

# Taylor-type focal cortical dysplasia: is the epilepsy always resistant to medical treatment?

Ennio Del Giudice<sup>1</sup>, Maria Cristina Bianchi<sup>2</sup>, Michela Tosetti<sup>2</sup>, Andrea Varrone<sup>3</sup>, Alfonso Romano<sup>1</sup>, Angela Francesca Crisanti<sup>1</sup>, Luigi Titomanlio<sup>1</sup>, Floriana Imperati<sup>1</sup>

<sup>1</sup> Department of Pediatrics, Child Neurology Unit, Federico II University, Naples

<sup>2</sup> Neuroradiology Department, S. Chiara Hospital and Stella Maris Scientific Institute, University of Pisa, Pisa

<sup>3</sup> National Research Council, Biostructure and Bioimaging Institute and Department of Radiology, Federico II University, Naples, Italy

Received December 20, 2005; Accepted July 12, 2006

**ABSTRACT** – Patients with Taylor-type focal cortical dysplasia (TTFCD) generally present with medically intractable epilepsy and impaired neurological and/or intellectual functioning. Surgery usually proves to be the only treatment approach leading to control of seizures. We describe a 17-year-old girl with TTFCD who exhibited a very long period of seizure remission. Combined clinical and neuroimaging findings were compatible with a diagnosis of a balloon cell-subtype TTFCD. As for the clinical course, partial motor seizures began at one year of age and ceased at five: our patient has had no seizure recurrence over a 12-year-follow-up. Moreover, throughout the 15-year follow-up, neurological examinations and cognitive abilities always remained within normal limits. Neuropsychological assessment clearly showed no impairments in executive functions: planning abilities, working memory, attention and impulse control, or constructive aspects of motor coordination. The predominant deficits pertained to verbal abilities in the context of borderline intellectual performances. To our knowledge, this case report documents the longest duration of seizure remission in a patient with TTFCD, thus emphasizing the possible benign course of such dysplastic lesions which usually have a poor prognosis, leading to early surgical treatment.

**Key words:** Taylor-type focal cortical dysplasia, dysplastic lesion, natural evolution, cortical dysplasia

---

**Correspondence:**

E. Del Giudice, MD  
Department of Pediatrics  
Child Neurology Unit  
Federico II University  
Via S. Pansini, 5  
80131 Naples  
Italy  
Tel.: (+00 39) 081 7462678  
Fax: (+00 39) 081 7463116  
<endelgiu@unina.it>

Taylor-type focal cortical dysplasia (TTFCD), also called focal cortical dysplasia type II (FCD II) according to the classification of Palmini *et al.* (Palmini *et al.* 2004), is a distinctive malformation of cortical development, characterized by laminar disorganization and dysplastic neurons. Classically, this condition includes the two

