finding,[7] we suggest that there is a defect of LPS responsiveness of monocytes to the induction of TNFα and IL10.

This case confirms the excellent response of CINCA syndrome to treatment with human IL1 receptor antagonist. Our results suggest that patients with this hereditary autoinflammatory disorder may exhibit a profound dysregulation of IL1 and TNFα synthesis. However, we cannot exclude the possibility that the inability to detect TNFα before application of IL1 receptor antagonist owed more to a rapid decay of TNFα rather than reduced production. As this dysregulation is reversed by treatment with IL1 receptor antagonist, one may argue that therapeutic inhibition of otherwise aberrant IL1β secretion results in a compensatory up regulation or less decay of TNFα to maintain the host's capacity to react to microbial agents and other types of danger signals. Furthermore, the overall up regulation of the TNFα pathway by interaction at the IL1 pathway illustrates that the cytokine imbalance is not due to a defect, but rather to a dysregulation. Finally, our results provide an explanation for the reason why TNF blocking agents are ineffective in certain autoinflammatory diseases.

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Reversible posterior leucoencephalopathy in scleroderma

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A 34 year old Chinese woman with limited scleroderma presented with rapid onset of mental confusion and generalised tonic-clonic seizures. Her blood pressure control had been unsatisfactory in the preceding 4 weeks despite the use of three anti-hypertensive agents, which included an angiotensin converting enzyme inhibitor. Malignant hypertension (blood pressure 240/140 mm Hg on admission) was evident, with typical fundoscopic abnormalities, microangiopathic haemolytic anaemia, and rapidly deteriorating renal function with acute oligouric renal failure (increase in serum creatinine from baseline of 86 to 495 μmol/l in 3 days). There was, however, no evidence of left ventricular failure.

Treatment was given in the intensive care unit with infusions of labetalol (up to 150 mg/h) and iloprost (up to 10 μg/h), large doses of captopril (150 mg/day), and haemodialysis. An urgent magnetic resonance imaging (MRI) scan

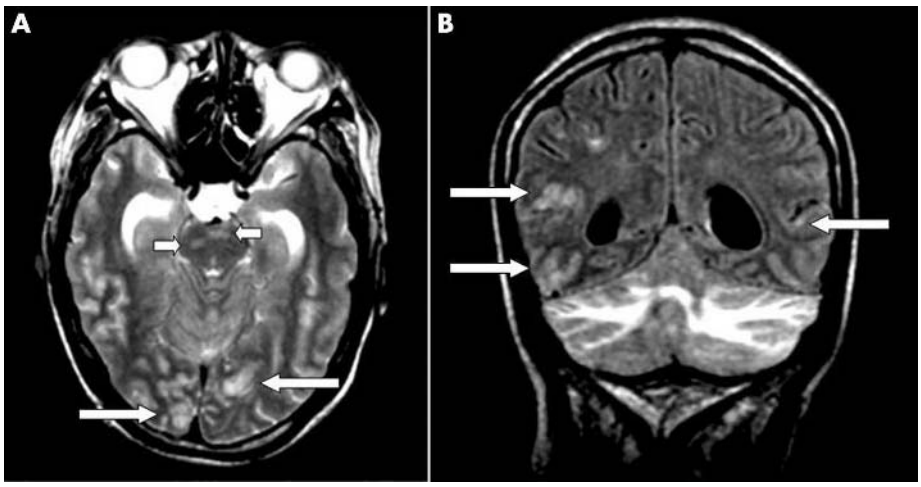

Figure 1 (A) Axial T_2 weighted and (B) coronal fluid attenuated inversion recovery (FLAIR) images showing bilateral abnormal hyperintensities in the white matter of the cerebellum, cortex, and subcortical white matter of the occipital lobes (long arrows), and in the brain stem (short arrows).

of the brain showed marked vasogenic oedema distributed symmetrically at the cortex, and subcortical white matter of the occipital lobes, the cerebellum, and the brain stem (fig 1). With control of hypertension and dialysis support, she gradually regained full consciousness without neurological deficits. A repeat MRI scan 2 weeks later demonstrated complete resolution of the lesions. The clinical picture was compatible with a reversible posterior leucoencephalopathy syndrome (RPLS).

