Letters

Neuropsychological functions in the follow-up of transient global amnesia

Sir: Since the description by Fisher and Adams,1 transient global amnesia has been defined as loss of short-term memory characterised by the inability to retain new information, with repetitive queries and retrograde amnesia, but with no other neurological signs and symptoms. Although patients of transient global amnesia seem to recover completely after an episode, Mazzuchi et al. have demonstrated that a persistent decrease in verbal IQ can occur.2 We have conducted a prospective analysis of 29 patients with transient global amnesia. The mean age of the patients at the time of their episode was 60.9 years (±8.0). All criteria for the diagnosis of transient global amnesia were present at the time of the episode: (1) transient amnesic attack with no direct relation to cranial trauma, (2) evidence given by a witness of the inability to form new memories, (3) repetitive queries, (4) apparently normal behaviour and orientation, (5) evidence given by a witness of normal long-term memory and (6) presence of retrograde amnesia at least during the episode. These criteria, more restrictive than those of other authors,3 rule out other possible causes. The patients were submitted to the Wechsler Bellevue Intelligence Scale six months after admission. A group of 29 control subjects with a mean age of 61.8 years (±7.3) were submitted to the same neuropsychological test. Student's t test was used for statistical evaluation.

The following values were obtained: transient global amnesia-verbal IQ 92.8 ± 15.4, Control-verbal IQ 90.2 ± 14.6 (p = 0.25); transient global amnesia-performance IQ 100.4 ± 12.0, Control-performance IQ 99.6 ± 15.9 (p = 0.42); transient global amnesia-Full IQ 95.0 ± 14.8, Control-Full IQ 94.1 ± 16.4 (p = 0.41). The most striking feature of the study was that no difference could be demonstrated between patients with transient global amnesia and control subjects. No difference was evident either in relation to the episode's duration, or in relation to the duration of the retrograde amnesia.

The sixteen patients described by Mazzuchi et al. had a verbal IQ and performance IQ greater than a control group and we think that the decrease in verbal IQ in relation to performance IQ could be due to a poor selection of the control group.

These authors interpreted their results as indicative of left hemisphere involvement in transient global amnesia, but our own results, the report of a patient with a mass in the non-dominant hemisphere, and a patient described by Ladurner et al. with a hypodense lesion in the right hemisphere demonstrated by CT examination seem to discount this hypothesis on the role of the left hemisphere in the production of episodes of transient global amnesia.

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References

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Neuropsychiatric symptoms in the course of Wegener's granulomatosis

Sir: Wegener's granulomatosis is an uncommon connective tissue disorder resembling polyarteritis nodosa; it causes granuloma and vasculitic lesions throughout the body, predominantly in upper respiratory tract, lungs and kidney.1 Treatment with cyclophosphamide (usually combined with steroids) produces survival rates of about 85%. In a review of 104 patients, Drachman2 reported that 54% had neurological involvement, predominantly peripheral lesions. Reports of central nervous system involvement are rare,3–5 and include a patient with immunosuppressant reversible dysphasia, thought to be secondary to cerebral vasculitis. The case reported here suggests that both neurologi- cal and neuropsychiatric disturbance may occur in the course of the disease as the result of central nervous system involvement. This has not been documented previously.

A 55-year-old woman presented with a three-week history of right-sided bloody nasal discharge. Biopsy of granular tissue from the right nostril suggested Wegener's granulomatosis, confirmed by biopsy of a right lower lobe bronchus lesion. Treatment was started with cyclophosphamide and prednisone. Despite resolution of her nasal symptoms, her relatives noticed that she was becoming drowsy and unsteady on her feet. She complained of blurred vision and polydipsia although blood glucose estimations were normal. Following development of a herpes zoster infection over her right hemithorax, the immunosuppressants were stopped. She rapidly became morose, apathetic, and prone to spells of tearfulness. This apparent depression was thought to be due to her having been widowed shortly before the onset of her illness. There was no family or past personal history of psychiatric disorder.

Examination revealed a pale, distressed woman, mildly clouded and slow to respond, with a marked expressive dysphasia. Her mood was fearful and depressed with secondary delusions of persecution by family and nursing staff. Cognitive testing showed impaired concentration with disorientation for time and a tendency to perseverate. She scored 17/37 on a standardised test of global cognitive function, with severe impairment (1/5) on the short-term memory sub-test. Apart from her dysphasia and an unsteady gait, there were no abnormal neurological signs. An EEG showed fluctuating delta components on both sides, superimposed on a slow dominant rhythm posteriorly indicative of a widespread or multi-focal organic disturbance. A diagnosis of sub-acute organic brain syndrome (ICD 293-1) with paranoid and depressive symptoms was made. Cultures of blood, sputum, urine and CSF failed to detect an infective cause. The CSF was normal.

Cyclophosphamide 150 mg daily and prednisone 60 mg daily were re-started because of her progressive deterioration. Within two weeks her mental state was much improved with significant resolution of her dysphasia and a measured increase in cognitive ability to 32/37. Her short-term memory impairment was unchanged. Her paranoid and depressive symptoms became less evident. An EEG recorded eight weeks after the first showed a return
to normal. She remained relatively well for eight weeks but then needed re-admission with a leucopenia (0·9 × 10⁹/l), recurrent herpes zoster and a chest infection. She was again confused with paranoid ideas. Her EEG showed diffuse changes, less pronounced than before. Prednisnone only was resumed and she slowly improved. She remains in clinical remission (18 months later) on prednisone 20 mg on alternate days. Her family report her personality as changed; she is socially inconsiderate, apathetic and lacking in spontaneity. Despite global improvement in cognitive function, she has slight residual dysphasia and short-term memory difficulties.