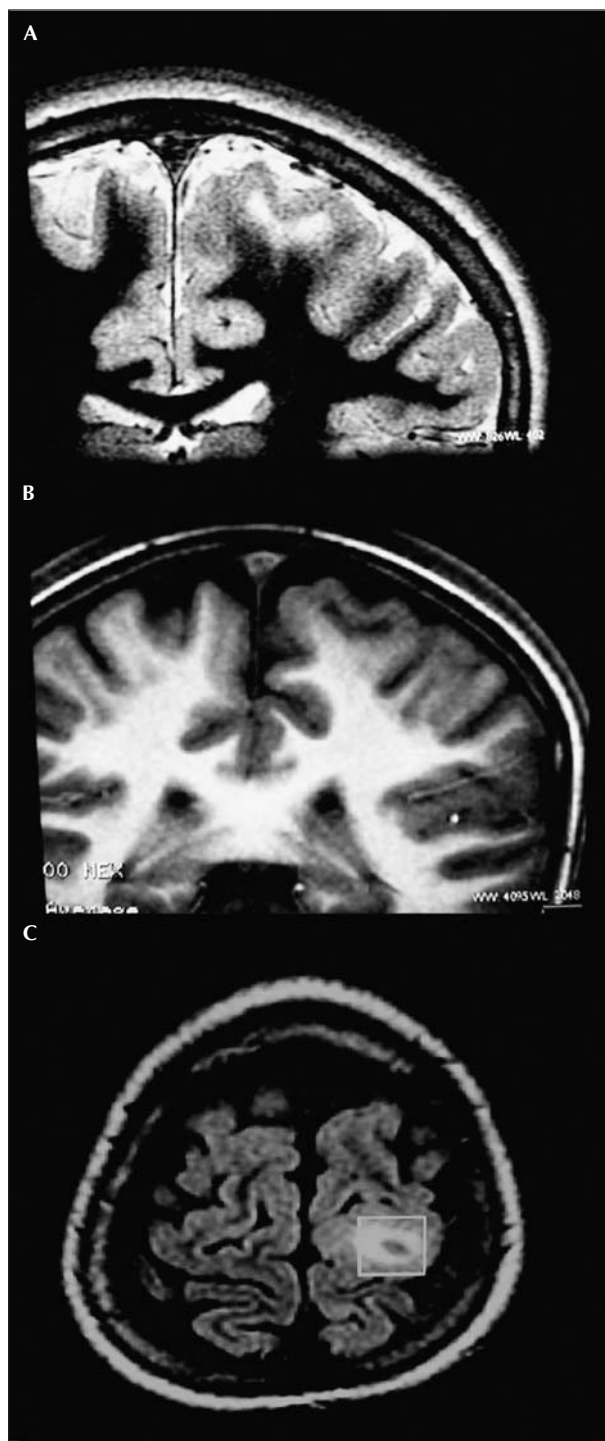
subtypes of dysplasia (TTFCD-D or FCD IIA) and balloon cells (TTFCD-BC or FCD IIB), on the basis of the presence or absence of balloon cells. Recently, Duchowny's group delineated two, distinct clinicopathological entities in the context of TTFCD (Lawson *et al.* 2005). MRI provides a neuroradiological hallmark: TTFCD-BC

characteristically appears, on fluid-attenuated inversion recovery (FLAIR) MRI, as a funnel-shaped lesion tapering from the cortex through the white matter to the lateral ventricle (Urbach *et al.* 2002). TTFCDs are often localized in the frontal lobe, and therefore in potentially eloquent cortex, thus raising the issue of the functional status of the regions involved (Marusic *et al.* 2002). Children with TTFCD usually present with severe, intractable epilepsy of early or very early onset, cognitive impairment, and focal neurological deficits such as hemiparesis (Lawson *et al.* 2005, Kloss *et al.* 2002). The TTFCD-D subtype is apparently associated with a more severe phenotype (Lawson *et al.* 2005). Conversely, adult-onset epilepsy in TTFCD, although rare, seems to be associated with a more favourable outcome (Siegel *et al.* 2005).

We report on a patient with left frontal TTFCD who showed early onset of partial seizures and subsequent, long-lasting remission.

