MRI of thoracic cord in tropical spastic paraparesis

Tropical spastic paraparesis (TSP) is a disease occurring in Afro-Caribbeans following HTLV-1 retro-virus infection. There is some evidence that the geographical and ethnic distribution of HTLV-1 illness is even wider[1] and HTLV-1 associated myelopathy (HAM) in Japan is probably the same disorder. Abnormalities are found on MRI of the brain in both TSP[2,3] and HAM.[4] High signal areas are found in the brain similar to those in multiple sclerosis (MS), though they tend to be less extensive. The thoracic cord (on which the brunt of the pathological process falls) has been examined in only three patients, one of whom had atrophy.[2] Since the clinical picture of TSP may resemble that of progressive MS, we have made a systematic comparison of the MRI characteristics of the thoracic cord in the two conditions.

Nine patients with TSP who were born in the Caribbean were compared with an age and sex matched group of European white patients with clinically definite MS,[5] all of whom had a progressive spastic paraparesis. Disability was scored using the Kurtzke Disability Status Scale.[6] The patients with TSP were anti-HTLV1 positive and had HTLV-1 genome integrated into leucocyte DNA. Eight were female. The mean age was 53 years (range 43–65 years), the mean symptom duration was 12 years (range 1·5–23 years), and the mean Kurtzke disability score was seven (range five to eight). The mean age of the MS patients was 42 years (range 35 to 53 years), the mean symptom duration was 11 years (range seven to 17 years), and the mean Kurtzke disability score was five (range 4 to 6). The spine was imaged by a Picker 0·5T superconducting machine with T1 weighted ($SE_{500/40}$) 5 mm contiguous parasagittal slices using a surface coil. All MS patients and five TSP patients had additional T2-weighted sequences ($SE_{1500/80}$, 5 mm contiguous parasagittal slices) to detect abnormal signal. Images were reported without knowledge of the individual diagnosis by one of the authors (EPGH du B).

Atrophy of the thoracic cord was seen in six of nine patients with TSP and five of nine patients with MS. Three of five patients with TSP who had T2-weighted images of thoracic cord had diffuse high signal and all three had atrophy (fig). Five of nine with MS had high signal return on T2 weighted images, one of whom did not have atrophy. The pattern of high signal was diffuse in two and focal or patchy in three (fig).

These results confirm the previous MRI finding of atrophy in the thoracic cord in a proportion of patients with TSP. However, a similar degree of atrophy is seen as frequently in patients with MS who had a progressive spastic paraparesis, a finding compatible with pathological studies where cord atrophy is present in 72% of patients with MS at necropsy.[7] There was some difference in the pattern of high signal seen in the two groups, with more diffuse and uniform high signal in TSP and focal or patchy high signal in MS. However, these differences in the MRI findings are slight and a reliable distinction between the two conditions cannot be made on these grounds.

Figure The MRI on the left shows diffuse high signal with atrophy of the thoracic cord in TSP. The right shows the patchy high signal typically seen in MS. ($SE_{1500/80}$, 5 mm sagittal slices).

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Lewy bodies and subacute sclerosing panencephalitis

The occurrence of Lewy bodies in the nervous system is relatively specific to Parkinson's disease.[1] Their association with other disorders may provide a clue to the aetiology of Parkinson's disease, especially when the cause of these disorders is known. We describe Lewy bodies in two patients with subacute sclerosing panencephalitis (SSPE). They are examples of long survival and the first has been reported for this reason.[2]

A 14 year old boy presented with intellectual deterioration and absence attacks. When seen at the National Hospital he had generalised epileptic seizures, multifocal myoclonus, emotional lability, dysarthria, mild chorea and ataxia. Serum measles virus titre was elevated. An EEG showed periodic complexes and cerebrospinal fluid (CSF) showed a paretic Lange curve. His condition stabilised, but at the age of 21 years he deteriorated again. Six years later he was bed-bound, and died of bronchopneumonia.

