pressure. It should be recognised that in the setting of a cerebellar or brainstem infarction, unilateral proptosis may herald increasing intracranial pressure mandating immediate treatment.

AMIR HALKIN JACOB ABLIN
Department of Internal Medicine, Hadassah Mt Scopus, Jerusalem, Israel
ISRAEL STEINER
Department of Neurology, Hadassah Ein Kerem, Jerusalem, Israel

Correspondence to: Dr A Halkin, Department of Internal Medicine, Hadassah Unniversity Hospital, Mt Scopus, Jerusalem 91240, Israel.


Normal frontal cortex histology and immunohistochemistry in patients with motor neuron disease

In the light of the association between frontotemporal dementia and motor neuron disease,1,2 two recent studies have examined neuropathological function, and distribution of cerebral blood flow3 or metabolism,1 in patients with motor neuron disease without overt clinical evidence of dementia. These authors showed subclinical evidence of the characteristic changes of frontotemporal dementia, with failure on tasks sensitive to frontal lobe function, and hypometabolism, or reduced cerebral blood flow, particularly in the orbitofrontal area.

Brains from patients with motor neuron disease with clinically evident frontotemporal dementia show both microvacuolation of the outer cortical laminae1 and ubiquitinated inclusions2 in neurons of the superficial layers of the frontal and temporal cortex. Inclusions are also seen in hippocampal granule cells. We have therefore examined the brains of 17 unselected patients referred for routine necropsy to a general pathology department with the clinical diagnosis of motor neuron disease, without dementia. Formal neuropathological testing had not been carried out. Brains were stained with haematoxylin and eosin for routine histological examination, and immunocytochemistry for ubiquitin, using standard techniques, for detection of inclusions. Ubiquitinated inclusions typical of motor neuron disease were present in the anterior horn cells of the spinal cord in all cases; frontal cortex was normal, with no evidence of either microvacuolation or inclusions.

Patients with motor neuron disease and frontotemporal dementia usually present with dementia, subsequently developing signs of amyotrophy. It is therefore possible that the neuropathological hallmarks of microvacuolation and inclusions are a relatively late feature. It will be important to examine pathologically brains from patients with motor neuron disease who have been prospectively tested in life; nevertheless others have failed to demonstrate frontal cortical atrophy in motor neuron disease without dementia,3 and it is possible that patients with motor neuron disease can seemingly have significant neuropathological and functional deficits without overt evidence of structural or pathological changes.

P N COOPER
Walton Centre, Rice Lane, Liverpool L9 1AE, UK
A S SIDONIUS
D M A MANN
Pathological Sciences, University of Manchester, Oxford Road, Manchester M13, UK

Correspondence to: Dr Cooper.


Very severe amnesia with acute onset after isolated hippocampal damage due to systemic lupus erythematosus

Neuropsychiatric lupus designates the whole range of behavioural and cognitive impairments occurring in systemic lupus erythematosus. Up to 75% of patients with systemic lupus erythematosus may be affected. Typical manifestations are strokes, seizures, dementia, psychosis, and confusional states. We describe a patient with acute onset of isolated, extremely severe, and persistent global amnesia due to systemic lupus erythematosus.

This 55 year old previously healthy farmer was confused after a nap in the afternoon. He had no known vascular risk factor. At admission, he was alert but confused for time and place and repeatedly asked the same questions about where he was and what had happened to him. Physical examination was normal. He could not repeat three words after a two minute delay. Routine blood tests were normal except for hypomagnesaemia. His CSF had a normal cell count, protein, and glucose content.

His behaviour was remarkable only for a most pervasive amnesia: the patient never recalled visitors, specifics from test sessions, or daily events. He always recognised his family and long time friends but never the examiners or other people on the ward. He easily oriented himself in his own home but did not find his way around on the ward, where he spent three months. Whereas he very remotely seemed preserved, he was unaware of events of the past 10 to 15 years. He easily recognised the photographs of cattle he had owned more than 15 years ago, but not those he had owned more recently. He further confabulated and then denied that he did not know the answers to questions. He was initially placid and unconcerned but became depressed after a month; he often cried and complained about his bad memory.

Neuropsychological evaluations established normal oral and written language, arithmetic skills, praxis, finger gnosia, and eight-left discrimination as well as constructive abilities, space exploration, and visual recognition of complex material. Intelligence was low average (Wechsler adult intelligence scale, IQ = 91; VIQ = 89; PIQ = 96).

Executive functions were normal and they were a cerebellar hemisphere infarction. Executive functions were initially deficient (in particular high rate of perseverations in fluency tasks) but reached the normal range in the course. The main finding was a profound amnesia, both anterograde and retrograde. In amnesia extending 10 to 15 years backwards. Semantic memory was normal, as evidenced by normal naming and verbal fluency. Motor learning in a mirror drawing task was normal.