## Case report

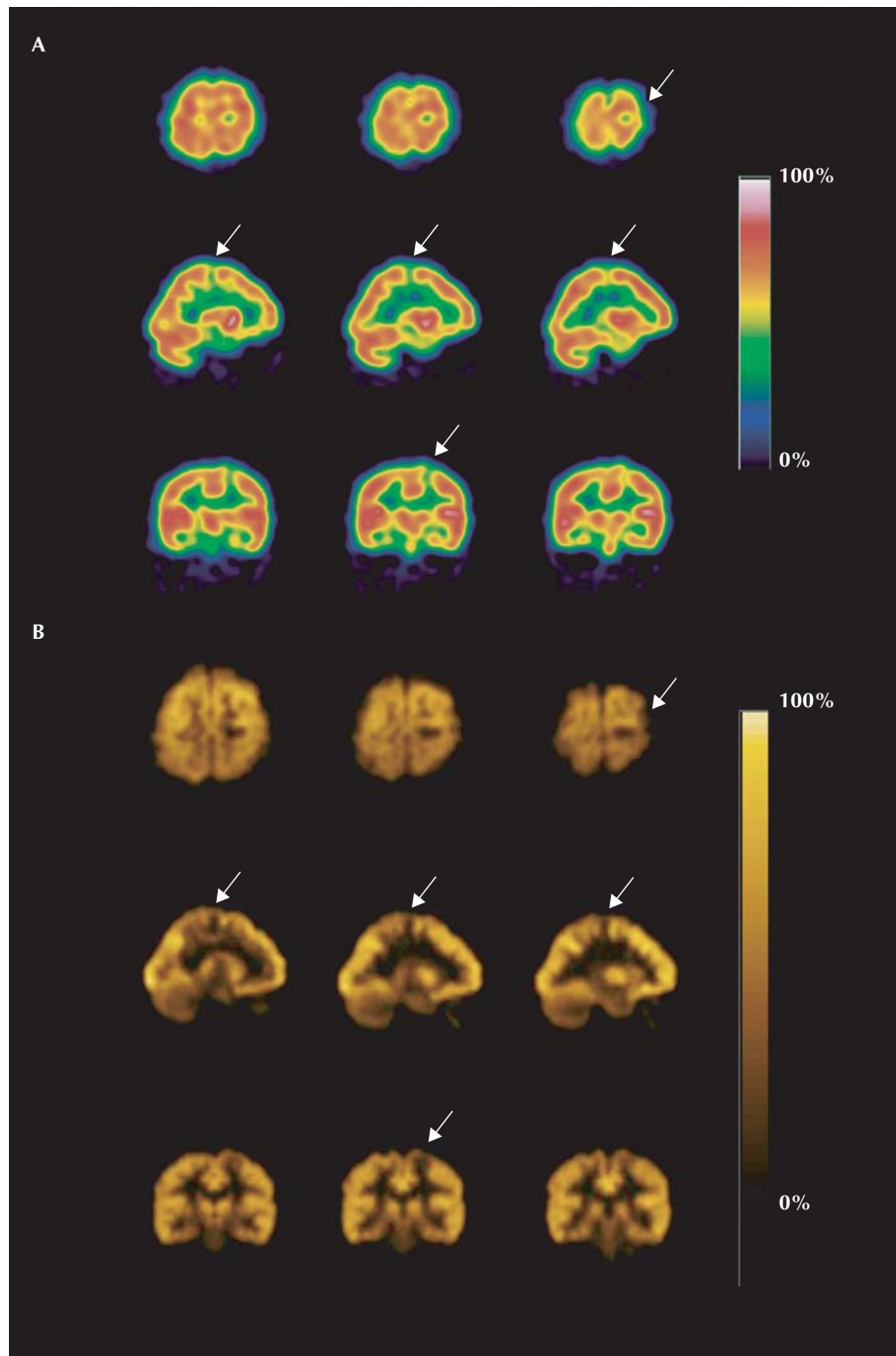
The patient was a 17-year-old girl, fully integrated in her social milieu. She was born after an uneventful pregnancy and delivery. Developmental milestones were reached at normal ages. Her first afebrile seizure occurred at the age of 12 months and lasted about three minutes. Symptoms included: impairment of consciousness with dystonic posturing of right arm followed by flaccid monoparesis, clonic twitching of right eyelid and lips. Further seizures ensued and were partially controlled on phenobarbital. The patient was admitted to our Child Neurology Unit at 24 months of age. At that time, neurological examination and psychomotor development were normal. Interictal EEGs showed spike-and-slow-wave complexes over the left rolandic area. Subsequent EEGs during the following 15 years remained unchanged. Seizure frequency was variable, ranging from two to six attacks per month. Carbamazepine (CBZ) plus Vigabatrin first reduced and eventually stopped the seizures when the girl was five years old: she remains seizure-free at the age of 17 on CBZ monotherapy. During the overall 15-year follow-up, neurological examinations and cognitive abilities have always been within normal limits. A detailed neuropsychological evaluation was performed at the age of 17 years and two months. Global intellectual functioning, assessed by means of the Wechsler Adult Intelligence Scale-Revised (WAIS-R), gave the following borderline scores: Full Scale Intelligence Quotient (FSIQ) 73; Verbal IQ (VIQ) 75; Performance IQ (PIQ) 77. Kaufman factorial analysis allowed a better definition of WAIS-R scores by demonstrating more clearly that performances on verbal abilities were poorer than those on perceptual organization and attention/concentration (Kaufman *et al.* 1975, Kaufman, 1990). Memory functions evaluated by means of the Italian version of the Reynolds' and Bigler's Test of Memory and



**Figure 1.** Brain MRI: coronal fast inversion recovery (FIR) T2-weighted (A), coronal spoiled gradient (SPGR) T1-weighted (B), axial fluid attenuated inversion recovery (FLAIR) (C). The rostral part of the left pre-rolandic cortex is thick and hollow, and the underlying white matter exhibits a tapered hyperintensity.

