Introduction

Cerebellar hypoplasia accounts for most of the congenital abnormalities that affect the cerebellar hemispheres, in which hypoplasia can be related to clastic or neurodegenerative processes [3]. Pontocerebellar hypoplasia (PCH) is a rare disorder with only about 20 patients described so far [9]. An autosomal model of inheritance has been proposed [7]. According to Barth, two forms of PCH can be distinguished by clinical and neuropathological changes [4, 6, 7]. Type 1 is characterized by the presence of spinal anterior horn degeneration, similar to infantile spinal muscular atrophy, with congenital contractures, neurogenic hypoventilation, and severe muscular hypotonia. Type 2 comprises severe chorea/dystonia, and spinal anterior horn pathology is absent. Neuropathologically, PCH2 differs from PCH1 in which a more extensive degenerative process involves anterior horns and various other gray matter structures [6]. Moreover, PCH2 is characterized by severe reduction in size of the ventral pons, inferior olive atrophy, dentate nucleus fragmentation, and thinning of the cerebellar cortex [21]. The lesions are indicative of an impaired maturation of the infratentorial structures, probably due to abnormal functioning of genes involved in patterning the formation of the central nervous system [15, 20]. By contrast, the normal cytoarchitecture of the supratentorial structures, associated with the slowly progressive atrophic process observed in the late stages of the disease, suggests that in PCH2 the cortico-striatal complex involvement arises through a different pathogenic process [20].

We describe two patients with PCH, from two unrelated families. One patient had clinical and neuroradiological findings similar but not identical to the picture
reported for PCH2. The other patient, presenting with a classical PCH2 phenotype, demonstrated microcephaly, severe dyskinesia/dystonia and recurrent dystonic crises that were well controlled by treatment with levodopa.

**Case reports**

**Patient 1**

This nine-year-old girl was the first child of healthy and second cousin-related parents. She was delivered at 38 weeks after an uneventful gestation. She weighed 3.2 kg; her head circumference (HC) was 32.5 cm (10th percentile), and length 48 cm. Her Apgar score was 9 at 5 minutes. Developmental delay was observed from the first months of life. At three months of age, examination showed marked hypertonicity of all limbs with opisthotonic posturing. Brain magnetic resonance imaging (MRI) detected severe pontocerebellar hypoplasia associated with enlarged temporal horns. Convergent strabismus was also noted. At one year of age, choreiform movements and dystonia of her limbs occurred, and these became more evident in the following years. During her first three years of life, she experienced four episodes of generalized tonic-clonic seizures (GTCS) with fever, which were treated with phenobarbital and never recurred subsequently. Around the fifth year of life, dystonic crises appeared. They were characterized by arrhythmic slow flexing movement of the upper limbs (more evident for the left arm) followed by a hypertonic symmetrical facial expression with choreo-atetotic movements of the left arm and dystonic posturing of the right leg in extension, and arrhythmic flexion-extension movements of the left leg associated with cephalic deviation towards the left were also observed. Psychomotor irritability and crying (possibly in response to pain) were also present. These episodes often occurred during the night and lasted from a few minutes up to five to six hours. No loss of consciousness occurred. One year later, nocturnal episodes of profuse sweating with tonic head nodding toward the left shoulder, tonic flexion of one upper limb and extension of the ipsilateral lower limb also appeared. These episodes occurred during the day and lasted from a few minutes to five to six hours. Several EEG recordings showed no clear paroxysmal activity. At seven years of age, she came under our care. Examination revealed axial hypotonia, hypertonia of the limbs, and severe dystonia with choreo-atetotic movements involving limbs, facial muscles and tongue, which increased with emotional stimulus and disappeared during sleep. Her HC was 46 cm (–3.1 SDS). During a long-term video-EEG examination, two typical dystonic crises were videotaped. On both occasions, interictal EEG activity, characterized by spike and spike-waves of high amplitude in the bifrontal region, remained unmodified during the dystonic crisis. Brain MRI showed severe pontocerebellar hypoplasia, associated with a thin corpus callosum, and thinning of the white matter, mainly in the parietal region (Fig. 1). Further investigations including biochemical screening for inborn errors of metabolism were normal or negative. The karyotype was normal as were nerve conduction velocity and electromyography. Based on this clinical history, 200 mg/day of levodopa in association with 50 mg/day of carbidopa was administered. During the clinical follow-up of one year, no dystonic crises reoccurred. In addition, her chorea and dystonic movements improved markedly.

**Patient 2**

This three-year-old girl was born to healthy and consanguineous parents. The pregnancy was complicated by polyhydramnios and markedly reduced fetal movements. From the sixth month of gestation, ultrasonographic examinations revealed reduced biparietal and occipito-frontal diameters. Delivery was at 37 weeks of gestation. Her Apgar scores were 6 at one minute and 8 at five minutes; birth weight was 2900 g; length 45 cm, and HC 29 cm (–3.6 SDs). Examination revealed marked muscular hypertonia and hyperreflexia. Dramatic startle responses with myoclonic jerks and tremulousness to external stimuli such as light, noise and touch were also observed. Prolonged apneic spells occurred and she required intubation. CT showed cerebellar hypoplasia, cerebral atrophy, and mild enlargement of the lateral ventricles. At three months, brain MRI demonstrated severe pontocerebellar hypoplasia associated with enlarged lateral ventricles and delayed white matter myelination. Pericerebral spaces were also increased. Her head growth was impaired, and microcephaly became progressively evident in the following months. In the first 18 months of life, she experienced four episodes of GTCS and was therefore placed on phenobarbital ther-

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**Fig. 1** Sagittal T1-weighted MRI. (A) Patient 1 (8 years old): pontocerebellar hypoplasia associated with cortical atrophy mainly in the frontal region. A thin corpus callosum is also observed. (B) Patient 2 (2 years old). Pontocerebellar hypoplasia is associated with a more severe cortical atrophy and a marked hypotrophy of the corpus callosum.