RPLS is a clinical syndrome characterised by headache, seizures, visual disturbances, and confusion. The MRI finding is often characteristic, with abnormal T_2 weighted hyperintensity affecting primarily the white matter of the territories of the posterior circulation.[1] The cerebral cortex and the anterior circulation territories may also be affected, but usually to a lesser extent. RPLS has been described in an increasing number of medical conditions, including hypertensive encephalopathy, eclampsia, neurotoxicity related to calcineurin inhibitors, and uraemic encephalopathy. Reversible vasogenic oedema is the underlying pathology of the abnormal MRI signal intensities. The exact pathogenesis of RPLS remains elusive but a break down of the autoregulation of cerebral blood flow and endothelial dysfunction resulting in leakage of fluid into the interstitium has been postulated.

RPLS has been described in many rheumatic diseases, including systemic lupus erythematosus, systemic vasculitides, and the overlap syndromes.[2 3] However, we believe that this is the first report of RPLS in adult patients with limited scleroderma. Prompt recognition and treatment of this condition is essential as it is potentially reversible.

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Experimental infection with *Plasmodium falciparum* does not result in the induction of anticardiolipin antibodies in healthy volunteers

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Antiphospholipid antibodies (aPL), particularly lupus anticoagulant or anticardiolipin antibodies (aCL), are diagnostic markers for the antiphospholipid syndrome, which is characterised by venous or arterial thrombosis or obstetric complications, or both.[1] aPL may also occur in association with a multitude of infectious agents. Asherson and Cervera, while reviewing infection related aPL, mentioned malaria as one of the parasitic infections that has been associated with the presence of aPL.[2] Indeed, two independent papers have described the high prevalence of aPL in patients with malaria. Jakobsen *et al* described the induction of IgM, but not IgG aPL during acute *Plasmodium falciparum* infection of Sudanese adults.[3] The aPL were reactive with cardiolipin, phosphatidylinositol, and phosphatidylcholine. Facer and Agiostratidou examined adult patients of diverse ethnicity with uncomplicated non-severe malaria.[4] They showed that *P falciparum* and *P vivax* infections are associated with the appearance of raised plasma levels of IgM and IgG aPL, and aCL were raised in over 75% of the patients with malaria. Patients with *P falciparum* had high aPL IgG levels, exceeding the levels seen in positive controls.[4] Because the observed association may lack a causal relation, we recently evaluated the induction of aPL in 10 healthy white volunteers upon infection with *P falciparum*.

Anopheles stephensi mosquitoes were infected with the chloroquine sensitive NF54 isolate of *P falciparum* at the insectary, as previously described.[5] Sets of female mosquitoes were allowed to feed on the forearms for 10 minutes. Subsequent dissection was performed to confirm the presence of sporozoites in the mosquito salivary glands. If not present, the feed was repeated until successful. Volunteers were carefully monitored by assessing blood films twice daily. Upon microscopic detection of parasites, volunteers were immediately treated with a standard curative regimen of chloroquine.

Blood was sampled one day before infection and 1, 7, 10, 12, and 20 days after infection. IgM and IgG aCL were analysed by commercial enzyme linked immunosorbent assay (ELISA; Pharmacia Diagnostics, Freiburg, Germany) in a serum dilution of 1:100. Results showed that all volunteers were negative for both IgM and IgG aCL before infection and remained negative for these antibodies during follow up. Thus, acute *P falciparum* infection does not result in the induction of aCL.

Nevertheless, although there seems to be no causal relation between malaria and aCL, the coexistence of aPL may further complicate malarial infection. For instance, thrombocytopenia is often (~60%) seen in patients with malaria, and