Learning (TOMAL) (Reynolds, 1995) were within normal limits. The Wisconsin Card Sorting Test (WCST) (Heaton, 1981) was used to assess response inhibition and mental flexibility at the cognitive level: no deficits were detected in any of the proposed tasks.

MRI revealed a focal cortical lesion involving the rostral part of the left prerolandic gyrus. The lesion was characterized by a thick and hollow cortex, appearing on the axial plane as a target-like image, and by indistinct sub-cortical white matter digitations on the coronal plane.



**Figure 2.** Transaxial (first row), sagittal (middle row), and coronal (bottom row) slices (3.9 mm thick) of SPECT (A) and FDG-PET (B) studies at the level of the prerolandic cortex. Both studies show a reduced tracer uptake (shown by the arrow) in the area corresponding to the dysplastic lesion on MRI.

The underlying white matter showed a tapered, abnormal hyperintensity pointing deeply toward the ipsilateral ventricle (*figure 1A, B, C*). No abnormal enhancement was detected after i.v. gadolinium administration.

Interictal single photon emission computed tomography (SPECT) and positron emission tomography with fluorodeoxyglucose (FDG-PET) showed a small area of reduced tracer uptake in the left prerolandic cortex corresponding to the dysplastic lesion detected by MRI (*figure 2*).

## Discussion

Taylor-type focal cortical dysplasia is a cause of refractory partial epilepsy and has a poor neurological prognosis. Surgery usually proves to be the only treatment approach leading to control of seizures. One possible explanation for drug resistance in TTFCD resides in the overexpression of drug resistance proteins such as multi-drug resistance gene-1 P-glycoprotein (MDR1) and multidrug resistance-associated protein 1 (MRP1) (Sisodiya *et al.* 2002). Conversely, no evidence has been put forward up until now regarding the mechanisms of drug responsiveness. Our patient has had no seizure recurrence during the last 12 years of follow-up. Only a few cases with transient seizure remission have been reported in the literature: in the quite large series of Stephen *et al.* nearly half of the patients with cortical dysplasia were found to be seizure-free at one-year follow-up (Stephen *et al.* 2001). Chassoux *et al.* studied a series of 28 patients with focal cortical dysplasia and found a transitory, seizure-free period lasting more than two years in nine cases (Chassoux *et al.* 2000). Gambardella *et al.* reported on spontaneous remission of childhood epilepsy in two patients with focal extraopercular cortical dysplasia: their seizure-free period was of five and six years duration respectively (Gambardella *et al.* 1997). In the series of 99 patients with intractable localization-related epilepsy reported by Takenaka *et al.* only ten patients had transient seizure remissions, which lasted for a maximum of eight years (Takenaka *et al.* 2000).

Interictal SPECT and FDG-PET studies have demonstrated reduced perfusion (Maehara *et al.* 1999, Sasaki *et al.* 2000) or decreased metabolic activity (Kim *et al.* 2000) in focal cortical dysplasias. In particular, the extent of the cortical abnormality is most often larger on FDG-PET than on MRI (Kim *et al.* 2000). In our patient, the hypoperfused/hypometabolic area was limited to the dysplastic region without apparent involvement of the surrounding cortex. This focal hypometabolism cannot explain the favourable course in our patient, since similar findings have been reported in patients with well established drug resistance (Chassoux, 2003). Notwithstanding this, based mainly on the long duration of the seizure-freedom and, to a lesser degree, on the limited extent of the hypometabolic area concordant with MRI abnormali-

ties, we are planning to gradually withdraw antiepileptic drug treatment.

The recent study by Lawson *et al.* (2005) has provided us with criteria apt to further delineate the TTFCD phenotype. Analysis of the clinical features in our patient—above all normal neurological examination and intellectual functioning—allowed us to entertain a diagnosis of a balloon cell-subtype TTFCD with reasonable certainty. In fact, TTFCD-BC never entails severe mental retardation (Lawson *et al.* 2005). Apart from the lesion subtype, the site of the lesion might be of importance. Cortical dysplasias or early lesions of the left hemisphere are reported to have a worse impact on language and cognitive development compared to right-sided lesions (Klein *et al.* 2000). Neuropsychological assessment in our patient clearly showed no impairment of executive functions: planning abilities, working memory, attention and impulse control, and constructive aspects of motor coordination. The predominant deficits pertained to verbal abilities in the context of borderline intellectual performances.

