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Case report

Symmetrical thalamic calcifications in a monozygotic twin: case report and literature review

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Abstract

We report the occurrence of symmetrical thalamic calcifications (STC) in one of a pair of monozygotic twins born at term without evidence of pre- or peri-natal asphyxia. STC is known to be an extremely rare condition in infants. Judging from the few cases reported in the literature, the clinical presentation is very severe: low Apgar score, no spontaneous movements, spasticity or marked hypotonia, impaired suck and swallow, facial diplegia. The prognosis is also very poor. The etiology is still a matter of debate: genetic, infectious, toxic or hypoxic-ischemic insults have been hypothesized. In our case, the presence of the lesion in one of a pair of monozygotic twins would rule out any genetic origin, nor was there any evidence of toxic or infectious disease. The only potential risk factor for fetal damage was hypoxic-ischemic insult related to the twin pregnancy.

Keywords: Thalamic calcifications; Twin pregnancy; Hypoxic-ischemic encephalopathy

1. Introduction

Symmetrical thalamic calcifications (STC) in infants are an extremely rare condition. The first cases were published in 1962 by Rosales and Riggs; since then, 26 more have been reported [1–6].

The etiology of this disorder is still a matter of debate and the clinical presentation is generally severe. It occurs sporadically: only Abuelo [1] described two cases in the same family.

We report on the occurrence of STC in one of a pair of monozygotic twins, discussing the possible etiology.

2. Case report

The patient was first seen at the age of 3 months due to persistent hypertonia since birth, with overlapping dystonic movements. The child was the first of twins born to a healthy 34-year-old primiparous mother. The parents were unrelated. The pregnancy and delivery were uneventful. The placenta was monochorionic. Apgar scores of 9 and 10 were recorded at 1 and 5 min, respectively. Birth weight was 2930 g (the birth weight of the twin brother was 3050 g), length 44 cm and head circumference 33 cm. No dysmorphic features were observed. Sucking and swallowing were apparently good. At 3 months old, the child was in relatively good general conditions. The head circumference was 41 cm (>50‰). Visual tracking was poor. The boy presented with a persistently hypertonic flexion posture of all extremities, with overlapping frequent, sudden episodes of very severe opisthotonic posture with retrocollis and tonic neck reflex, often accompanied by crying. Dystonic movements involving the face, mouth and tongue were also noted. The tendon reflexes were brisk.

CT scan of the brain at the age of 2 months revealed mild cortical atrophy with ventricular widening and symmetrical non-enhancing hyperdense areas bilaterally in the region of the thalamus. (Fig. 1).

MRI at the age of 3 months showed bilateral areas of increased and decreased signal intensity in T1- and T2-weighted images, respectively, in the region of the thalamus (Fig. 2).

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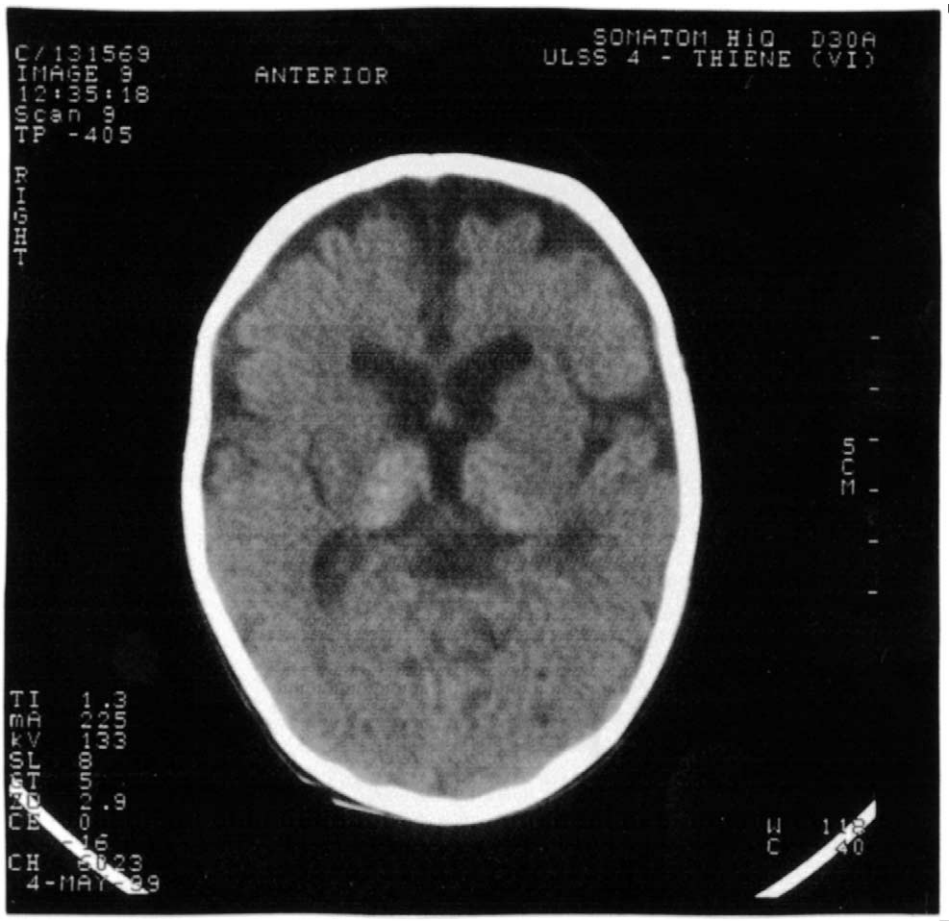