Brain MRI was performed three times. In the initial MRI 10 days after onset, both hippocampi seemed discretely swollen with blurring of the cortical sulci. In the subsequent MRIs after three and 10 months, both hippocampi appeared considerably smaller than in the initial scan (figure). No additional lesions were found; in particular, there was no macroscopic or microscopic infarction or other small ischemic or thalamic vascular lesions.

Transcranial and carotid Doppler ultrasound examination and echocardiography were normal. Thrombocytopenia persisted (15 to 31 x 109/l). Haemoglobin and leucocyte count, renal function, and liver enzymes were normal. A bone marrow biopsy showed normal haematopoiesis. Antinuclear antibodies, anti-double stranded DNA antibodies, and anti-smooth muscle antibodies were raised. No antibodies were detected against ENA-Sm, phosphoryl, thrombocytes (anti-GPIIb/IIIa and anti-GPIB/IX), or neurotrophic viruses. No anti-neuronal antibodies were found (sought after five months when antineuronal antibodies were no longer detectable). Complement factor C4 was slightly decreased (135 mg/l). Family and personal history disclosed no deposits of IgG, IgM, and C3 along the basal membrane. These findings were consistent with a diagnosis of systemic lupus erythematosus according to the American Rheumatism Association criteria.

The patient was treated with prednison (75 mg daily for 12 weeks), cyclophosphamide (150 mg daily for 10 weeks), and
Letters of Summary

Wechsler memory MRI shows (TRITE - per bocytopenia, although full The Rey-Osterrieth complex of Test California verbal learning test:
Trial 5 Interference list Short delay free recall Short delay, cued recall Long delay free recall Long delay, cued recall Recognition, hits Recognition, false positives Rey-Osterrieth complex figure: Delayed recall Rey visual designs learning test: Long delay free recall Recognition, hits Recognition, false positives Autobiographical memory interview: Childhood Early adulthood Recent facts Autobiographical Childhood Early adulthood Recent facts

The full list of tests and references can be obtained from the authors.

intravenous immunoglobulin (0.4 g/kg body weight per day for five days) with no improvement of the amnesia or the thombocytopenia, although the antinuclear, anti-

MRI (TRITE: 2900/80; coronal slices) of the medial temporal lobes. Ten days after onset (A) the MRI shows discrete enlargement of both hippocampi with blurring of the cortical structure. Ten months after onset (B) both hippocampi show considerable atrophy.

...ds-DNA, and anti-ss-DNA antibodies disappeared. After six months, a single generalized tonic-clonic seizure occurred. At a follow up examination after 11 months, the amnesia was still extremely severe (table). At 20 months, both the amnesia and the thombocytopenia were unchanged. No new seizure or additional cognitive or other sequelae of systemic lupus erythematosus had occurred.

Anterograde amnesia of comparable severity, often with temporally graded retrograde amnesia, has previously been reported after bilateral medial temporal lobe damage involving the hippocampus and adjacent cortex due to resection for epilepsy treatment, stroke, herpes encephalitis, or trauma.1 In our patient, the MRI indicated isolated bilateral medial temporal lobe damage with initially swollen, then atrophied, hippocampi. To our knowledge, this is the first account of systemic lupus erythematosus presenting with acute, extremely severe, and persistent global amnesia with radiological evidence of circumscribed medial temporal lobe damage.

Neuropsychiatric manifestations in systemic lupus erythematosus have been attributed to brain infarction due to cardiac embolism or to vascular occlusion associated with antiphospholipid antibodies, thrombotic thombocytopenic purpura, infections, medication, or autoimmune processes.1,3 Vasculitis is rare. There was no evidence for thombocytopenic purpura or infection in our patient. Cardiac embolism may simultaneously damage both medial temporal lobes. This mechanism was initially suspected in our patient because of the acute onset but is highly unlikely in view of the MRI, which did not disclose any vascular lesion. An autoimmune mechanism is more likely. Antibodies against neurons, nucleofilament protein, ribosomal protein, and phospholipid have been implicated in the pathogenesis of neuropyschiatric lupus erythematosus.2 Autoimmune processes may selectively affect the medial temporal lobe: limbic encephalitis, a paraneoplastic syndrome with complex-partial seizures and progressive cognitive decline, has been associated with an antibody against neuronal nuclei (anti-Hu).4 Limbic encephalitis usually develops insidiously but acute onset similar to viral encephalitis has been reported.1 These findings support the contention that our patient’s bilateral hippocampal damage was based on an autoimmune process. The lack of improvement after immunosuppressive treatment may indicate irreversible damage to the medial temporal lobe or persistence of the presumed antibody, as suggested by the persistence of thombocytopenia despite normal haematopoiesis.

The study was supported by grant No 32-040 432 from the Swiss National Science Foundation to Dr. Schneider.

ARMIN SCHNIDER
CLAUDIO BASSETTI
Department of Neurology
ARMIN SCHNIDER
KLEMENS GUTBROD
Division of Neuropsychological Rehabilitation
CHRISTOPH OZDOBA
Division of Neuroradiology, University Hospital, Bern, Switzerland

Correspondence to: Dr med Armin Schneider, Abt für Neuropsychologische Rehabinilitation, Inselspital, CH-3010 Bern, Switzerland.

