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 had occipital lobe epilepsy since the age of 18. Seizures consisted of frequent and prolonged visual auras (hallucinations, palinopsia, photopsias) followed by reversible but progressive visual loss, as well as complex partial and secondary generalised seizures. Clinical findings were suggestive of complex partial seizures, with hearing loss, visual field loss, 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 encephalopathy 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 epilepsy and not a fixed structural pathology of the cortex.

Reversible cortical abnormalities have been shown by MRI in generalised and partial status epilepticus. The appearance may be misdiagnosed as a neoplastic or ischaemic stroke if the transient nature and temporal relation to status epilepticus is not recognised. 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. 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. 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. Those patients with idiopathic cerebellar ataxia-P who develop severe autonomic failure are subclassed under the broader category of multi-system atrophy. Another group of patients is clinically characterised by a pure
cerebellar syndrome. These patients usually have cerebellar cortical atrophy.^

Autosomal dominant cerebellar ataxia resembles idiopathic cerebellar ataxia in many respects. Like idiopathic cerebellar ataxia, 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 phenomenological similarities have prompted the hypothesis that at least some cases of 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.^

The recent discovery of an expanded trinucleotide repeat mutation in the SCAl region in American families with autosomal dominant cerebellar ataxia offers the opportunity to search for this mutation in isolated patients with idiopathic cerebellar ataxia by the polymerase chain reaction.

We have analysed DNA from 61 patients with idiopathic cerebellar ataxia with a mean age (SD 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 consanguinity or consanguinity of parents. All diagnoses were made after exclusion of possible symptomatic causes (alcoholism, other toxic causes, malignancy, hypothyroidism, vitamin deficiency, inflammations, 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.^

Polymerase chain reaction analysis was performed, as described by Orr et al. 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 inherited from Sibera was included, in which the SCAl expansion has been demonstrated and sequenced.

A diagnosis of SCAl heterozygocity 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 SCAl in German families with autosomal dominant cerebellar ataxia of about 25%. By contrast, the SCAl expansion was found in none of the 61 cases of idiopathic cerebellar ataxia.

The present results argue against the hypothesis of a high penetrance number of cases of idiopathic cerebellar ataxia due to a trinucleotide expansion at the SCAl locus. The importance of our failure to show a mutation of the SCAl gene in patients with idiopathic cerebellar ataxia is underlined by the finding that the SCAl expansion is present in a considerable proportion of German families with autosomal dominant cerebellar ataxia. This may indicate that the possibility that some cases of idiopathic cerebellar ataxia are due to spontaneous mutations at other gene loci associated with autosomal dominant cerebellar ataxia. Larger studies are required to determine if there are at least two other gene loci (SCAl2 and SCAl3) for autosomal dominant cerebellar ataxia.^

The hypothesis that idiopathic cerebellar ataxia is due to a mutation at one of these loci cannot be tested at present because SCAl2 and SCAl3 genes are not identified. It is unlikely that a recessive gene defect accounts for many cases of 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 non-inherited.

This hypothesis is supported by a recent study reporting discordance for idiopathic cerebellar ataxia in monzygous triplets. 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 ophthaloplegia, pyramidal signs, dystonia, and hypertrophy are found in more common in autosomal dominant cerebellar ataxia. Pathological and neuroradiological studies show that there is frequent spinal cord and cerebellar involvement in idiopathic cerebellar ataxia but not in idiopathic cerebellar ataxia.

Finally, postmortem studies have shown the presence of oligodendroglial intracytoplasmatic inclusions in the brains of patients with sporadic olivopontocerebellar atrophy, but not in the brains of patients with dominantly inherited olivopontocerebellar atrophy.^

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Life threatening epilepsy in a child

Epilepsy is known to cause a variety of arrhythmias that sometimes lead to sudden death.^

Arrhythmias are evoked by abnormal autonomic activity to the heart.^

We encountered a patient with epilepsy who developed torsades de pointes. Torsades de pointes—an ECG manifestation in which wide QRS like ventricular tachycardia continuously appears with periodically changing polarity—sometimes leads to ventricular fibrillation, which can cause sudden death.^

To our knowledge, this is the first report of evidence of epilepsy that caused torsades de pointes.

A 7 year old girl, who had been investigated for two attacks of epilepsy during the previous six months, was admitted to our institution after respiratory arrest. There was no relevant family history. Her pupils were dilated and there was no light reflex. An ECG showed ventricular fibrillation.

After intubation, two attempts at cardioversion with 200 J and 300 J were unsuccessful. Anti-arrhythmic treatment, having been tried without success, was also unsuccessful. The fourth attempt with 350 J changed the fibrillation pattern to a torsades de pointes (figure). Xylocaine was ineffective, but diazepam finally terminated both the convulsion and the torsades de pointes. Serum electrolyte concentrations (K 5 mmol/l, Ca 2·5 mmol/l, Mg 2·1 mmol/l, and PaO2 280 mmHg) were all normal at this time. Thiamylal sodium (3 mg/kg/h) was given for the next three days. During this period the ECG was also normal, with no prolongation of the QT interval. The patient became able to talk two days after barbiturate withdrawal. Myocarditis and cardiomyopathy were ruled out on the basis of echocardiographic findings, and she was negative for all the viral antibodies tested. An EEG obtained in the interictal period was normal. Cranial CT also showed no abnormalities.

The arrhythmia was diagnosed as torsades de pointes evoked by generalised seizures. After having been placed on oral anticonvulsant treatment, the patient was transferred to another institution without complications days later without any neurological deficits.

The two points of interest in this case were the induction of torsades de pointes by generalised seizures and the termination of both the seizures and the arrhythmia by diazepam. In this patient, the epileptic focus was not determined, so the attacks were classified as generalised seizures on the basis of their clinical features, and the development of torsades de pointes was preceded by a generalised seizure, the arrhythmia was assumed to be attributable to the seizure.

There have been no similar reports. As both conditions developed almost simultaneously, diazepam was initially given to terminate her torsades de pointes without prolongation of the QT interval, but proved to be ineffective. Then it was decided to apply other agents or overdrevce pacing. Both conditions were terminated, however, by the diazepam that was subsequently given to control the seizure. Diazepam specifically acts on the sinoatrial node. Considering that arrhythmias secondary to seizures are mediated by a limbic-forbrain...
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