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Crossed cerebellar diaschisis secondary to refractory frontal seizures in childhood☆

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We report a girl with refractory partial seizures since 7 years of age, secondary to right frontal cortical dysplasia, who developed MRI and SPECT abnormalities in the contralateral hemicerebellar cortex. These became more marked, leading to left hemicerebellar atrophy. Crossed cerebellar diaschisis has been described mostly in hemispheric stroke and supratentorial tumours, but less often in epilepsy. It is usually a transient phenomenon. This report shows that crossed cerebellar diaschisis can develop within two years of seizure onset and evolve over time.

Key words: cerebellar diaschisis; cortical dysplasia; corticopontocerebellar pathway; epilepsy; frontal lobe; SPECT.

INTRODUCTION

Secondary cerebellar lesions in patients with epilepsy are uncommon. They classically consist of bilateral atrophy of the cerebellar cortex with some degree of gliosis[1, 2]. Various causes have been implicated, including status epilepticus[2, 3], complex partial seizures[2–5], subclinical epileptic activity[2, 3] and phenytoin therapy[1–3]. We describe a patient with refractory partial seizures who developed hemicerebellar involvement contralateral to a frontal epileptogenic focus. This phenomenon of crossed cerebellar diaschisis has been described mostly in stroke, infections and tumours.

Case report

A 7-year-old girl with an unremarkable past medical history presented with brief stereotyped episodes of clonic movements of the left lower face and left hand with preserved consciousness and no other symptoms or signs. The episodes started 4 weeks before presentation occurring about once a week, with no apparent precipitating factors. Clinical examination was normal. Electroencephalography (EEG) showed right frontal discharges interictally. Magnetic resonance imaging (MRI) showed mild enlargement of subarachnoid spaces overlying the right frontal lobe (Fig. 1a) and normal appearance of the cerebellum (Fig. 1b). Seizure frequency increased despite various combinations of carbamazepine, sodium valproate, vigabatrin, lamotrigine, gabapentin, topiramate and clonazepam. Phenytoin was stopped after a single dose following an anaphylactoid reaction. Courses of steroids were effective but side effects limited their use. By the age of 9, her behaviour was characterised by reduced attention span and emotional blunting. Psychometric evaluation (K-ABC test) showed global cognitive deficit (score of 70, mean = 100, SD = 15), poor visuo-spatial and abstract memory (score of 4, mean = 10, SD = 3) and difficulties in perceptual organisation (score of 2, mean = 10, SD = 3).

She had eight episodes of status epilepticus between the age of 9 and 14. Five of these were controlled with benzodiazepines and phenobarbitone. The others necessitated barbiturate coma or even lignocaine and halothane. Interictal and ictal EEG continued to show right frontal discharges. Interictal bicisate Tc-99m single photon emission computerised tomogram (SPECT) at the age of 10 showed decreased activity in the right frontal region, no asymmetry being present

