Multiple sclerosis in association with dialysis encephalopathy syndrome

Sir: Since its first description in 1972, the syndrome of dialysis encephalopathy has occurred in numerous centres in the United States, Europe, and Australia. This condition is characterised by speech and language changes and seizures. A typical electroencephalographic abnormality precedes the clinical symptoms by six to eight months, continuing throughout the illness. In nearly every instance, the course of the disease is inexorable, resulting in death in less than a year. The pathogenesis of this condition, in spite of several theories, has not been elucidated. We have observed a patient with a typical dialysis encephalopathy, who also developed multiple sclerosis, suggesting that immunological features of dialysis encephalopathy do not preclude the development of the demyelinating illness. To our knowledge this association has not been previously recorded.

A 37-year-old white female was admitted to the Brigham and Women's Hospital with a speech and gait disorder of several months' duration. She had been on home dialysis for ten years, for the most part using untreated tap water. Renal biopsy had shown chronic glomerulonephritis. She had had rheumatic valvular disease with an aortic-valve replacement following staphylococcal endocarditis. Medications upon admission included coumarin and an aluminium-containing oral antacid. On admission the patient was disorientated and inattentive, and both recent and remote memory were impaired. Speech was dysemiplastic and was punctuated by frequent arrests, as well as by numerous literal paraphasias. Comprehension and repetition were relatively spared. She had poor penmanship with frequent spelling errors although she sometimes preferred to communicate in the written mode. Her drawings and constructions were impaired. The cranial nerves were normal. She was generally wasted with increased tone, hyperreflexia and extensor plantar responses. Both lower limbs were weak, the right slightly more than the left. She had a spastic gait with inversion of the right foot on walking. Sensory examination was unreliable, but it appeared that there was a sensory loss over the right lower trunk and upper thigh. Routine laboratory values were unremarkable. She had a serum aluminium of 31, normal being less than 50 mEq per 100 ml. Lumbar puncture revealed spinal fluid with a glucose of 62 mg per 100 ml, a protein of 22 mg per 100 ml, and a gamma globulin of 3-8 mg per 100 ml. A CT scan showed evidence of mild cerebral atrophy. A myelogram was normal. An EEG revealed bursts of high-voltage delta waves occurring anteriorly with intermittent spikes and sharp waves. Visual evoked potentials were abnormal (right eye 145 ms, left eye 117 ms, normal 108 ms). Somatosensory evoked potentials could not be satisfactorily recorded.

Despite an initial favorable response on EEG and clinical testing to diazepam and later to clonazepam, she had a progressive downhill course. Weakness, hyperreflexia, pseudobulbar signs, painful flexor spasms, facial and limb myoclonus, seizure activity, progressive dementia, and speech difficulty all developed. Valproic acid, phenobarbital, and phenytoin, as well as intravenous ACTH, had no effect. She died three months after admission. At necropsy the patient's kidneys showed end-stage renal disease with cystic degeneration. On gross external inspection the brain showed mild frontal atrophy. Serial coronal sectioning of the cerebral hemispheres revealed scattered, irregular, sharply defined small zones of gliosis and myelin loss. These were present about the lateral and third ventricles and in the white matter of the centrum semiovale. Serial en bloc horizontal sections of the brainstem and cerebellum revealed occasional similar lesions in the white matter of the brainstem. Histological examination of these lesions showed them to be demyelinated plaques of multiple sclerosis. Some were active, other quiescent. The active lesions showed a lymphocytic-macrophage infiltrate at the advancing edge. The older lesions contained only rare mononuclear cells and were gliotic.

The syndrome of chronic dialysis encephalopathy has a fairly consistent clinical picture. In the majority of patients, there is a speech and language disorder characterised by a halting, hesitant dysarthria with frequent speech arrests, literal and phonemic paraphasias, and relatively preserved comprehension. The speech disorder may vary according to the dialysis schedule; worsening during and after dialysis. Multifocal myoclonic movements are seen involving the limbs and face, with seizures appearing later in the course of the illness. Various psychiatric symptoms may appear, all against a background of progressive dementia. Electroencephalographic changes occur early in the illness, appearing as bursts of high-voltage delta waves predominantly anteriorly with random sharp spikes and triphasic waves with a relatively normal background. This EEG and set of clinical symptoms have been shown to respond initially to diazepam or clonazepam or both, however, in all but a few instances, the clinical course is inexorable, with death occurring in 1 to 15 months after the onset of the illness. A body of evidence has accumulated, linking
the disease to aluminium toxicity, particularly to untreated water used to make the dialysate although possibly also to orally ingested antacids. The pathological changes in the brain at necropsy have consistently been nonspecific and have not furnished an explanation as to the nature of the process.

