs of severe lupus activity, despite being strongly immunosuppressed. Her clinical presentation was not characteristic of multiple sclerosis: optic neuritis was unilateral; blindness was permanent; evoked potentials were delayed but also had short amplitude; and MRI lesions had no enhancement after gadolinium administration and were not progressive in time and space.

In our opinion, the main diagnostic issue was the differentiation between an inflammatory and/or a thrombotic mechanism. Antiphospholipid syndrome is common in lupus and is frequently associated with central nervous system involvement, namely transverse myelitis [1–3]. Also, abrupt-onset, unilateral and irreversible optic neuritis is more commonly ischaemic than inflammatory/demyelinating [1]. Our patient had transiently positive antiphospholipin antibody and presented with stroke, thrombocytopenia and extensive livedo reticularis, suggesting underlying antiphospholipid syndrome. A good response to anticoagulation has been reported in similar cases [2, 4].

Overall, we felt that a demyelinating syndrome as part of her lupus with secondary antiphospholipid syndrome was more probable than classical multiple sclerosis occurring coincidentally in this patient. We agree with Drs Chan and Liu that it would be interesting to study the specific autoantibody marker for neuromyelitis optica (NMO-IgG) [5]—this may well give further help in characterizing these clinically difficult patients.

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Effect of rituximab in refractory SLE: inhibition of Th1?

Sir, The report by Tokunaga et al. [1] clearly demonstrates that rituximab, a chimeric monoclonal antibody specific for human CD20, is highly effective against the life-threatening disease systemic lupus erythematosus (SLE). Furthermore, the authors demonstrate that rituximab not only reduces B-cell numbers and IgG levels, but also down-regulates CD40 and CD80 on B cells of treated patients. Interestingly, all of the five patients they studied had central nervous system (CNS) involvement (two had consciousness disorder and three had sensory disorder).

The balance between T-helper type 1 cells (Th1 cells) and Th2 cells in SLE patients remains controversial. Some reports have suggested that SLE is a disease in which the actions of peripheral...
Th2 cells predominate over those of Th1 cells [2, 3]. Other reports, however, suggest a predomiance of Th1 cells in SLE patients having class IV lupus nephritis as defined by the World Health Organization (WHO) [4]. We recently reported that the level of the Th1 chemokine interferon-inducible protein 10 (IP-10)/CXCL10 is increased in the cerebrospinal fluid of patients with CNS lupus and demonstrated that CNS involvement in SLE is an immunological disorder of Th1 predominance [5].

Several reports have shown that both CD40/CD40L and CD80/CD28 interactions are a prerequisite for the development of Th1 lineage cells [6–8]. Therefore, rituximab-inhibited down-regulation of CD40 and CD80 on B cells might inhibit the activation and development of Th1 dominance by preventing CD40/CD40L and CD80/CD28-mediated downstream interactions, and thereby result in the suppression of Th1-predominant immunological disorders such as CNS lupus. Given the inhibitory effects of rituximab on interactions between CD40/CD40L and CD80/CD28, this drug is somewhat analogous to CTLA4-Ig, a human fusion protein combining the extracellular portion of the cytotoxic T-lymphocyte-associated antigen 4 (CTLA4) with the Fc region of human IgG [9]. In this case, however, rituximab inhibits not only B-cell functions but also Th1-cell activation and has an advantage over CTLA4-Ig, which is reported to inhibit only CD80/CD28 interactions. A comparative clinical study between rituximab and CTLA4-Ig is needed to reveal whether rituximab is more effective than CTLA4-Ig, which is reported to inhibit only CD80/CD28 interactions.

As we pointed out previously, clinicians should be aware of the risk of the development of severe infections following treatment with rituximab [10]. In this regard, the strategy proposed by Tokunaga et al. is well considered since they successfully treated their patients with only a few injections of rituximab. The authors have declared no conflicts of interest.

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