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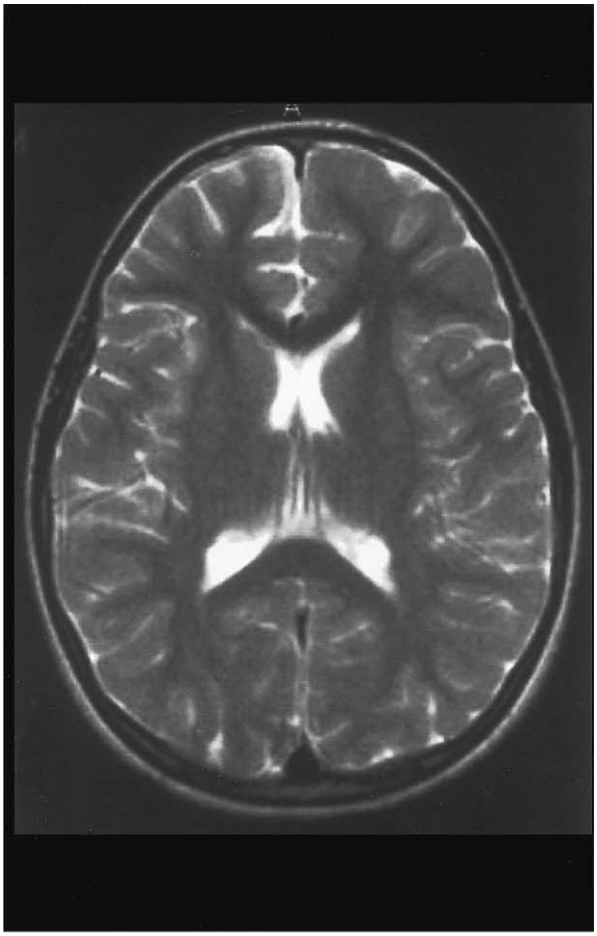
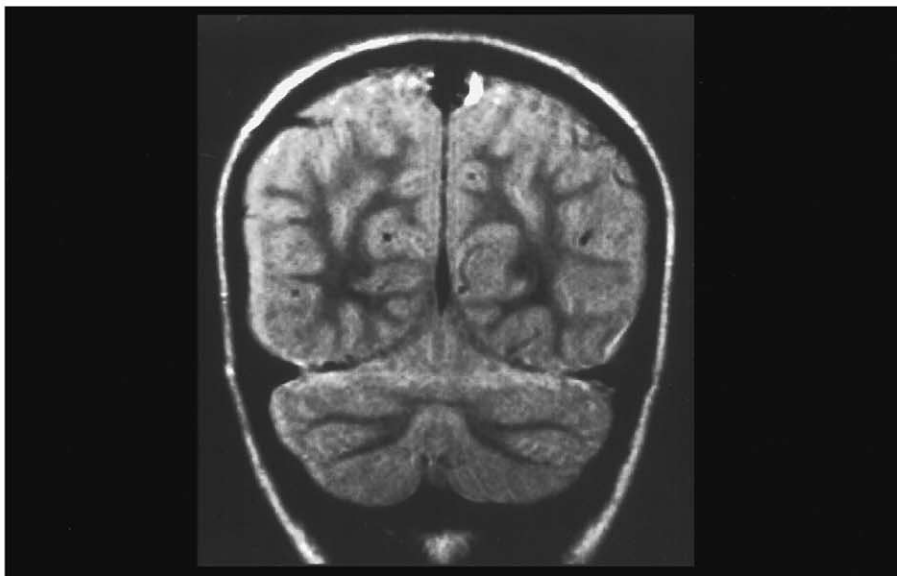


(a)



(b)

Fig. 1: (*a*) Axial T2-weighted MRI spin echo sequence showing mild enlargement of subarachnoid spaces of the right frontal lobe. (*b*) Coronal proton density-weighted MRI spin echo sequence showing normal cerebellum.

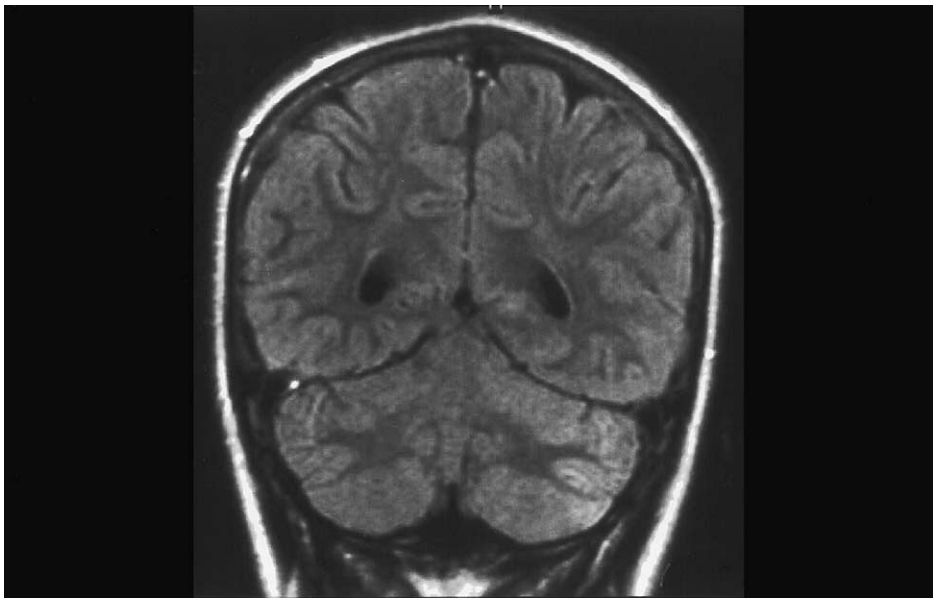


Fig. 2: MRI coronal flair sequence showing mild hyperintensity of left cerebellar cortex, otherwise of normal volume.

