Abnormalities of cortical development and epilepsy

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Neuroimaging of focal cortical dysplasia: neuropathological correlations

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ABSTRACT − Focal cortical dysplasia is a well-known cause of intractable epilepsy with early onset of seizures, and is potentially amenable to surgical therapy.

It was first described by Taylor in 1971 as a peculiar malformative disorganisation of the neocortex characterised at histology by loss of cortical lamination and accompanied by giant, dysmorphic neurones and, most frequently, by ‘balloon cells’ littered throughout the cortex and sub-cortical white matter. While in the past decades the term ‘cortical dysplasia’ has referred to various malformations of cortical development, such as agyria, pachygyria, polymicrogyria, heterotopia and hemimegalencephaly, it is now widely accepted that the entity identified by Taylor should be considered separately, from both histological and neuroimaging standpoints. More recently, the recognition of various histological subtypes of focal cortical dysplasia characterised by different degrees of cortical disruption with or without cytological abnormalities has generated several classifications that are still unsatisfactory. With better magnetic resonance capability, subtle and very small focal cortical dysplasias may now be visualised and the differential magnetic resonance aspects of the histological subgroups can be established. We will discuss the problem of histopathological classification and magnetic resonance imaging differentiation of the various subtypes of focal cortical dysplasia in the light of personal data collected from a large series of epileptic patients who underwent surgery and had a histological diagnosis of focal cortical dysplasia.

KEY WORDS: focal cortical dysplasia, epilepsy, MR imaging, neuropathologic classification, epilepsy surgery

Several structural abnormalities of the brain can be found in patients with partial epilepsy, including malformations of cortical development (MCD), neoplasms, arteriovenous malformations and cavernous hemangiomas, scars and atrophic processes.

Focal cortical dysplasia (FCD) is a peculiar developmental anomaly of the cortex, first identified by Taylor [1] in lobectomy specimens obtained from drug-resistant epilepsy patients. It was described as an area of neocortical laminar disruption in which abnormal dysmorphic neurones were littered in all the cortical mantle and more or less associated with the so-called ‘balloon cells’ (BC), representing cells of uncertain lineage.

Taylor separated this entity from other MCD such as agyria, pachygyria, polymicrogyria, heterotopia and...
hemimegalencephaly, frequently referred to in the literature using the general term ‘cortical dysplasia’. Based on subsequent neuropathological observations, it has become clear, nevertheless, that the term FCD encompasses a wide spectrum of abnormalities of differing severity.

For a long time, confusing terminology and classification of the different forms of FCD were used in the literature: while Taylor’s FCD (TFCD) was unanimously recognised as the most severe form, with well defined histopathological features, the less severe forms of FCD were variably called ‘microdysgenesis’ or ‘mild cortical dysplasia’, and heterogeneous microscopic abnormalities were considered, in isolation or together, as being distinctive of them [2-13].

Our group recently proposed a simplified, three-category classification of FCDs, based on easily recognised histopathological characteristics, that avoids complicated terminology (Table 1) [14, 15].

With the common use of magnetic resonance (MR) images to investigate epileptic patients, FCDs have been visualised with increasing frequency, and some characterisation of their differential aspects [16-25] has been achieved.

Since the preoperative recognition of lesions on MR imaging can modify the diagnostic work-up of patients who are candidates for surgery, the most appropriate MR technique should be employed and the study should be carefully focussed on the clinical presentation [26-28]. Sequences in three different anatomical planes should always be acquired to assure the best visualisation and characterisation of the pathology.