While our patient had all of the typical features of dialysis encephalopathy, she had a superimposed demyelinating disease with the neuropathological findings of multiple sclerosis. It is of interest that the multiple sclerosis, a disease in which immune mechanisms are felt to play a central role, proceeded at a rapid pace in spite of the relative immunodeficiency occasioned by the setting of renal failure and chronic dialysis. We report this unusual case in the belief that understanding of the cause of dialysis encephalopathy may come from knowledge of which diseases may occur in its company.

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References

Circling movements in human viral encephalitis

Sir: Rotational and somersaulting movements have been observed secondary to experimental irritative lesions in monkeys at or near the vestibular association cortex in the temporal operculum. Circling or rotational movements as part of seizure disorder have occasionally been described and have been associated with lesions such as tumours, vascular infarcts, depressed fracture and aneurysm in the frontotemporal region. The following case documents circling movements in a child with presumed viral encephalitis.

A 5½-year-old right handed female child was hospitalised on 25 September 1980. Her birth and early development were normal. She developed persistent high grade fever without rigors lasting for four days two weeks prior to admission. Three days after the onset of fever she had two successive generalised tonic-clonic convulsions following which she remained unconscious for the next two days. She could not talk, hear or comprehend when she regained consciousness, and was incontinent of urine and faeces. She could sit and stand on her own, but each time she was made to stand she would rotate around her own axis toward the left.

On examination, at the time of admission, she was conscious but had a vacant look and could not recognise her parents. She did not talk or cry. She would open her mouth and bite any object brought near her. Ocular movements and the optic fundi were normal. There was a partial right facial paresis. There was no overt weakness in the extremities, but the right sided deep tendon jerks were brisk and the right plantar response was extensor. The most striking sign was the presence of circling movements. She would rotate in an anticlockwise (left) direction at a rate of 20-25 times/min, with her head and eyes turned to the left, whenever she was made to stand (fig A). This activity continued until she was put to bed. She would revert back to anticlockwise rotation whenever forcibly rotated in the clockwise direction. The frequency of circling decreased one week after admission, and three weeks later it stopped. Instead she walked around aimlessly and grabbed at any object coming in front of her to put it in her mouth. This oral tendency decreased and disappeared after one month. At a recent follow up (19 January 1982), her mood was normal, she responded to her name and could comprehend some simple commands. She now recognised her parents and elder brother, and was able to communicate by gestures for food and urination, and she had begun to speak a few words. Normal investigations included routine haematology, urine analysis, blood biochemistry, cerebrospinal fluid (CSF), negative syphilis serology and radiographs of chest and skull. Viral serological data on paired CSF samples showed no significant titre of complement-fixing antibody against measles, mumps, varicella-zoster, cytomegalovirus and herpes simplex. No virus was isolated in tissue culture. The first EEG recording obtained during sleep on 26 September 1980 showed bitemporal predominantly delta slowing with suppressed voltage over the fronto-temporal region of the left hemisphere. There were no sharp complexes. The second EEG recorded a week later showed almost identical findings. Subsequent EEGs disclosed a tendency for reorganisation of the background with theta activity. In addition, prolonged bursts of spike discharge, well represented on the right hemisphere was evident. A CT scan (fig B) done on 30 December 1980 showed low density lesions bilaterally in the temporal regions, more on the upper and anterior part of the temporal lobes, much more evident on the left side. There was no mass effect and the lesion showed no enhancement with the contrast.

This patient had a rapid onset of illness associated with fever, convulsions and unconsciousness. The subsequent course was one of progressive recovery. She lost recognition of objects and people and speech and exhibited marked oral tendencies and emotional lability. The clinical syndrome is compatible with lesions of both temporal lobes (cf the Kluver-Bucy syndrome in experimental animals). The clinical and anatomical findings in our patient indicate a herpes simplex viral encephalitis. However, virological proof is missing, so the diagnosis is presumptive. Other viruses like canine distemper virus and the virus of foot and mouth disease are known to cause encephalitis associated with circling movements in the wild hedgehog, Erinaceus europaeus.* These viruses were not tested in our patient. The

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