Fig. 1. Axial CT image at the age of 2 months shows mild cortical atrophy, ventricular widening and symmetrical hyperdense areas bilaterally in the region of the thalamus.

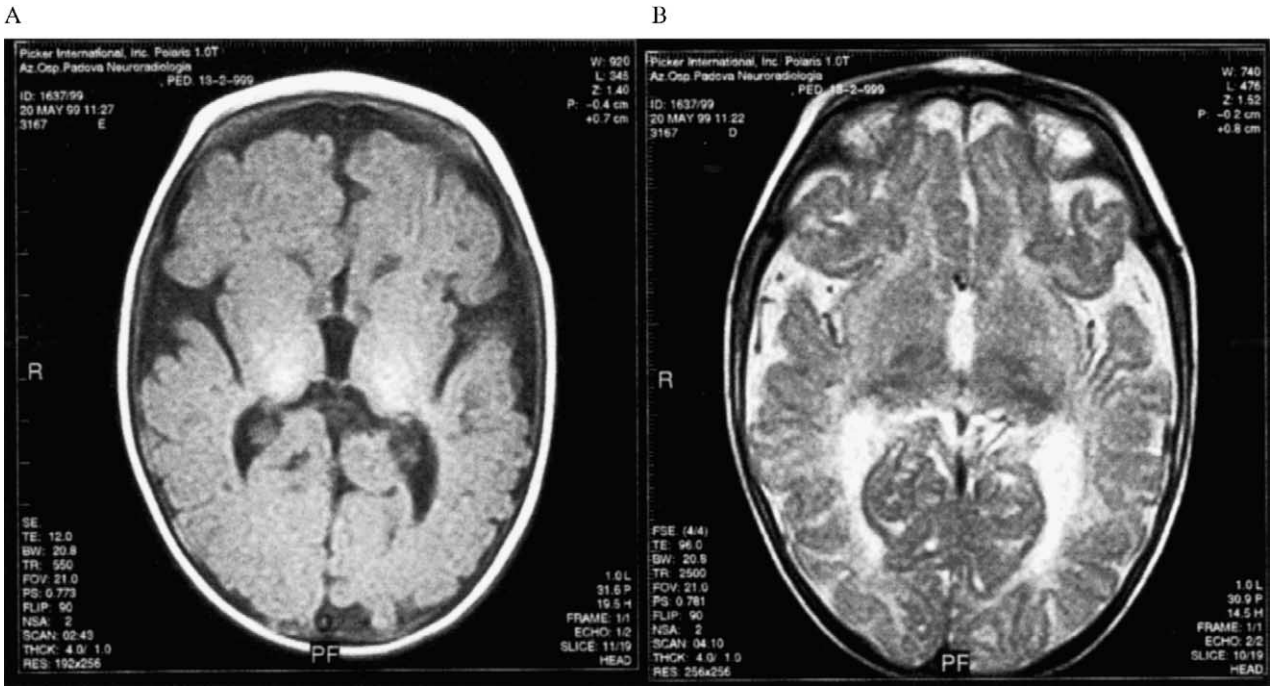

Fig. 2. Age 3 months. (A) Axial SE 550/12 MR image shows bilateral areas of high signal intensity in the region of the thalami. The internal capsula appears poorly myelinated. (B) Axial FSE 2500/96 MR image shows slight hyperintensity in the same region.

EEG was characterized by a diffuse slow background activity.

The ophthalmologic examination was negative.

Visual and auditory evoked potentials and EMG with nerve motor conduction velocity were normal.

Viral (TORCH, HIV) and metabolic investigations (urine acids, plasma and urine amino acids, very long fatty acids), and CSF examination for protein, glucose and lactate were all normal with no cells.

At 10 months old, the child had a severe spastic dystonic tetraparesis and mental retardation.

The twin brother has also been followed up: his neurological development is completely normal.

3. Discussion

STCs are known to be a pathological feature of hypoxic-ischemic encephalopathy in infants [7,8], but have also been reported in a few severely disabled infants with no evidence of pre- or perinatal asphyxia [1–6].