The brain showed severe atrophy associated with widespread neuronal and myelin loss, gliosis, and occasional neurofibrillary tangles. Very few nerve cells remained in the substantia nigra with a couple of Lewy bodies present in each unilateral section. Lewy bodies were also present in the locus

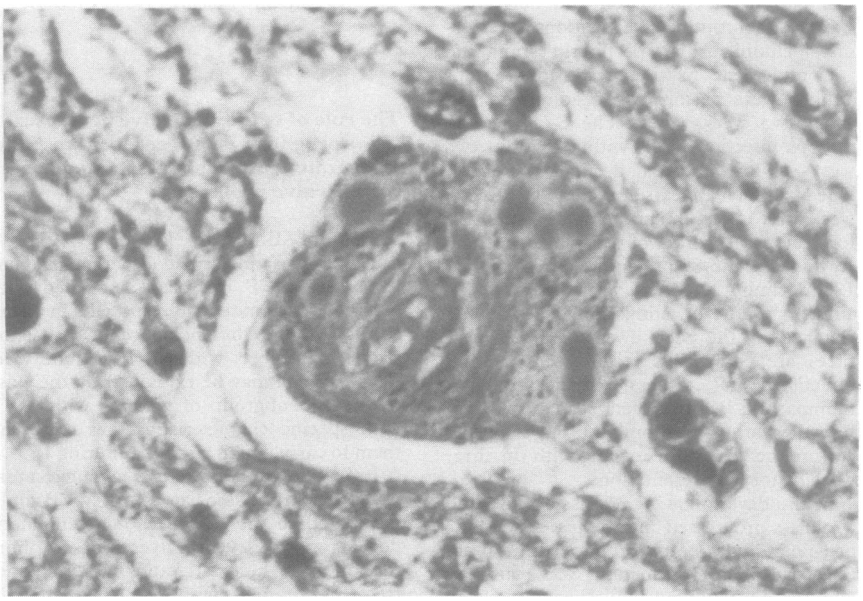

Figure Locus coeruleus neuron containing a neurofibrillary tangle surrounded by a number of smaller Lewy bodies. Haematoxylin and eosin × 1500.

coeruleus, but not in the dorsal vagal nucleus, nucleus basalis, cerebral cortex, spinal cord, superior cervical sympathetic ganglia, and coeliac ganglia.

The second case was a nine year old boy presenting with intellectual deterioration and an epileptic seizure. A month later, when admitted to Hôpital Ste-Justine, Montreal, he was unable to obey simple commands, his affect was inappropriate and there was mild orofacial chorea. The left plantar was extensor and his gait ataxic. He developed generalised myoclonus with occasional opisthotonus, and within weeks showed decorticate posturing. Serum measles virus titre was 1024. CSF protein was 0·54 g/l, with no cells, and the measles complement fixation titre was 128. An EEG was dominated by low voltage slowing and periodic high voltage slow-wave complexes.

His condition stabilised, but he remained bed-bound and died at the age of 19 years. The brain showed generalised atrophy, with profound neuronal loss and gliosis in the cerebral cortex and hippocampus with a few microglial nodules and tangles. Some remaining neurons showed intranuclear inclusions. All central grey nuclei showed severe neuronal loss with glial and microglial reactions and several tangles. There was severe neuronal loss in the substantia nigra and locus coeruleus with tangles and Lewy bodies (fig). Lewy bodies were not found in the dorsal vagal nucleus, cerebral cortex, spinal cord or autonomic nervous system.

These patients with SSPE showed long survival of 13 and 10 years respectively. Tangles occur even in patients dying at a young age,[3] but Lewy bodies have not been described in other cases. They were present in the substantia nigra and locus coeruleus, but not in other areas usually susceptible to Lewy bodies. We know of a third case of SSPE with onset at 21 years, and a nine year survival. In this case there were very few nerve cells in the substantia nigra, and some pale bodies, which are normally seen in Lewy body diseases.[4]

Apart from the Lewy body–Parkinson's disease spectrum Lewy bodies are confined to a small group of rare degenerative disorders.[1] They may be by-products of attempted regeneration, rather than of degeneration, thus explaining their occurrence in long-standing cases of SSPE showing periods of relative stability. SSPE is a destructive inflammatory process due to persistent measles infection, but the aberrant immunological mechanisms are not fully understood. Although there is no direct evidence for an infectious aetiology for Parkinson's disease, there are parallels with SSPE which results from an infectious agent acquired in early life, leading to a progressive disorder associated with disconcordance in identical twins,[5] and Lewy bodies pathologically.

