Short report

Acute cerebral demyelination: clinical and pathological correlation with computed tomography

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SUMMARY A 30-year-old woman died eleven weeks after the onset of an acute illness during which she developed quadriplegia, dysphasia, incontinence, confusion, emotional lability and gaze palsies. The CT scan demonstrated large white matter low attenuation lesions with no mass effect and minimal contrast enhancement. At necropsy the lesions were shown to be those of massive cerebral demyelination.

Cranial computed tomography (CT) has been shown to be of considerable value in the assessment of patients with demyelinating diseases. In addition to atrophic lesions, areas of low attenuation in the periventricular, central and cortical white matter can be demonstrated. In a small number of patients it has been possible to correlate these radiological findings with histological study of demyelinating lesions obtained by biopsy or at necropsy. A patient with acute fulminant demyelination is described, in whom it was possible to correlate the clinical and radiological features with histological findings.

Case report

M.D., a 30-year-old woman had enjoyed good health until two weeks prior to her admission to hospital, when she developed light-headedness followed by increasing weakness and ataxia of the right leg and arm and subsequently neglect of the right side of the body, dysarthria and blurred vision. Examination at another hospital confirmed dysarthria and right spastic hemiparesis with cortical sensory deficit; general examination was normal. Investigations showed normal haematological and biochemical findings. A technetium brain scan showed slightly increased uptake of isotope in the left parietal region and a left carotid angiogram was normal. The initial EEG was normal, but a repeat one week later showed continuous delta activity in the left hemisphere. The cerebrospinal fluid taken on the 13th day of the illness was under normal pressure and contained 2 white cells and protein 0-20 g/l with gamma globulin slightly increased at 13-6%. An autoimmune antibody screen and serological tests were negative. In view of her continuing deterioration, she was given dexamethasone and transferred to this neurological unit on the 23rd day of her illness. She was now slightly obtunded, dysarthric, dysphasic and dyslexic. There was an incomplete right homonymous hemianopia, the fundi were normal and external ocular movements were full. There was a marked spastic right hemiparesis, involving the face, bilateral hyperreflexia and clonus, more so in the right limbs, and a right hemisensory loss to all modalities. There was no meningism and general examination was normal. A CT scan on the 24th day of the illness showed low attenuation in the white matter of the cerebral hemispheres with discrete lesions (measuring at 16 Hounsfield units) in the internal capsules, tempororo-occipital and parietal lobes, and adjacent to the roof of the right lateral ventricle (fig 1). Slight enhancement was seen in the right periventricular region. Repeat CSF examination on the 26th day of the illness showed 15 lymphocytes, protein 0-38 g/l with slightly raised gamma globulin at 12%. Other serological tests, viral antibody studies, haematological and biochemical indices were negative or normal. Visual evoked responses to binocular flash stimulation showed prolonged latencies with P2 at 148 ms on the right and 135 ms on the left. Treatment was continued with ACTH on the basis of an acute demyelinating illness. A repeat CT scan 8 days later showed more extensive white matter lucencies with slight peripheral contrast enhancement of one. She continued to deteriorate becoming quadriplegic, more dysphasic and dysarthric, developing vertical and subsequently horizontal gaze palsies, incontinence and mental confusion. Emotional lability ensued with frequent out-
Enhanced CT scan on admission showing discrete low attenuation lesions in the internal capsules, left temporo-occipital and parietal white matter (a), and diffuse low attenuation throughout most of the white matter of the right hemisphere (b). There is no contrast enhancement.

Bihemisphere section (at level of superior corpora quadrigemina) showing large paraventricular areas of demyelination surrounded by smaller discrete areas of demyelination often with areas of partial demyelination (shadow plaques). (Stain = Weil for myelin) (b) Area of total fairly acute demyelination with large masses of lipid-laden macrophages ("compound granular corpuscles") and glial fibre formation. (Stain: PTAH for glial fibres.) × 100.
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bursts of screaming and crying. She died in the 11th week of her illness.

Pathological findings

Autopsy revealed an acute pyelonephritis. The brain was of normal size and weight, and there was no external abnormality. Coronal sections revealed extensive greyish to yellow lesions of the central white matter, which involved both hemispheres, and were most extensive in the occipital region. The lesions were slightly granular, bilateral and roughly symmetrical. The edges of these lesions were clearly defined, and their shape was irregular. Extensive lesions abutted on to the lateral ventricles, which were considerably enlarged. Subcortical white matter was intact. There were no obvious lesions within the cerebellum or brain stem.

Large sections were examined after staining with haematoxylin and eosin, Klüver Barrera and Weil stains for myelin, phosphotungstic acid haematoxylin, Gheel stains for axons and neutral fat stains. The affected white matter consisted of areas of extensive demyelination. Small foci within the larger lesions contained patchy, poorly staining myelin remnants. Within the demyelinated areas, there were numerous foamy macrophages which stained positively for neutral fat. Macrophages were particularly numerous in perivascular sites. Large, reactive astrocytes were present, and gliosis was marked within the affected areas, although of varying density (fig 2). There was perivascular cuffing by lymphocytes, with occasional plasma cells, and such reactions extended to the edge of the demyelinated areas in irregular fashion. Many axons were preserved, but others were fragmented and exhibited irregular clubbing. There was some oedema at the periphery of the lesions. Sections through the cortex, optic nerves, midbrain, pons, medulla and cerebellum were normal and no further plaques were found.

Discussion

The initial clinical presentation of this patient raised the possibility of vascular or neoplastic pathology in the left hemisphere, but subsequent developments suggested a rapidly evolving demyelinating disease, the precise classification of which remains problematic. The absence of other readily identifiable aetiological factors, however, raises the diagnostic possibility of acute cerebral multiple sclerosis.6 The histological findings of shadow plaques and gliotic areas within the demyelinated central white matter may be taken as supportive evidence for this view, but it was noted that true dissemination of white matter lesions outside the hemispheres was not present.

The CT scan provided evidence of multiple white matter lesions in the hemispheres: characteristically these lesions showed low attenuation and lack of space occupation both of which have been observed in all the previously reported cases of multiple sclerosis7-8 with one notable exception.7 Contrast enhancement was, however, relatively insignificant in this patient. Enhancement on CT scan occurs either by pooling of contrast in abnormal vasculature or by leakage through a damaged blood brain barrier;10-11 the latter may be stabilised by steroid drugs which may then prevent contrast enhancement12 13 as could have occurred in this patient. Moreover it is now appreciated that contrast enhancement in acute demyelinative (multiple sclerosis) lesions is more likely to be detected if a higher-than-normal dose of contrast is administered and thin sections (5 mm) are taken after a delay of 1–2 hours,14-16 none of which were employed in this patient. The validity of the above observations has been disputed, however, by the demonstration of significant diffuse enhancement in a biopsy-proven demyelinating (multiple sclerosis) lesion during the stage of clinical and pathological regression and while the patient was receiving steroids.

The present case illustrates the ability of the CT scan to demonstrate white matter disease and to aid accurate diagnosis in individual patients, whilst lending some support to the view that contrast enhancement in myelinoclastic lesions may not be closely related to the phase of demyelination, duration of symptoms and steroid treatment.

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References


