

Variability of Serial CT Scans in Subacute Necrotizing Encephalomyelopathy (Leigh Disease)

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Computed tomographic (CT) brain scans of patients with subacute necrotizing encephalomyelopathy (SNE) may reveal focal lesions that correspond to sites of anatomic involvement of the disease. Three patients with SNE were followed with serial CT brain scans. In two patients radiographic abnormalities appeared well after the onset of clinical symptoms. In all three patients the radiographic lesions changed with time. This variability seen with serial scanning is an important feature of SNE.

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Introduction

Subacute necrotizing encephalomyelopathy (SNE, Leigh disease) is an autosomal recessive neurodegenerative disease, characterized by multiple symmetric foci of necrosis in the basal ganglia, brainstem, cerebellum, and spinal cord. It commonly begins in infancy or early childhood and is manifest by developmental delay, feeding difficulty, cranial nerve palsies, nystagmus, blindness, disorders of tone, movement, and respiratory abnormalities [6]. Rarely, juveniles and adults are affected [3,9]. The evolution of clinical signs varies from one patient to another, and may vary within members of an affected kindred [5,9]. Although clinical and laboratory evidence suggests that

SNE may represent a disorder of brain pyruvate metabolism [1,6,7,8], no specific biochemical marker has been identified so that antemortem diagnosis of SNE is difficult to establish with certainty [1,7,8].

Bilateral symmetric radiolucencies in the basal ganglia, thalamus, brainstem, and cerebellum have been demonstrated in CT scans of patients with documented SNE [2,10].

We report three patients with variable changes of their serial CT scans.

Case Reports

Cases 1 and 2. Twin infants, products of a marriage between first cousins, once removed, were delivered at 35 weeks gestation by Caesarean section due to premature labor and breech presentation. Their prenatal and early postnatal courses were normal; both twins progressed normally during the first month of life. At two months of age, both had poor head control, roving eye movements, and poor visual fixation. By six months of life, examination demonstrated no head control, bilateral optic atrophy, conjugate roving eye movements, and spasticity. Each patient had a metabolic acidosis. Urine screening tests for amino acids, serum electrolytes, serum transaminases, calcium, creatinine, and examination of cerebrospinal fluid were normal. Visual evoked responses were absent. Electroretinograms suggested diffuse inner retinal dysfunction. Brainstem auditory evoked response testing of both infants revealed conduction abnormalities at the level of the pons. Electromyography, motor nerve conduction velocities, and EEG were normal. CT scans were normal (Fig 1-A). The patients continued to deteriorate, and by ten months of age they developed dysphagia and intermittent apnea. Examination at that time indicated poor head control, minimally reactive pupils, spasticity, hyperreflexia, and dystonic posturing. A mild metabolic acidosis with partial respiratory compensation was documented. CT brain scans of both patients indicated identical radiolucencies of the basal ganglia and midbrain tegmentum (Fig 1-B).

Over the next seven months the patients' clinical condition continued to slowly deteriorate. Intermittent periods of apnea increased in frequency and on one occasion one of the twins was brought to the emergency room by paramedical personnel with a respiratory arrest requiring resuscitation.

At 17 months of age CT scans were obtained which demonstrated marked cortical atrophy and ventricular enlargement (Fig 1-C). The previous well-defined lucencies of the basal ganglia were no longer present in either twin. The first twin died at twenty months of age from respiratory failure. The second twin was found dead at home one month later.

Autopsy examination was denied for the first twin but performed on the second. Complete neuropathologic examination disclosed necrotic lesions and cavitation involving the midbrain and pons as

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A

well as linear areas of cortical cavitation. The basal ganglia appeared mildly discolored but no gross necrotic cavitation was evident. Microscopic examination of the basal ganglia disclosed mild cell loss, vascular proliferation, and reactive astrocytosis. Microscopic brainstem involvement was characterized by significant cell loss, vascular engorgement, and marked reactive astrocytosis.

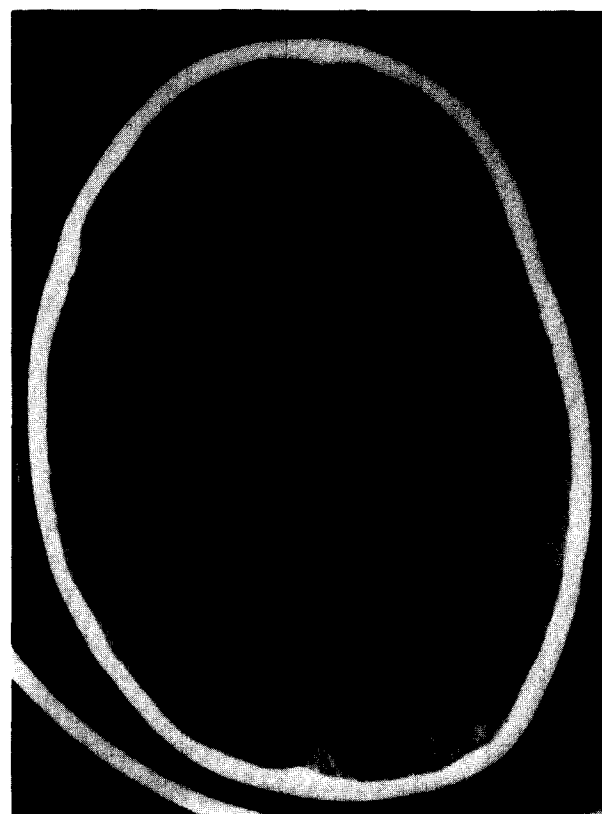
The family history was remarkable for an older brother, who at three months of age was found to have blindness, optic atrophy, developmental delay, hyperreflexia, and seizures. He had a respiratory arrest at ten months of age. Limited neuropathologic examination revealed vascular proliferation and reactive astrocytosis of the periventricular white matter.

