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Computed Tomography in Alexander's Disease

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Summary. Two cases of biopsy-proven Alexander's disease are described with computed tomographic changes which, in our experience and on survey of the literature, have not occurred in any other condition. Such changes in a child with a progressive condition consistent with Alexander's disease, strongly support the diagnosis.

Key words: Leukodystrophy – Alexander's disease – Computed tomography

Computed tomography (CT) has extended the scope of neuroradiology to include the leukodytrophies in which the predominant feature is more or less symmetrical reduction in the attenuation of the cerebral white matter. In some of these diseases, including globoid and metachromatic types, the diagnosis is made by biochemical tests, but in others including spongiform degeneration and Alexander's disease [1], it can be established positively only by brain biopsy. CT has made an important contribution to our knowledge of the natural history of these diseases and our concepts of the clinical spectra have been modified by it. Somewhat similar symmetrical low attenuation of white matter also occurs in other conditions most, but not all of which, can be distinguished from the leukodystrophies by the clinical context or by biochemical tests [2].

Despite the fact that there is no specific treatment for Alexander's disease, a positive diagnosis is important for the exclusion of a treatable condition, and to establish the prognosis. A specific abnormality on a less invasive test may abolish the necessity for brain biopsy and for this reason we are presenting two patients with CT appearances which, as far as we are aware, have occured in no other condition.

Case Reports

Case 1

R. S., a white boy presented when 7 months old for investigation of developmental retardation. There was no family history of neurological illness. Following a normal pregnancy there was arrest of labour with foetal distress, culminating in lower segment caesarian section. There were no neonatal problems and development appeared to be normal until 5 months, when the child was unable to sit but could follow with his eyes.

Further development ceased from this time and there was some regression with loss of head control. Six weeks prior to admission he started to vomit frequently and one generalised fit was observed.

On examination the head was large with sunsetting eyes and a tense fontanelle. Muscle tone was diminished and head control was absent.

Haematology, enzyme studies and blood chemistry were normal. A CT scan was performed at 7 months of age and a small brain biopsy was obtained from the right parietal lobe under the same anaesthetic.

Plain CT (Fig. 1) showed symmetrical well demarcated low attenuation in the deep cerebral white matter, sparing the subependymal regions. It was considerably more extensive in the frontal lobes than elsewhere. There was moderate dilatation of the lateral ventricles. After contrast medium there was symmetrical enhacement of the caudate nuclei, of the anterior columns of the fornices, of the periventricular brain substance and in the central part of the forceps minor and the region of the optic radiation (Fig. 2).

Brain biopsy showed the typical appearances of Alexander's disease.

The cortical architecture was preserved but the molecular layer contained abundant eosinophil structures with the characteristic appearance and usual

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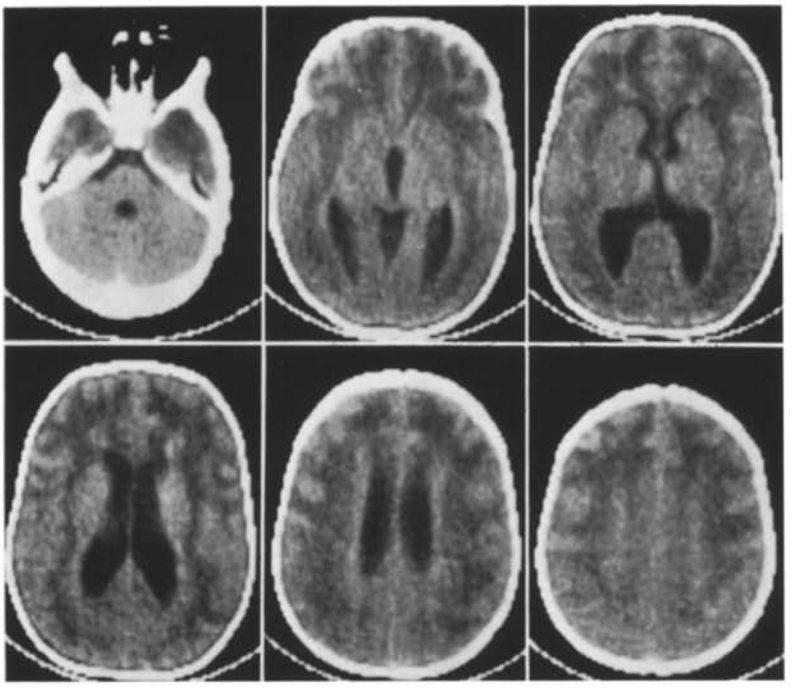

Fig. 1. Plain scan. There is symmetrical low attenuation in deep white matter, more extensive in frontal lobes

