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PRE- AND POSTMORTEM MRI FINDINGS IN INFANTILE NEURONAL CEROID-LIPOFUSCINOSIS

Poster

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Infantile neuronal ceroid lipofuscinosis (INCL) is a recessively inherited progressive encephalopathy. The aim of the study was to demonstrate the course of INCL with brain MRI, and to correlate MRI with histopathological findings. The authors also wanted to ascertain by quantitative analysis at what age the first pathological changes could be measured—since storage material is known to be present even in the fetus¹—the location of these changes, and their rate of progression. 21 patients aged three months to 11 years, 46 neurologically normal controls of the same age, and eight formalin-fixed brains of INCL patients (children's age range at death seven to 13 years) were examined by MRI at 1.0T. In addition to visual evaluation, the signal intensity of the premortem MRIs was measured in numerous locations. The prenatal and postnatal development of the central nervous structures began normally, as demonstrated by MRI and in conformity with the neuropathological findings², at least until the age of three months. However, pathological findings were detected both visually and quantitatively even before clinical signs. The radiological picture of the brain varied with the duration of the disease. Generalized cerebral atrophy, more obvious than cerebellar, strong thalamic hypo-intensity in the white matter and basal ganglia, and thin periventricular high-signal rims from 13 months onward on T₂-weighted images with the typical clinical picture were pathognomonic findings in the early stage of INCL. Wallerian degeneration^{2,3} and increased interstitial fluid in the white matter may account for the increased white matter intensity.

The authors suggest that the decreased T₂ signal intensity in the thalami is due to the change in the components of the storage material. According to the quantitative analysis, they also assume that in the early stages of INCL more storage material accumulates in the thalami than in the basal ganglia. In the final stage, after the age of four years, cerebral atrophy is extreme and the grey matter is hypo-intense compared with the white matter, the reverse of normal. The signal intensity of the white matter is higher than that of the cerebrospinal fluid. MRI findings of the final stage of the disease and of the postmortem examinations did not differ significantly. The drastically altered relative intensities of the grey and white matter structures on MRI reflected incomplete replacement of the neurons with abnormal hypertrophic astrocytes and/or macrophages filled with storage material. The abnormalities progress on MRI during the first four years of life, then stabilize, in conformity with the clinical and histopathological picture of INCL.

References

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CEREBROTENDINOUS XANTHOMATOSIS IN CHILDREN

Poster

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Cerebrotendinous xanthomatosis (CTX) is a rare, autosomal recessive lipid-storage disease which is caused by an enzymatic defect (hepatic 27-hydroxylase) in the synthesis of bile acids out of cholesterol, leading to the accumulation of cholestanol and cholesterol in the tissues. Biochemical diagnosis is made by the determination of excessive urinary excretion of bile alcohols and by the ratio of serum cholestanol and cholesterol levels. Clinical characteristics of the disease are premature cataract, formation of tendinous xanthomas, premature coronary heart disease and neurological abnormalities, *i.e.* dementia, pyramidal and cerebellar signs, and peripheral neuropathy. Although in many patients the onset of symptoms is in childhood, CTX is seldom diagnosed

before 20 years of age.

The authors describe five children varying in age from seven to 29 years at diagnosis. Their clinical course, laboratory findings and development after starting therapy are presented and the results are discussed. In all five children (seven to 20 years) the diagnosis CTX was biochemically proven. All patients had abnormal bile alcohols in their urine. Serum cholestanol content exceeded the 40 µmol/L (reference value: 3.3 to 12.5 µmol/L), and the cholestanol/cholesterol ratio varied from 1.21 to 2.19 (normal value: 0.08 to 0.21). Clinical characteristics of the patients were intractable diarrhoea, bilateral cataract, mild to moderate mental retardation and delay of motor development in three (aged seven, 12 and 13 years), and cerebellar signs in two patients (aged 17 and 20 years). After the start of therapy with chenodeoxycholic acid, the diarrhoea disappeared with an improvement of subjective well-being and mental functioning. Determination of the enzymatic activity of the mitochondrial 27-hydroxylase and the defect at the DNA level is in progress. CTX is seldom diagnosed in childhood. The onset of typical neurological symptoms and signs are nearly always in the second decade. Intractable non-infectious diarrhoea has not been described earlier regarding any clinical spectrum of CTX. This diagnosis should be considered in any combination of cataract, diarrhoea and neurological symptoms and signs.

VIGABATRIN VERSUS ACTH AS FIRST-LINE THERAPY IN WEST SYNDROME

Poster

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ACTH is the most recommended drug for the treatment of spasms in West syndrome, but it is frequently associated with serious side-effects. Research for alternative therapies with greater benefits is the object of many studies. The authors compared vigabatrin (GVG) and ACTH as first-line therapy for West syndrome. Patients were randomly assigned to GVG 100 to 150mg/kg/day or to ACTH depot 0.1mL/day. After 20 days, if there was no significant clinical/EEG improvement, the other drug was given to the patient. 35 newly diagnosed and untreated patients with West syndrome were included in the trial: 20 males and 15 females, aged four to nine months. 18 patients, four cryptogenic and 14 symptomatic, received ACTH as their first drug. Disappearance of spasms was observed in nine patients (9/18; 50 per cent) treated with GVG (three cryptogenic and six symptomatic) and in 10 patients (13/17; 77 per cent) treated with ACTH (six cryptogenic and seven symptomatic). GVG response occurred within eight days. Treatment intolerance was observed in two cases, one treated with GVG and one treated with ACTH. Disappearance of interictal EEG abnormalities was faster in patients treated with ACTH than in those treated with GVG. Nine patients not responding to GVG had a good response when treated with ACTH. Three of four patients not responding to ACTH, had a good response when treated with GVG. After three months, relapses were more numerous in patients treated with ACTH. These data demonstrate that GVG is effective in 50 per cent of cases with West syndrome, both cryptogenic and symptomatic; its safety profile is good. This drug can be suggested as a first-choice treatment for infantile spasms, before starting ACTH treatment.

NEW AND PROMISING DRUGS FOR EPILEPSY

Invited Lecture

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In approximately 20 per cent of patients with epilepsy, seizures are resistant to long-established drugs. Development of new therapy remains important. Seizures occur under three main conditions: impaired GABA-mediated inhibition, enhanced glutamate/aspartate transmission, and endogenous bursting of subsets of pyramidal neurons. Brain GABA is increased by vigabatrin, tiagabine and stiripentol. Of these, only vigabatrin, an effective drug for partial seizures and infantile spasms, is licensed. Lamotrigine impairs glutamate/aspartate transmission, has a wide profile and is useful for typical and atypical absences, drop attacks and partial seizures. Remacemide, a