Such patients have several neurological and neuropathological features in common (Table 1). They are usually infants born at term or beyond 34 weeks of gestation. The pregnancy is generally normal, though there have been reports of polyhydramnios in six cases [3,4], abnormal cardiotocography in four [4] and sudden loss of fetal movements in two [2,4].

Clinical presentation at birth is severe: low Apgar scores [1,3,4], no spontaneous movements [3,4,6], spasticity or hypertone [1,4–6], or marked hypotonia, feeding problems caused by impaired suck and swallow [3–6], facial diplegia and tongue fasciculations [3].

The prognosis is generally very poor, with lack of psychomotor development and death within days or months.

Table 1
Clinical and neuroradiological findings in infants with STC

Reported patients (26)		Present case
Gestational age range	32–42	
Median gestational age	38	+
Polyhydramnios	7/26	−
Apgar score at 1 min ≤4	10/17	−
Apgar score at 5 min ≤6	8/14	−
No spontaneous motor activity	11/26	−
Hypertonia	19/26	+
Absent suck and swallow	21/26	−
Neonatal convulsions	8/26	−
Evidence of thalamic calcification on CT scan	12/13	+
Death within 1 month	11/26	−
Death within 6 months	8/26	−
Neuropathological examination		
Thalamic lesions	18/18	
Basal ganglia affected	4/18	
Brain stem involvement	7/18	

Long-term follow-up is only available for two patients, both suffering from severe neurological impairment [3].

CT scan reveals STCs. In some cases, the thalami are normal or hypodense, despite mineralized neuronal necrosis being found at autopsy [1,3].

MRI is negative or may show delayed myelination [4,6].

The pathology is characterized by bilateral symmetrical lesions in the thalami, mostly involving the lateral portion [3,4], with gliosis, neuronal mineralization and neuronal loss. In some cases, the brain stem [3,4], striatum [1,4] and hippocampus [3] present similar lesions.

The cause of this anatomo-clinical disorder is still a matter of debate. The severe clinical course, especially the marked spasticity already evident at birth or within a few days after birth, would suggest a prenatal origin of the damage.

Congenital infections can be ruled out because serologic tests are always negative and the cerebral lesions show no signs of inflammation at autopsy in any of the reported cases.

A toxic event has been hypothesized, given the presence of axonal spheroids in two patients [2,3]. In fact, in one case the mother had suffered from salicylate intoxication: the newborn's brain damage may, however, have been related to hypotension and acidosis, rather than to any direct toxic effects.

No data are available in the literature as regards a potential genetic etiology. The report from Abuelo [1] on two siblings with STC cannot entirely rule out the possibility of hypoxic-ischemic insults occurring in both cases.

The vast majority of authors consider prenatal hypoxic-ischemic damage responsible for this disorder.

The selective vulnerability of the thalamus and basal ganglia to hypoxic-ischemic insult has been documented both experimentally and clinically. This is more frequent in full-term than in preterm infants [3,9]. The pathogenesis of the damage appears to be related primarily to glutamate-induced neuronal damage [7].

The association of gliosis with neuronal loss and/or mineralization in these patients suggests a destructive lesion. The time it takes for appreciable tissue calcification to become visible after a hypoxic insult is 2 or more weeks [4]. In some cases, in fact, the CT scan was normal postnatally and the STC were only discovered several weeks later [1], on repeat CT or at autopsy.

As mentioned earlier, there is no clear reason to justify an intrapartum or postpartum asphyxia in most reported cases, but careful investigation into the history of the pregnancy pinpoints a noxious event capable of causing fetal hypoxia in some, e.g. polyhydramnios [3,4], abnormal cardiotocography several days before delivery [4], sudden loss of fetal movements some weeks before birth [2,4], breech presentation [3,4], maternal trauma with subsequent labor, and salicylate intoxication [3]. This would support the claim that the poor condition of these patients observed at birth may have already existed, instead of being a consequence of perinatal asphyxia.

The prognosis of STC is generally very poor. Only the cases described by Di Mario survived more than 3 years [3].

As far as our patient is concerned, the clinical and neuroradiological characteristics are similar to those of other cases reported in the literature. As stated by van der Knaap, the finding of STC in one of a pair of monozygotic twins (as in our case) goes against any genetic origin and supports the assumption that this condition is acquired [6].

The investigations performed rule out any congenital infections, toxic events, or neurodegenerative disorders. The Aicardi-Gouitières syndrome can be ruled out because the CSF was normal. The pregnancy and delivery were uncomplicated. The only risk factor might be related to the twin pregnancy.

The incidence of brain damage in monochorionic twins is relatively high (approximately 30 versus 3% in dichorionic gestations) and it is due to either mechanical factors (transient disturbance of umbilical blood flow due to compression, distortion or placental circulatory stasis) or placental vascular anastomoses leading to feto-fetal transfusion and iniqual circulation [7,10].

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