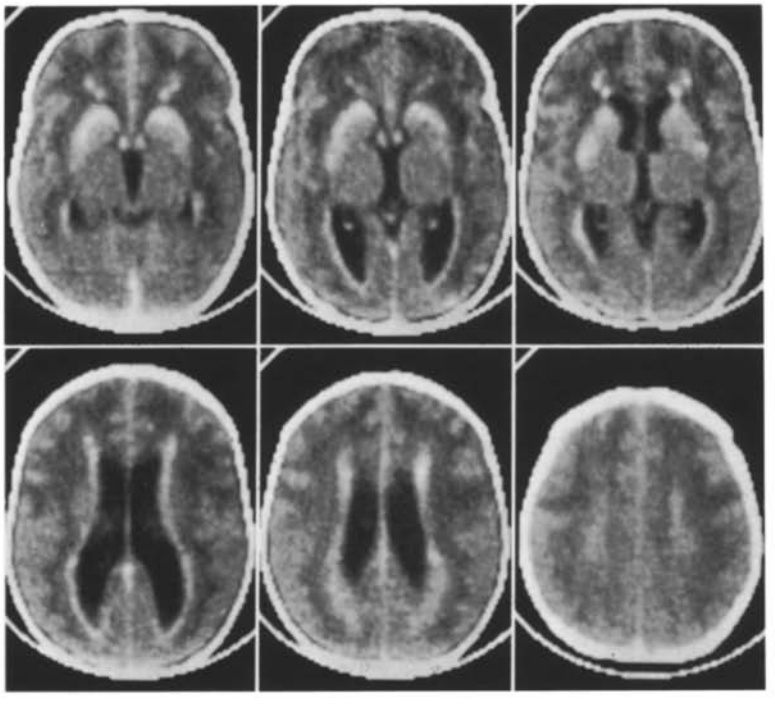

Fig. 2. After contrast medium. Enhancement of caudate nuclei, anterior columns of fornices, periventricular brain substance and region of forceps minor and optic radiation

staining reactions of Rosenthal bodies. Rosenthal bodies were also shown aggregated around blood vessels and scattered within the poorly myelinated white matter.

Case 2

This case has been previously illustrated [2] but only briefly described and is reported here in more detail.

C. W., a white girl presented at 7 months for investigation of mental retardation. There was no family history of neurological illness. Delivery, following induction at 37 weeks gestation for pre-eclamptic toxaemia, was normal. There were no neonatal problems. She smiled at 6 weeks, but she never developed good head control. After 4 months the parents noticed some loss of muscle strength in the baby's neck. Focal fits commenced at 6 months.

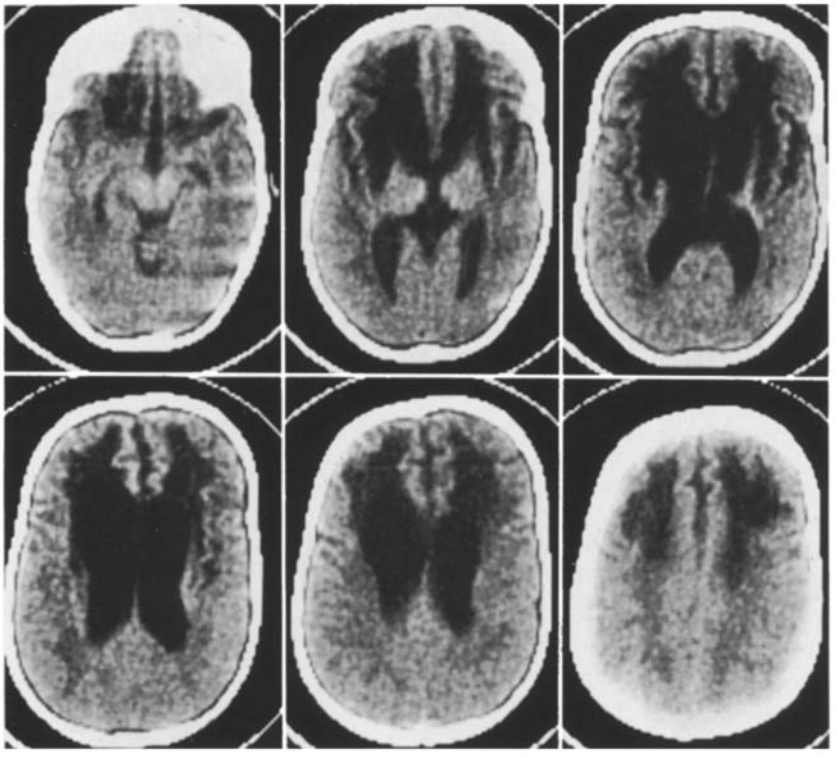

Fig. 3. Plain scan. Marked symmetrical low attenuation in white matter of both frontal lobes, caudate and lentiform nuclei, anterior limbs of internal capsules and narrow band close to ependyma in parietal and occipital lobes