To our knowledge, this case documents the longest duration of seizure remission in a patient with TTFCD, thus emphasizing the possible benign course of such a dysplastic lesion, which usually carries a poor prognosis leading to early surgical treatment. □

## References

- Chassoux F, Devaux B, Landre E, *et al.* Stereoelectroencephalography in focal cortical dysplasia: a 3D approach to delineating the dysplastic cortex. *Brain* 2000; 123: 1733-51.
- Chassoux F. Stereo-EEG: the Sainte-Anne experience in focal cortical Dysplasias. *Epileptic Disord* 2003(Suppl. 2): S95-S103.
- Gambardella A, Le Piane E, Luciano Olivieri R, *et al.* Spontaneous remission of childhood epilepsy in two patients with focal extraopercular cortical dysplasia. *Brain Dev* 1997; 19: 422-5.
- Heaton RK. *A manual for the Wisconsin Card Sorting Test*. Odessa: Psychological Assessment Resources, 1981.
- Kaufman AS. Factor analysis of the WISC-R at 11 age levels between 6<sup>1/2</sup> and 16<sup>1/2</sup> years. *J Cons Clin Psychol* 1975; 43: 135-47.
- Kaufman AS. *Assessing adolescent and adult intelligence*. Boston: Allyn and Bacon, 1990.
- Kim SK, Na DG, Byun HS, *et al.* Focal cortical dysplasia: comparison of MRI and FDG-PET. *J Comput Assist Tomogr* 2000; 24: 296-302.
- Klein B, Levin BE, Duchowny MS, *et al.* Cognitive outcome of children with epilepsy and malformation of cortical development. *Neurology* 2000; 55: 230-5.
- Kloss S, Pieper T, Pannek H, *et al.* Epilepsy surgery in children with focal cortical dysplasia (FCD): results of long-term seizure outcome. *Neuropediatrics* 2002; 33: 21-6.
- Lawson JA, Birchansky S, Pacheco E, *et al.* Distinct clinicopathologic subtypes of cortical dysplasia of Taylor. *Neurology* 2005; 64: 55-61.

- Maehara T, Shimizu H, Yagishita A, *et al.* Interictal hyperperfusion observed in infants with cortical dysgenesis. *Brain Dev* 1999; 21: 407-12.
- Marusic P, Najm IM, Ying Z, *et al.* Focal cortical dysplasias in eloquent cortex: functional characteristics and correlation with MRI and histopathologic changes. *Epilepsia* 2002; 43: 27-32.
- Palmini A, Najm I, Avanzini G, *et al.* Terminology and classification of the cortical dysplasias. *Neurology* 2004; 62: S2-S8.
- Reynolds CR, Bigler ED. Test of Memory and Learning (TOMAL). Trento: Erickson, 1995; (Italian version by Ianes D).
- Sasaki K, Ohsawa Y, Sasaki M, *et al.* Cerebral Cortical dysplasia: assessment by MRI and SPECT. *Pediatr Neurol* 2000; 23: 410-5.
- Siegel AM, Cascino GD, Elger CE, *et al.* Adult-onset epilepsy in focal cortical dysplasia of Taylor type. *Neurology* 2005; 64: 1771-4.
- Sisodiya SM, Lin WR, Harding BN, *et al.* Drug resistance in epilepsy: expression of drug resistance proteins in common causes of refractory epilepsy. *Brain* 2002; 125: 22-31.
- Stephen LJ, Kwan P, Brodie MJ. Does the cause of localisation – related epilepsy influence the response to antiepileptic drug treatment? *Epilepsia* 2001; 42: 357-62.
- Takenaka J, Aso K, Watanabe K, *et al.* Transient seizure remission in intractable localization-related epilepsy. *Pediatr Neurol* 2000; 23: 328-31.
- Urbach H, Sceffler B, Heinrichsmeier T, *et al.* Focal cortical dysplasia of Taylor's balloon cell type: a clinicopathological entity with characteristic neuroimaging and histopathological features and favorable postsurgical outcome. *Epilepsia* 2002; 43: 33-40.