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Early mortality in systemic small cell vasculitis

The largest reported study of systemic small cell vasculitis (SSCV) claimed that the balance of current treatment regimens is skewed towards over-immunosuppression, and that the greatest threat in the first year is from adverse effects of therapy rather than vasculitis.

Reporting new data to show how different factors contribute to early mortality in SSCV, Dr Mark Little (Renal Institute, University of Birmingham) argued that when treating a patient with systemic vasculitis, the key decision for the clinician is the intensity of immunosuppression to use.

Dr Little and his colleagues analysed data from 523 patients representing the entire spectrum of SSCV disease severity. The burden of therapy was quantified using a severity of score (1–4) for leucopenia, infection and other adverse events, and an additional weighting for follow-up duration. A single combined burden of therapy (CBOT) score was generated for each patient.

As the CBOT score reaches >7, there is an exponential increase in the risk of mortality, rising to a 60% 1-year mortality with CBOT scores of >9.

Dr Little reported that there were 56 deaths at 1 year, with an overall 1-year mortality probability of 11.1%. He added that 50% of deaths were the direct result of infection, but only 14% of active vasculitis itself. Some 66% of patients developed at least one adverse event.

Dr Little said: 'There is a very fine balance between therapy to prevent active tissue destruction secondary to vasculitis and the adverse effects of that therapy. It presents a very difficult decision for all clinicians treating patients with vasculitis.'

He concluded: 'Recording burden of therapy scores may be a useful component of patient care. Once certain thresholds are reached in clinical practice – such as CBOT scores of 4 and 8 – this should trigger a full review of therapy intensity.

'We should be particularly vigilant in the elderly and those patients with reduced renal function. Accumulation of adverse events, as monitored using this simple scoring method, should prompt a reduction in immunosuppression.'

Stephen Pinn

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Treatment of lupus nephritis without maintenance steroids

Induction therapy with rituximab may obviate the need for maintenance steroids in patients with lupus nephritis. Furthermore, according to new research, patients willing to undergo repeat biopsies for suspected residual proteinuria may find they have no active lesions and do not require further treatment.

Dr Ruth Pepper (Imperial College Kidney and Transplant Unit, Hammersmith Hospital, London) reported that steroids are routinely used to treat lupus nephritis but cause substantial morbidity, patient distress and some mortality.

She said that mycophenolate mofetil is appropriate for induction and maintenance treatment of lupus nephritis, while rituximab is increasingly used as a lupus rescue therapy, and has a history of safe use in many autoimmune and other disorders.

'However,' she cautioned, 'rituximab has yet to have its role in induction and maintenance therapy fully defined, and steroid-free regimens have not been tried to any extent in lupus nephritis.'

Since February 2006, Dr Pepper and her colleagues had piloted a protocol for the treatment of lupus nephritis using rituximab + prednisolone for induction, and mycophenolate mofetil without any oral steroids for maintenance.

Rituximab (1 g) and prednisolone (500 mg) were given in two doses, 2 weeks apart. Maintenance therapy was mycophenolate mofetil alone (1–3 g in divided doses titrated to trough levels). She reported the latest data on 25 patients who had reached at least 12 months' follow-up.

At 1 year, there was complete remission in 17 patients (68%), partial remission in seven patients (28%) (stable or improved creatinine and 50% improvement in proteinuria) and one non-responder (4%).

Stephen Pinn

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Gene expression in lupus and vasculitis

Gene expression profiling may guide future treatment choice and lead to better patient outcomes in systemic lupus erythematosus and vasculitis.

Professor Kenneth Smith (Head of Division of Renal Medicine, School of Clinical Medicine, University of Cambridge): reported: 'The risk for both these autoimmune diseases is polygenic. There is no single gene that drives that risk – rather a combination of genetic factors contributing a small amount to the overall risk.'

Of particular interest in systemic lupus erythematosus is the inhibitory receptor FcγRIIb acting as a brake on the immune system. Expression of FcγRIIb is controlled by interleukin-4 (IL-4). The physiological role of FcγRIIb in terms of the inflammatory response is to balance resistance to infection and the risk of septic shock.

An FcγRIIb polymorphism (T232) abolishes the inhibitory function of the receptor in systemic lupus erythematosus, enhances B-cell activation and increases pro-inflammatory cytokine production – in lupus, but not in systemic vasculitis.

Stephen Pinn

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