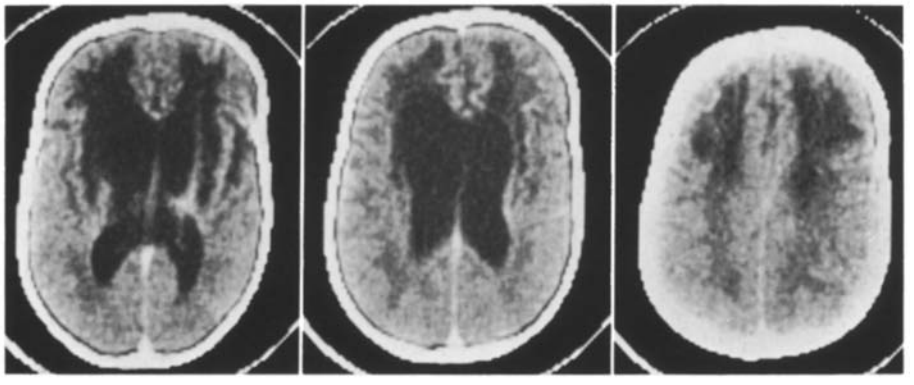

Fig. 4. After contrast medium. There is no abnormal enhancement

Examination revealed a head above the 98th percentile with a tense fontanelle. She was able to follow objects with her eyes, but she had no head control and her limbs were hypotonic with athetoid movements. General examination revealed no abnormality.

Haematology, blood enzyme studies and chemistry were normal except for a raised serum folic acid (28 mg/ml). An EEG at this time showed a patchy distribution of abnormalities with focal discharges in the left anterior frontal and parietal regions. Air encephalography showed minor dilatation of the left lateral ventricle. Brain biopsy was obtained from the right frontal lobe at 9 months of age.

Over the following years there were numerous admissions for recurrent chest infections, 'cerebral irritability' and increased incidence of convulsions. Retention of urine was noted during a recent admission for social reasons. A CT scan was performed at 6 years of age.

Plain CT (Fig. 3) showed marked symmetrical low attenuation of the white matter throughout both frontal lobes and also of the caudate and lentiform nuclei and of the anterior limbs of the internal capsules. There was in addition, a narrow band of low attenuation lateral to the subependymal region in the parietal and occipital lobes. There was quite marked dilatation of the frontal horns and moderate dilatation of the remainder of the lateral and third ventricles. There was no abnormal enhancement (Fig. 4).

Brain biopsy showed intensely eosinophilic droplets within distended cortical astrocytes. Similar,

often rod-shaped bodies were present beneath the pia, within the parenchyma and around blood vessels. These stained intensely with PTAH and Luxol fast blue. Histochemistry showed no neuronal storage and there was almost complete lack of myelin in the white matter. There were numerous sudanophilic macrophages, more evident deep in the white matter where there were also focal areas of calcification. The appearances were typical of Alexander's disease.

Discussion

Alexander's megalencephalic leukodystrophy is a rare condition of uncertain pathogenesis. All proven cases have been sporadic except for one in which the family history strongly suggested that three siblings of an autopsy-proven case were affected [3]. The brain is large and shows grey softened white matter. Microscopical examination of the white matter shows little stainable myelin. However, the characteristic feature of the condition is the presence of masses of Rosenthal bodies clustered around blood vessels. Numerous Rosenthal bodies are also regularly found in the subpial region of the molecular layer of the cerebral cortex and periventricularly adjacent to the ependyma. On the basis of electron microscope structures Schlote [4] concluded that these bodies originate from degenerating glial fibres.

The disease is usually manifest clinically during the first year of life, with slow enlargement of the head, progressive retardation, symmetrical spastic weakness and convulsions. Occasional cases present later in early childhood, with the history extending back to the first year [5]. A single case has been described presenting in adult life [6]; megalencephaly was absent and progression was very slow, simulating multiple sclerosis.

The distribution of the low attenuation and enhancement in the first of our cases, and of the low attenuation and atrophy in the second, has not to our knowledge been described in any other condition and is probably pathognomonic of Alexander's disease. The presence or absence of abnormal enhancement may depend on the timing of the CT studies, which was early in the first and very late in the course of the disease in the second case.

Another autopsy-proven case described by Boltshauser et al. [7] was a child with clinical onset at 2 years who died at 4 years. CT showed low attenuation in the frontal white matter and progressive atrophy mainly involving the frontal lobes. Kazner et al. [8] illustrated the CT appearances of three siblings showing low attenuation throughout the frontal, parietal and occipital white matter associated with dilatation of the lateral ventricles but without involvement of the basal ganglia. Though claimed to be Alexander's disease, it is not clear whether there was histological proof in these cases. Only one further case with CT findings has been mentioned [2]. This was a markedly retarded child with a family history of death of a sibling at the age of 9 months from a similar condition. CT at the age of 1 year showed diffuse cerebral atrophy only. This case had many atypical features and, since histology is not available for review, it can not be considered a proven example of Alexander's disease.

We believe that computed tomographic appearances similar to those in our proven cases of Alexander's disease are sufficient in the clinical context to suggest the diagnosis, and that when such changes are present cerebral biopsy is not essential. Absence of the characteristic changes does not exclude Alexander's disease.

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Note added in proof. Delouvrier and Nahum (Xtract **9**, 12–19, 1980) have recently described a case of biopsy proven Alexander's Disease in an 11-month-old child with megalencephaly and mental retardation. CT showed diffuse low attenuation throughout the cerebral white matter, more marked frontally, without contrast enhancement.