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Combined neuroleptic malignant syndrome and the central anticholinergic syndrome

The neuroleptic malignant syndrome (NMS) is an idiosyncratic reaction to neuroleptic drugs characterised by encephalopathy, rigidity, dysautonomia and hyperthermia.[1] Dopamine receptor blockade appears central to the pathophysiology of the rigidity,[2] and possibly the encephalopathy.[3] Because cholinergic receptor blockade can also cause encephalopathy, the differential diagnosis of NMS includes the central anticholinergic syndrome (CAS).[1] Nevertheless, anticholinergics, which are used to treat Parkinsonism associated with neuroleptic use, are often used to treat the rigidity in NMS.[3] However, anticholinergics could theoretically exacerbate the encephalopathy of NMS, possibly spawning the development of combined NMS and CAS. We report the first case of combined NMS and CAS.

After four months of lithium therapy, a 28 year old man with bipolar affective disorder was given 15 mg of daily haloperidol. One week later he was brought to the emergency room confused, agitated and hallucinated. Neurological examination disclosed a fever of 101°F, cogwheel rigidity, resting tremor, and dysmetria. Serum glutamic oxaloacetic transaminase 128 IU/l (normal 5–35), serum glutamic pyruvate transaminase 65 IU/l (normal 5–30), lactic dehydrogenase 373 IU/l (normal 90–220) were all increased in concentration. His creatinine phosphokinase was 7700 IU/l (normal 25–145). All other laboratory studies, including computed tomography of the brain, and lumbar puncture were normal. The haloperidol and lithium were stopped.

Treatment included levodopa/carbidopa 25/250, and 4 mg of intramuscular benztropine over two hours. Several hours after receiving the benztropine, his mental status deteriorated from being agitated and confused to comatose, and his temperature increased from 101°F to 104°F. The rigidity was unchanged, but he developed urinary retention, decreased bowel sounds and large pupils, suggesting anticholinergic toxicity. Six mg of intravenous physostigmine was administered. Within minutes he was able to follow simple commands. His temperature decreased from 102°F to 99·5°F over the next hour.

The differential diagnosis of NMS includes CAS. In a recent review, Guze and Baxter state that a response to physostigmine is sufficient to differentiate between NMS and CAS.[1] However, this case suggests that the two disorders can coexist in the same patient. Furthermore, since drugs that cause NMS have anticholinergic properties, cholinergic blockade by neuroleptic drugs may make patients more susceptible to CAS from even low doses of anticholinergic agents.

Two points are illustrated by this unusual case. First, anticholinergic agents, which do not have demonstrable efficacy in NMS[3] are probably contraindicated in NMS. Second, patients with NMS should be carefully monitored for signs of anticholinergic toxicity.

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Intraoperative aneurysms rupture during the predissection stage

Much has been written about intracranial aneurysms which rupture as they are being dissected, probably because of the frequency of this event (24% in one well known series).[1] Less has been written about rupture of aneurysms during the period after the craniotomy is started and before the aneurysm is exposed, the predissection stage, discussed by Batjer and Samson.[2] Fortunately, this is uncommon (Yasargil 1984, Charles G Drake and John L Fox: personal communications). Batjer and Samson encountered it four times in a series of 307 consecutive aneurysm operations and questioned whether the operations should have been aborted. I report an experience of rupture of an aneurysm before dissection.

A 59 year old right handed white woman experienced the acute onset of severe headache 48 hours before admission. She had no neurological symptoms and the only abnormal finding was neck stiffness. Computerised tomography (CT) of the head was normal but lumbar puncture disclosed grossly bloody fluid under an opening pressure of 210 cm. Left carotid angiogram showed an anterior communicating artery aneurysm 3 mm in diameter pointing forward and down.

During opening the patient was given 50 gm of 20% mannitol, but spinal fluid was not drained. A slow drip of nitroprusside was started. As the chiasmatic cistern was opened, and before the aneurysm was displayed, the aneurysm ruptured and the brain herniated massively into the craniotomy opening. A hand held brain retractor was left in place to allow escape of blood. At the time of rupture the patient's blood pressure was 100/80 mm Hg but within a few minutes had risen to 180/95 mm Hg. Immediately after rupture the patient was given 40 mg of nitroprusside and 20 mg of dexamethasone intravenously. Five minutes after rupture nitroprusside was stopped and a nitroglycerin drip (40 mg in 50 cc of 5% dextrose and water) was started. Within two minutes, that is seven minutes after rupture, the brain suddenly returned to its pre-rupture position and the BP fell to 60/40 mm Hg. Frontal lobe amputation, which had removed only 5 cc of brain, was terminated and the BP was allowed to rise slowly over the next 45 minutes. No further attempt to