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 Pathology,
Hadassah Ein Kerem,
Jerusalem, Israel

Correspondence to: Dr A Haklin, Department of Internal Medicine, Hadassah Unanimity 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 neuropsychological function, and distribution of cerebral blood flow3 or metabolism,4 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 related 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 laminae5 and ubiquitinated inclusions6 in neurons of the superficial layers of the frontal and temporal cortices; inclusions are also seen in hippocampal granule cells.7 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 neuropsychological testing had not been carried out. Brains were stained with haematoxylin and eosin for routine histological evaluation, and immunostained 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, and it is clear that patients with motor neuron disease can seemingly have significant neuropsychological and functional deficits without overt evidence of structural or pathological change.

P N COOPER
Walton Centre for Neurology,
Liverpool L9 1AE, UK

N ASSIDJON
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 hippocampal damage, 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 thrombocytopenia (26 x 109/l). 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 very remote memory 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 never confabulated and always 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 left-right 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 found intact. Very simple tasks required lower levels of cognitive processing. 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 memory impairment (preserved immediate memory span was normal, he was unable to recall any previously acquired explicit information, independent of the presentation modality). He was able to perform time-based recognition tasks, he denied any familiarity with the items and had a high rate of false positives in forced choice recognition tasks.

An autobiographical interview and a test of knowledge of place disclosed a temporally graded retrograde 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 distinctly swollen with bulging of the cortical plates. The MRI taken after 3 months, both hippocampi appeared considerably smaller than in the initial scan (figure). No additional lesions were found; in particular, there was no implication of small hemispheric 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 haemopoiesis. Antinuclear antibodies, anti-DNA, anti-Ro/SSA, anti-La/SSB, anti-smooth muscle, anti-centromere, anti-protein, and anti-neutrophilic cytoplasmic antibodies were raised. No antibodies were detected against ENA-Sm, phospholipid, thrombocytes (anti-GPIb/IIIa and anti-GPIb/IX), or rheumatoid factor. No anti-neuronal antibodies were found (sought after five months when antinuclear antibodies were no longer detectable). Complement factor C4 was slightly decreased (135 mg/l). Family and maternal, sibling, and first degree relative deposits of IgG, IgM, and C3 along the basal membrane. These findings were consistent with a diagnosis of systemic lupus erythematosus according to the 1971 American Rheumatism Association criteria.

The patient was treated with prednisone (75 mg daily for 12 weeks), cyclophosphamide (150 mg daily for 10 weeks), and
intravenous immunoglobulin (0.4 g/kg body weight per day for five days) with no improvement of the amnesia or the thrombocytopenia, although the antinuclear, anti-ds-DNA, and anti-ss-DNA antibodies disappeared. After six months, a single generalised 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 thrombocytopenia 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. 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 thrombocytopenic purpura, infections, medication, or autoimmune processes. Vasculitis is rare. There was no evidence for thrombocytopenic 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, neurofilament protein, ribosomal protein, and phospholipid have been implicated in the pathogenesis of neuropsychiatric lupus erythematosus. 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). Limbic encephalitis usually develops insidiously but acute onset similar to viral encephalitis has been reported. 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 thrombocytopenia despite normal haematopoesis.

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

Correspondence to: Dr med Armin Schneider, Abt für Neuropsychologische Rehabilitation, 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. 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. Carbamazepine may control idiopathic trigeminal neuralgia by suppressing Na+ currents either in the trigeminal causal nucleus directly, or in the ganglion. Recently, a novel antiepileptic drug lamotrigine has become available, and this is at least as potent as carbamazepine in inactivating Na+ currents, 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 along right third 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 lamotrigone 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 lamotrigine was 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 by mouth. After two months, however, the economic burden on the patient led to Fogarty percutaneous compression of the gasserian ganglion, with analgesia at short term follow up only.

Patient 4 was a 72 year old man who had frequent attacks of idiopathic trigeminal neuralgia in the left second and third branches for a few months. A sense of burning in the gums was reported laterly. Notably, 50% of the attacks presented at night. Speaking and chewing triggered intolerable pain. Carbamazepine at 200 mg twice a day initially controlled the attacks, but very soon produced cardiovascular intolerance. Carbamazepine was replaced with lamotrigine and attacks were completely controlled at 400 mg in divided doses over four months.

Lamotrigine may cause initial ataxia, diplopia, nausea, vomiting, and blurring of sight in 15–35% of the patients treated for epilepsy, but these disappear or are much reduced after dose adjustments. An allergic skin rash is seen in 3–17% of the patients. This can be reduced to no more than 10% if the drug is started at 50 mg once a day for four days, then doubled to 100 mg for another two week, then doubled to 200 mg for another two weeks, and then brought to a maintenance dose of 200–400 mg in divided daily doses. A similar regimen may be applied for idiopathic trigeminal neuralgia, and infrequently faster doses, although perhaps necessitating an increase schedule for rapid control. Doses of lamotrigine can be as high as 1300 mg daily. Carbamazepine and phenytoin speed up the elimination of the drug, whereas valproate slows it.

Lamotrigine is a potent antigelutamatergic agent. Depression of excitatory transmission in the trigeminal causal nucleus is believed to be part of the range of action of this anti-idiopathic trigeminal neuralgia drug, and thus lamotrigine relief of idiopathic trigeminal neuralgia may not necessarily be due to Na+ current inactivation.

Our preliminary data require confirmation with a placebo controlled study.

Correspondence to: Dr S Canavero, Via Montemagno 46, 10132-Torino, Italy.