Lamotrigine control of idiopathic trigeminal neuralgia

Carbamazepine is the drug of choice for idiopathic trigeminal neuralgia, being effective initially in 75% of patients; no other available drug is as effective, although pilocarpine and oxcarbazepine may be superior.2 Unfortunately, up to one third of patients cannot tolerate the drug in the doses required to alleviate the pain, and carbamazepine may cause aplastic anaemia, agranulocytosis, and hypersensitivity reactions.3 Carbamazepine may control idiopathic trigeminal neuralgia by suppressing Na+ currents either in the trigeminal causal neurons directly, or in the gasserian ganglion. Recently, a novel antiepileptic drug lamotrigine has become available, and this is at least as potent as carbamazepine in inactivating Na+ currents,4 with fewer side effects. A search of the medical literature did not disclose previous studies of lamotrigine effects on idiopathic trigeminal neuralgia. Thus we obtained authorisation to prescribe lamotrigine in four patients with idiopathic trigeminal neuralgia, from whom informed consent was obtained.

Patient 1, a 55 year old man, developed typical idiopathic trigeminal neuralgia paroxysms in the second right trigeminal branch. Oral carbamazepine (200 mg twice daily) almost completely controlled the paroxysms. In view of possible complicating side effects, the patient accepted the switch to lamotrigine. Carbamazepine was then stopped and replaced with lamotrigine on the following day (at which time the paroxysms had recurred) at 50 mg once a day by mouth, increased by 50 mg aliquots each day. At 100 mg twice daily paroxysms were controlled to a large degree, and relief grew to complete control at 100 mg three times a day. No adverse effects have been seen over six months.

Patient 2 was a 31 year old woman who developed typical idiopathic trigeminal neuralgia attacks involving the first three right branches. Carbamazepine at 200 mg twice a day almost completely controlled the paroxysms, with some attendant somnolence. At 600 mg daily, control was complete, but the patient was severely ataxic and could not drive. Discontinuation of treatment resulted in relapse. Lamotrigine produced complete relief at 400 mg in divided doses, without side effects, over six months.

Patient 3, a 75 year old woman, developed typical idiopathic trigeminal neuralgia in 1973 in the first and second left branches. Carbamazepine was effective only at 2000 mg (complete relief), with considerable side effects. Alcohol injection of the gasserian ganglion gave complete remission for three years. Subsequent recurrences were again treated with alcohol injection, but relief was always shorter. Glycerol injection was effective for four months. Idiopathic trigeminal neuralgia recurred. There were no sensory deficits or dysaesthesiae. Lamotrigine, begun as for patient 1, gave 90% relief at 150 mg three times a day. After

Clinical evaluation of vasospasm in subarachnoid haemorrhage by in vivo microdialysis

Patients in whom subarachnoid haemorrhage is complicated by vasospasm are at risk of developing cerebral infarction. Preserving a patent circulation may, unfortunately, be difficult. Animal experiments have shown that cerebral ischaemia is associated with raised extracellular glutamate concentrations, which can be measured by in vivo microdialysis. We attempted to demonstrate a relationship with subarachnoid haemorrhage in whom extracellular glutamate was monitored, by in vivo microdialysis, for four hours every day for four days after operation.

A 38 year old farmer reported to the hospital with a five day history of severe frontal headaches, nausea, and vomiting. Before admission he had an episode of right sided numbness and vomiting lasting 24 hours. He also complained of photophobia and mild neck stiffness. Except for the neck stiffness no focal neurological findings were evident on examination. Lumbar puncture was performed and revealed 120 cells, 2% polymorphs, with a raised pressure of 298-09 (19-9) mmHg. This was "high" in comparison with the baseline normal in humans (20-25 mmHg) as previously reported.6 An angiogram one day later showed severe focal vasospasm (no filling of the right anterior cerebral artery. Subsequent CT showed bilateral frontal hypodensities suggesting ischaemic changes (fig 1). The early severe focal vasospasm dramatically improved, and angiography on day 4 revealed a "normal" circle of Willis.

Intracerebral microdialysis was performed as previously described8 after stabilisation of the patient in the intensive care unit. The catheter was inserted via the right carotid artery. Intracerebral microdialysis was performed as previously described after stabilisation of the patient in the intensive care unit. The catheter was inserted via the right carotid artery. Intracerebral microdialysis was performed as previously described8 after stabilisation of the patient in the intensive care unit. The catheter was inserted via the right carotid artery. Intracerebral microdialysis was performed as previously described8 after stabilisation of the patient in the intensive care unit. The catheter was inserted via the right carotid artery. Intracerebral microdialysis was performed as previously described8 after stabilisation of the patient in the intensive care unit. The catheter was inserted via the right carotid artery.