in the cerebellum. MRI showed mild right frontal atrophy. Flair sequences showed discrete hyperintensity of left hemicerebellar cortex on T2-weighted images (Fig. 2). Concordant electroclinical and neuroimaging findings coherently suggested a right frontal epileptogenic focus. Surgery was considered but the family were reluctant. At the age of 13, following bouts of uncontrolled seizures, she developed transient left hemiparesis and became increasingly sexually disinhibited. At 14, mild left hemiparesis became persistent following refractory status epilepticus. Repeat MRI showed more pronounced right frontal atrophy with thickening of overlying diploe (Fig 3a) and abnormal diffuse hyperintensity of left cerebellar cortex, of smaller volume than the right (Fig. 3b). Repeat interictal SPECT showed marked hypoperfusion of both the right frontal lobe and the left cerebellar hemisphere. She subsequently underwent anterior frontal lobectomy with improved seizure control. Histopathology showed disrupted neuronal organisation with loss of normal cortical lamination, moderate loss of neurones, clusters of neuronal dysplasia and ischaemic lesions as well as secondary gliosis in frontal cortex and subcortical white matter. These findings are consistent with cortical dysplasia.

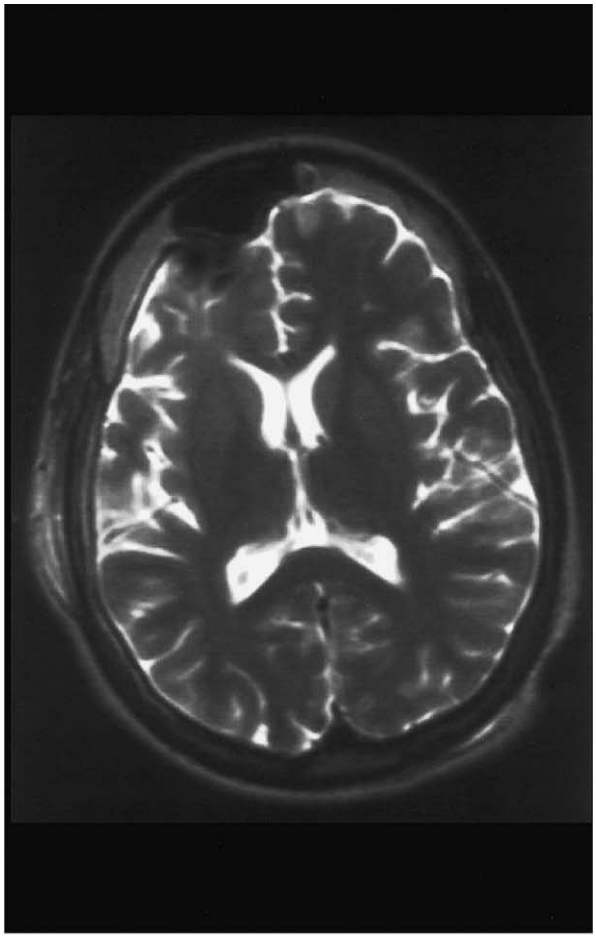
DISCUSSION

This patient with refractory seizures originating from the right frontal lobe developed contralateral unihemispheric cerebellar involvement, i.e. crossed cerebellar diaschisis (CCD). Diaschisis is characterised by depression of regional brain perfusion, metabolism or neuronal activity remote from a diseased cortical area[6]. Proposed mechanisms underlying CCD include disconnection of glutamatergic corticopontocerebellar tracts[6, 7]. These fibres arise mostly from the frontal cortex, follow the pyramidal tract and project onto the contralateral cerebellar cortex[8]. Cerebellar involvement can be documented by MRI[9], although functional imaging such as PET[4, 7] or SPECT[10, 11] is more sensitive. CCD often resolves with time[5] although the mechanisms by which cerebellar metabolism returns to normal are unknown.