Case 3. A 2½-year-old male product of a nonconsanguineous marriage was born to a 19-year-old female after an uneventful pregnancy, labor, and delivery. The infant developed normally until the age of six months, when he was found to have irregular eye movements and tremulousness of the hands and arms. He was unable to walk without assistance at 12 months of age and was exceedingly clumsy, falling frequently. At 20 months of age he had the onset of recurrent vomiting that persisted for 3 months.

Examination at 22 months of age documented bilateral optic atrophy, nystagmus, and ataxia of the trunk and limbs. A serum lactic acidemia was present and a CT scan of the brain demonstrated a right caudate lucency and bilateral lucent lesions in the midbrain (Fig 2-A). Visual evoked responses were absent, and brainstem auditory evoked responses indicated a pontine level conduction defect.



B



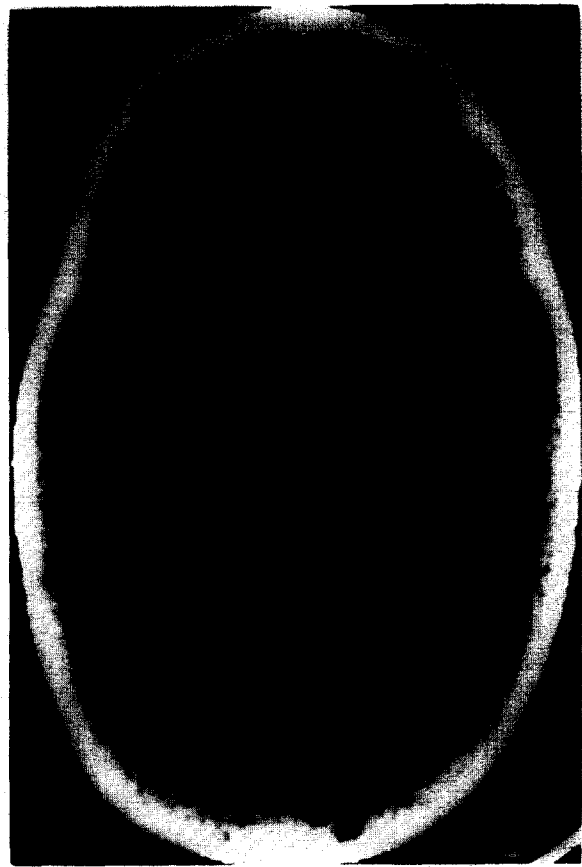
C

Figure 1. CT scans of Twin. (A) Normal unenhanced CT scan at six months of age; (B) Unenhanced CT scan at ten months of age with lucency of the putamen, bilaterally (arrows); (C) Unenhanced contrast CT scan at 17 months of age. Cortical atrophy and enlarged ventricles are present while the previous lucencies of the putamen have disappeared.



A

Figure 2. CT scans of Case 2. (A) Unenhanced CT scan at 22 months of age. Lucencies present in the right caudate nucleus and midbrain bilaterally (arrows); (B) Unenhanced CT scan at 30 months of age. Lucencies of the putamen bilaterally (arrows) are now present with disappearance of previous right caudate lesion. Thin sections through the midbrain region failed to disclose the previous midbrain lucencies.



B

A CT scan at 30 months of age revealed bilateral lesions in the putamen, with disappearance of the previous right caudate and midbrain lucencies (Fig 2-B).

Discussion

Previous reports document that radiolucencies may be present in the basal ganglia, thalamus, brainstem, and cerebellum of patients with SNE [2,10]. These radiographic lesions have corresponded to the necrotic lesions found at autopsy, and it has been advocated that the CT findings can be useful in establishing the antemortem diagnosis. These reports have not documented any temporally associated changes in the appearance of these radiolucencies in SNE, nor have they considered the importance of serial CT scans.

Our patients demonstrate that CT findings of SNE are dynamic. They may appear after the onset of clinical symptoms, and vary with time. The twin patients first had clinical signs at two months of age; yet CT scans at six months of age uncovered no abnormality. By ten

months of age both patients had typical CT scan radiolucencies in the basal ganglia and midbrain. Repeat scans three months prior to their demise demonstrated cortical atrophy and enlarged ventricles; the previous basal ganglia and midbrain lucencies were no longer present. The CT scan of the third patient was abnormal at 22 months of age with a right caudate and bilateral midbrain lucencies. Eight months later these lesions were no longer evident but new lesions were now apparent in the putamen bilaterally.

Pathologically SNE is characterized by symmetric foci of variable necrosis with vascular proliferation, spongiform loosening of the neuropil and reactive microgliosis. The lesions tend to be symmetric and predominate in the dorsal brainstem, basal ganglia, thalami, dentate nuclei of the cerebellum, and spinal cord. Although the pathologic lesions resemble those of Wernicke encephalopathy, the mammillary bodies are usually spared.

The absence of gross necrosis and cavitation of the basal ganglia at autopsy of the second twin suggests that these pathologic changes are not required for CT detection. CT may be a sensitive means of detecting active lesions with vascular proliferation and

spongiform loosening of the neuropil. While some of these lesions will progress to frank necrosis and cavitation, others will remain as areas of variable spongiosis or appear as microscopic astrocytic gliosis. The latter condition may not be easily detected with CT. This variation in the pathologic process may account for the variation that we observed on CT.

The variable CT findings appear to be an additional feature of SNE which should distinguish its radiographic appearance from other causes of basal ganglia lucencies [4]. The CT scan continues to be the best means of establishing the antemortem diagnosis in the absence of a definitive biochemical marker.

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