Reversible cortical oedema mimicking cortical dysplasia in mitochondrial disorder

Partial seizures are invariably associated with focal brain pathology. Optimised MRI in the evaluation of these patients for surgery has greatly improved the detection of a spectrum of lesions. Imaging findings, however, are not always specific for a particular pathology, and may transiently mimic a fixed structural lesion.

We briefly report the clinical and laboratory findings of a patient who has had occipital lobe epilepsy since the age of 18. Seizures consisted of frequent and prolonged visual auras (hallucinations, palinopsia, photopsia) followed by reversible but progressive visual loss, as well as complex partial and secondary generalised seizures. Clinical findings were stare, partial stator, severe hearing and visual loss, mild ataxia, and dysarthria. The patient’s mother had a stroke at the age of 34 followed by seizures and dementia.

Visual evoked potentials showed abnormal latencies. Monitoring with EEG showed non-specific interictal slowing of background rhythms and focal seizures arising from left and right occipital lobes.

A mitochondrial cytopathy was confirmed by the presence of ragged red fibres and abnormal mitochondrial ultrastructure in the muscle biopsy. Magnetic resonance imaging during a period of increased seizure activity showed thickening of the cortical ribbon of the right parieto-occipital cortex in T1 weighted images. Increased signal was seen in the T2 weighted sequences (fig 1). A diagnosis of cortical dysplasia was considered and the patient was referred to our centre for surgical evaluation. Repeat MRI five months later no longer showed the lesion (fig 2). Retrospectively, it became apparent that the abnormality was due to transient cortical oedema associated with focal status epilepticus and not a fixed structural pathology of the cortex.

Reversible cortical abnormalities have been shown by MRI in generalised and partial status epilepticus.1,3 The appearance may be mimicked as a neoplastic or ischaemic stroke if the transient nature and temporal relation to status epilepticus is not recognised.4,5 The unusual linear and pericortical extent of the reversible signal abnormality in our patient led to the initial misdiagnosis of a migrainous disorder and the patient was referred for evaluation for surgery for epilepsy. Further investigation showed a mitochondrial disorder in our patient and the transient cortical oedema may indeed be secondary to altered cerebral energy metabolism and the pathogenetic mechanisms causing severe seizures in this condition.1,4 This case report illustrates that transient functional MRI abnormalities may mimic fixed structural lesions.

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Absence of SCA1 mutation in idiopathic cerebellar ataxia

Idiopathic cerebellar ataxia refers to a group of sporadically occurring cerebellar degenerations of unknown aetiology, which are clinically characterised by progressive ataxia with an onset in adult life.1 Neuro-pathological and clinical studies suggest that there are at least two types of idiopathic cerebellar ataxia. One group of patients presents with additional non-cerebellar symptoms, such as parkinsonism, autonomic failure, and pyramidal symptoms (idiopathic cerebellar ataxia-P). The underlying pathology in many of these patients is olivopontocerebellar atrophy.2 Those patients with idiopathic cerebellar ataxia-P who develop severe autonomic failure are subsampled under the broader category of multiple system atrophy.3 The other group of patients is clinically characterised by a pure...
cerebellar syndrome. These patients usually have cerebellar cortical atrophy.2

Autosomal dominant cerebellar ataxia resembles idiopathic cerebellar ataxia in many respects. Like idiopathic cerebellar ataxia, an autosomal dominant cerebellar ataxia is a late onset disorder that may present as a pure cerebellar disorder or in combination with non-cerebellar symptoms. Neuropathological findings in idiopathic cerebellar ataxia and autosomal dominant cerebellar ataxia are often indistinguishable. These phenomological similarities have prompted the hypothesis that at least some cases of idiopathic cerebellar ataxia from spontaneous mutation of a gene responsible for autosomal dominant cerebellar ataxia, from non-paternity, or falsely appear sporadic due to incomplete pedigree data.3,4 The recent discovery of an expanded trinucleotide repeat mutation in the SCA1 region in American families with autosomal dominant cerebellar ataxia offers the opportunity to search for this mutation in isolated patients with cerebellar ataxia by the polymerase chain reaction.5

We have analysed DNA from 61 patients with idiopathic cerebellar ataxia with a mean age of 12.8 years and mean disease duration of 9.2 (SD 47) years. All patients satisfied the following diagnostic criteria: (a) progressive, otherwise unexplained ataxia, and (b) family history without evidence of heredity or consanguinity of parents. All diagnoses were made after exclusion of possible symptomatic causes (alcoholism, other toxic causes, malignancy, hypothyroidism, vitamin deficiency, inflammation, metabolic, or vascular causes). Twenty-five patients had a pure cerebellar syndrome (idiopathic cerebellar ataxia-C), whereas 36 had additional non-cerebellar symptoms (idiopathic cerebellar ataxia-P). Of these, 17 fulfilled the clinical criteria for probable multiple system atrophy.6 Polymerase chain reaction analysis was performed, as described by Orr et al.7 For comparison, DNA from 144 patients with autosomal dominant cerebellar ataxia was analysed. As a positive control, DNA from families with autosomal dominant cerebellar ataxia from ABIbergen was included, in which the SCA1 expansion has been demonstrated and sequenced. A diagnosis of SCA1 heterozygosity was made in five out of 19 German families with autosomal dominant cerebellar ataxia for which the family history was medically documented. This corresponds to a prevalence of SCA1 in German families with autosomal dominant cerebellar ataxia of about 25%. By contrast, the SCA1 expansion was found in none of the 61 cases of idiopathic cerebellar ataxia. The present results argue against the hypothesis of a higher number of cases of idiopathic cerebellar ataxia due to a trinucleotide expansion at the SCA1 locus. The importance of our failure to show a mutation of the SCA1 gene in patients with idiopathic cerebellar ataxia is underlined by the finding that the SCA1 mutation is present in a considerable proportion of German families with autosomal dominant cerebellar ataxia. However, our data do not exclude the possibility that some cases of idiopathic cerebellar ataxia are due to spontaneous mutations at other gene loci associated with autosomal dominant cerebellar ataxia. Like studies of unstable markings on chromosomes, there are at least two other gene loci (SCA2 and SCA3) for autosomal dominant cerebellar ataxia.5,6 The hypothesis that idiopathic cerebellar ataxia is due to a mutation at one of these loci cannot be tested at present because SCA2 and SCA3 genes are not identified. It is unlikely that a recessive gene defect involves mutations of both of the idiopathic cerebellar ataxia because recessive inheritance of a late onset ataxic disorder has been documented only very rarely. It therefore seems likely that most cases of idiopathic cerebellar ataxia are of the non-inherited late onset type. This hypothesis is supported by a recent study reporting discordance for idiopathic cerebellar ataxia in monzygotic triplets.4 In addition, detailed clinical, neuroradiological, and neuropathological investigations show subtle differences between idiopathic cerebellar ataxia and autosomal dominant cerebellar ataxia. Thus age of onset is more variable and tends to be lower in autosomal dominant cerebellar ataxia. Additional non-cerebellar features of idiopathic cerebellar ataxia are often parkinsonism and autonomic failure, whereas ophthalmoplegia, pyramidal signs, dystonia, and dysarthria are more common in autosomal dominant cerebellar ataxia. Pathological and neuroradiological studies show that there is frequent spinal fluid involvement in idiopathic cerebellar ataxia but not in idiopathic cerebellar ataxia.2 Finally, postmortem studies have shown the presence of oligodendrogliarial intracytoplasmatic inclusions in patients with sporadic olivopontocerebellar atrophy, but not in the brains of patients with dominantly inherited olivopontocerebellar ataxia.2

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