Despite the lack of direct histological evidence, there are strong grounds for suggesting that the neuropsychiatric disorder observed was the result of central nervous system involvement in the Wegener's granulomatous process. The polydipsia and visual difficulties, noted early on may have been consequent upon contiguous invasion by granulomatous tissue from the nose or paranasal areas. The generalised disturbance, with evidence of cortical deficits appears more probably related either to remote cerebral granulomata or vasculitits than to further local extension. The fact that the neuropsychiatric disturbance arose following cessation of immunosuppressants and resolved following their reintroduction, makes their role as causal confusional agents improbable, nor could an infective or metabolic cause be detected.

Reviewing the few existing reports of pathologcal change in the brains of patients with Wegener's granulomatosis, it seems that diffuse cerebral involvement may occur with necrotic foci in optic nerves, thalamus, cerebellum and cortex. Recently Oimomi et al3 partially resected a lesion from the right parietal lobe of a patient with Wegener's granulomatosis in which granulomatus foci and necrotising angiitis coexisted. In that case, as in this, there was no evidence of renal involvement, an observation also made by Sahne4 in his patient with a reversible dysphasia. These patients conform to the concept of limited Wegener's granulomatosis, in which it appears effective to treat the neurological complications with glucocorticoids.

In the present case, the persistence of memory difficulties, language problems and personality change, suggests that structural damage has occurred. The patient's depressed and withdrawn presentation was initially attributed to her recent bereave-

ment partially obscuring the eventual diagnosis of a cerebral granulomatosis responsive to treatment. Neuropsychiatric symptoms appearing in a patient with Wegener's granulomatosis should alert the clinician to this possibility.

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References

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Chronic meningitis in Fabry's disease

Sir: The usual neurological manifestations of Fabry's disease are two-fold: bouts of pain in the extremities due to peripheral nerve damage and cerebro-vascular accidents due to the thickening of vessel walls in the brain. Both are a consequence of the intracellular deposition of trihexosylceramide. The cerebro-spinal fluid (CSF) is normal or shows transient abnormalities. We report a case of Fabry's disease presenting as a chronic meningitis.

A 54-year-old man was first admitted to hospital because of an unexplained fever. For ten years, he had had painful paraesthesia of hands and feet, oedema of the lower limbs, cardiomegaly and deafness. Six months before admission, he had developed fever, diarrhoea, back pain and lymph node enlargement. A lymph node biopsy specimen showed numerous macrophages with foamy cytoplasm. The diagnosis of Whipple's disease was proposed, although a biopsy of the jejunum was not conclusive. Oxytetracycline was given for nine months but proved ineffective. Upon readmission, the findings were similar with the exception of anaemia, leucopenia and thrombocytopenia. A bone marrow aspiration was normal. After a few days, the patient complained of headache. The neurological signs and symptoms were unchanged. The ESR was 120 mm/hour. CSF analysis showed 26 white cells and low glucose level. Repeated lumbar punctures confirmed the diagnosis of chronic meningitis (table.) No infectious disease was found (tuberculosis, brucellosis, listeriosis, mycosis, syphilis). A liver biopsy specimen was normal. There was no evidence of sarcoidosis or malignancy. The patient received isoniazid, rifampin and ethambutol for four months without effect. Steroids (1·0 mg/kg/day) were then added. They produced some improvement in clinical and laboratory abnormalities, but relapses occurred whenever the dose of steroid was reduced. Eighteen months later, a rise in the blood creatinine level (198 nmol/l) disclosed renal failure. The uroanalysis was normal. A kidney biopsy specimen showed intracellular deposits of lipid in the glomeruli and tubules. The diagnosis of Fabry's disease was further substantiated by a decrease alpha-galactosidase activity in the plasma: 0·23 nmol/ml/h (control: 7-9), in the white blood cells: 6-2 nmol/h/mg protein (control: 39) and in the urine: 1·1 nmol/ml/h (control: 13·8). Thin layer chromatography showed a massive excretion of trihexose and digalactosyl ceramide in the urine. A history of deafness and death in early adulthood of several male relatives had been recorded in the family. The patient died of peritonitis, after a perforation of the small bowel while still on steroids.

In the present case, the discovery of a chronic meningitis was misleading since Fabry's disease is not listed among the many causes of chronic meningitis. The hypothesis that the meningitis was due to an intercurrent disease is unlikely as no other cause was found during the two year follow-up. CNS involvement in Fabry's disease seldom produces permanent changes in the CSF. Although intracellular deposits of lipid in the brain are common, sometimes extending to the arachnoid, the CSF remains normal or shows a mild increase in protein. Cellular changes have been occasionally noticed in the wake of cerebral attacks. Low glucose level was never mentioned. We believe that this is the first documented case of chronic meningitis in Fabry's disease. Fabry's disease should be added to the ever-growing
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