Neuropsychological analysis in patients with systemic lupus erythematosus: a case control study

Neuropsychiatric involvement is considered an ominous sign in systemic lupus erythematosus. More recently, neuropsychological testing has been carried out in patients with SLE. Marked cognitive impairment was observed in some patients even when there was no overt evidence of nervous system involvement. Mental performance did not appear to be related to disease activity or cortisol. Cognitive impairment has been regarded as a possible marker of subclinical neuropsychiatric involvement.

We carried out neuropsychological tests on a group of patients with SLE, without clinical evidence of neuropsychiatric involvement, and compared them with a control group of healthy subjects. The hospital at Jerez is a referral centre for a population of 350,000. We have 63 patients registered as fulfilling the criteria for SLE established by the American Rheumatological Association. Twelve had clinical neuropsychiatric involvement. From the remaining patients we randomly selected 20 subjects for a prospective neuropsychological study and another 20 sex matched healthy volunteer subjects as the control group. Both, patients and controls were recruited from the same population. The age and educational levels were similar.

A complete clinical examination, standard blood tests and immunological study were carried out. The disease activity was measured by the SLE-DAI system. Neuropsychological assessment included: Wechsler Adult Intelligence Scale (WAIS), Verbal fluency was evaluated by the Set test, and depressive symptoms were assessed by the Hamilton Scale for depression. The neuropsychologist examiner was unaware of the clinical situation of subjects.

Statistical analysis was performed using a non-parametric test (Mann-Whitney U test) for mean comparisons between the two groups.

The table shows the mean (SD) for neuropsychological tests. The average age of patients with SLE was 33.2 (range: 17–63) and that of the controls 36.6 (range: 16–61). There were 19 women in both groups. The mean duration of the disease was 71 months (range 12–240). The mean of disease activity was 8.65 (range: 2–21).

Fourteen patients were receiving treatment with less than 15 mg of prednisone, two with more than 15 mg and four were not treated with corticosteroids.

The differences on neuropsychological tests were not significant according to the Mann-Whitney U test (p>0.1).

We concluded that the patients with SLE without clinical neuropsychiatric involvement have a mental performance similar to healthy subjects. Because of the small sample size the results should be interpreted with caution. However, we did not find gross differences between the two groups.

Observing subtle differences in neuropsychological tests that could be used as a marker of subclinical neuropsychiatric involvement, we believe that large randomised studies are needed to resolve this question.

Acute diffuse muscular pain following initiation of methotrexate therapy

We report two cases of an apparently previously undescribed reaction to low dose oral methotrexate therapy for rheumatoid arthritis. Both cases have been reported to the Committee for the Safety of Medicine.

A 70 year old woman with a 20 year history of seropositive rheumatoid arthritis but with no significant evidence of disease complications was reviewed in the outpatient department. She had previously been treated for six years with enteric coated sulphasalazine to a maximum dose of 500 mg daily; higher doses had made her non-specifically unwell. In 1992 vague abdominal discomfort had caused her to discontinue sulphasalazine but she continued to take diclofenac and coproxamol for pain and stiffness. Due to the presence of active synovitis she was started on methotrexate 5 mg weekly.

After the first dose which she took in the evening she awoke the same night with “severe pain in the whole body” which she felt was distinct from her usual joint pain in that it appeared to be located in her muscles rather than her joints. She was unable to move for seven hours due to the pain and stiffness which she described as “like being pinned”. She felt non-specifically unwell for a further two days. Having felt that this was probably coincidental she took the first dose the following week but developed identical symptoms which again lasted two days. She has now continued the methotrexate and not experienced any further similar symptoms. Before starting the methotrexate her plasma viscosity was 1.84 cp (NR 1.5–7.2), haemoglobin 11.1 g/dl and immediately after the medication the plasma viscosity was 1.68, haemoglobin 12.5 g/dl. No other investigations were performed since at the time the patient did not report on the adverse reaction or that she had stopped the methotrexate.

A 48 year old woman had an 18 month history of seropositive erosive rheumatoid arthritis and bronchiectasis. She had previously been treated with traditional (discontinued due to proteinuria) and sulphasalazine (discontinued due to diarrhoea). Her other medication included coproxamol, diclofenac, prednisolone 2.5 mg daily, ranitidine, bisacodyl, and salbutamol and beclomethasone inhalers. Due to persistent synovitis she was started on oral methotrexate 5 mg weekly. Three hours after the first dose at 5 pm she felt as if she had “gotten flu”, ‘a cold’, her joints and muscles ached, she was unable to move due to weakness and pain. She also developed blistering of the mouth. The symptoms lasted three days and fully resolved. They recurred in indental fashion following two further doses of the methotrexate. Before starting the methotrexate her plasma viscosity was 1.76 cp, following the initial dose it rose to 1.83 cp. The full blood count and differential remained unchanged as did her serum biochemistry; creatinine kinase was normal at 31 IU/l (NR 25–200). Since discontinuing the methotrexate there have been no further similar episodes.

The consistent temporal relationship to the methotrexate dose would seem to make a true association likely. We have been unable to uncover any previous reports of a similar adverse event. Unfortunately, in both cases the episode was not witnessed by a physician, and neither patient was willing to undergo rechallenge under observation due to the severity of the symptoms. The rapid time course is intriguing, suggesting either an immediate hypersensitivity reaction or a pharmacological effect. The onset of action is compatible with the known rapid absorption
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P J Modrego, J P Venegas, M S Cuenca, R S Moreno and A J Delgado

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