CCD occurs in a relatively high proportion of unilateral supratentorial stroke[9]. It has also been reported in encephalitis[12], following intracarotid amytal injections[11] and in tumours[7]. In the latter CCD occurs with a higher incidence in frontal tumours, with a positive correlation with tumour size[7]. Conversely, CCD may manifest as frontal dysfunction contralateral to primary cerebellar pathology[13]. In general clinical signs of cerebellar dysfunction are absent[4, 7, 10].

Few reports have described CCD in adults with refractory seizures[4–6]. Proposed pathophysiology includes a direct effect of epileptic activity through excitotoxicity, ictal energy failure and postictal anterograde transneuronal degeneration[14]. In our patient, aberrant connections in relation with cortical dysplasia might also be involved[15]. Previously described cerebellar changes include Purkinje cell loss and gliosis of molecular layer with possible granular cell layer involvement[1]. In their retrospective review Tien and Ashdown[4] found that patients with MRI evidence of crossed cerebellar atrophy had

(a)



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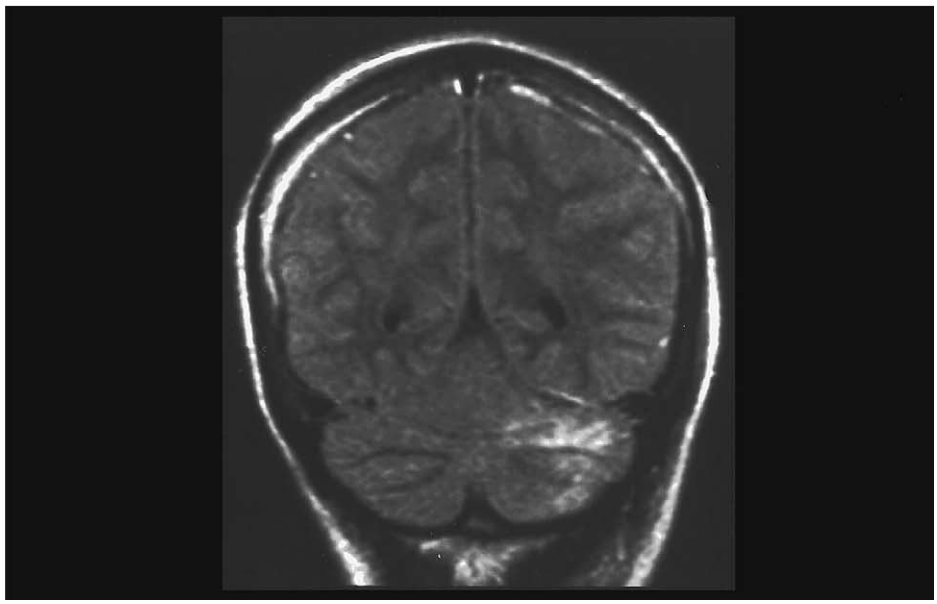

Fig. 3: (*a*) Axial T2-weighted MRI spin echo sequence showing diffuse cortical atrophy of right frontal lobe with enlargement of subarachnoid spaces, marked pneumatisation of right frontal sinus and enlargement of overlying diploe. (*b*) Coronal flair MRI sequence showing diffuse abnormal hyperintensity of left cerebellar cortex with moderate degree of atrophy.

long-standing intractable focal seizures since birth or childhood. The underlying aetiology in these patients was encephalitis. However, demonstration of cerebellar involvement was relatively late with respect to seizure onset and no scans were obtained before the appearance of hemicerebellar atrophy. The duration of clinical signs and symptoms in the group with crossed cerebellar atrophy was on average 9.5 years (range 6–15 years)[4]. Our report shows that CCD can occur within two years of seizure onset and evolve towards cerebellar atrophy.

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