**MR technique.** Our examinations using a 1.5 T magnet (Philips ACS NT) included: transverse spin-echo (SE) DP-T2W images of the whole brain (2 000-2 500/20-90) [TR msec/TE ms], 1 avg, 128 × 256 matrix, 230 mm field of view, 4-5 mm slice thickness with 10% intersection gap; coronal turbo spin-echo (TSE) TW2 images (2 300/100) [TR msec/TE ms], 4 avg, 256 × 256 matrix, 230 mm field of view, 3 mm-thick sections with 10% intersection gap, turbo factor of 15; coronal TSE fluid-attenuated inversion-recovery (FLAIR) T2W sequence (6 000/100/2 000) [TR msec/TE msec/inversion time msec], 3 avg, 238 × 256 matrix, 230 mm field of view, 3 mm-thick sections with 10% intersection gap, turbo factor of 15; coronal T2W images (3 000/20/400) [TR msec/TE msec/inversion time msec], avg, 256 × 256 matrix, 230 mm field of view, 3 mm-thick sections with 20% intersection gap, turbo factor of 4. Coronal sequences were acquired over the area of the brain suspected of being the epileptogenic zone (EZ), that is, the area of seizure generation, based on electro-clinical data. In most patients, 3D volume Fast Field Echo (FFE) T1-W images are also obtained in the sagittal plane (30/4.6) [TR msec/TE msec], 30° flip angle, 1 avg, 512 × 512 matrix, 230 mm field of view, 1 mm-thick contiguous slices, and source images are subsequently reformatted in transverse and coronal sections. Additional sagittal TSE FLAIR T2W images are sometimes acquired to obtain further definition of hippocampal/parahippocampal pathology.

No contrast medium is usually injected.

To investigate temporal lobe epilepsy, transverse images are acquired along the major axis of the hippocampus, and coronal images perpendicular. For extra-temporal lobe epilepsies, sections are obtained parallel and perpendicular, respectively, to the anterior-posterior commissural (AC-PC) line.

**Table 1. Neuropathological classification and findings of FCDs.**

- A) Architectural (AD) - heterotopic neurones in the WM - disarray of cortical lamination
- B) Cytoarchitectural (CD) - heterotopic neurones in the WM - disarray of cortical lamination - giant neurones
- C) Taylor’s (TFCD) - heterotopic neurones in the WM - disarray of cortical lamination - giant + dysmorphic neurones - without or with balloon cells (BC)

**Personal data**

FDCs were found in approximately 23% of the histopathological specimens from our total series of 360 patients undergoing surgery during the preceding six years. To find distinctive MR findings for the different subgroups of FCDs, we conducted a retrospective study correlating imaging and histopathology in a group of 49 patients, selected on the basis of their histological diagnosis of FCD, among 224 patients who underwent surgery between May 1996 and November 2000 and for whom a clinical follow-up of at least one year was available. According to the adopted neuropathological classification, 15 TFCD (13 with BC; 2 without BC) (30.6%), 6 cytoarchitectural dysplasia (CD) (12.2%) and 28 architectural dysplasia (AD) (57%) were identified in this series.

Differences were found at imaging between TFCD and the other two categories of cortical dysplasia (non-TFCD), even though some overlapping of MR features was observed [29].

The most striking features of Taylor’s FCD included: focal thickening of the cortex with poor definition of the grey-white matter junction; decreased signal of the subcortical white matter on T1-W sequences that increased on T2-W images and frequently tapered as it extended to the ventricle (figures 1, 2). Cortical gyri were most frequently normal or slightly wider. Calcifications, peripheral oedema or mass effect were usually absent. TFCD favoured an extra-temporal location with a predilection for the frontal lobe. Our data are therefore consis-
tent with the literature for both characteristic MR appearance and site of TFCD.

**Architectural dysplasia** was mainly characterised by focal volume loss of the involved brain with shrinkage of the white matter, which exhibited variable increased signal on T2-W images and mild blurring with the overlying cortex. Normal cortical thickness was usually observed. The temporal lobe was the most common location for this subtype of cortical dysplasia (figure 3). This quite peculiar MR aspect of AD is not sufficiently underlined in the literature.

**Figure 1.** MR images of Taylor’s FCD with balloon cells. Coronal turbo spin-echo inversion-recovery T1-weighted image (3 000/20/400) (A) shows thickening of the frontal cortex on the right, with blurring of the grey-white matter junction and decreased signal of the white matter, tapering towards the ventricle. Coronal turbo spin-echo T2-weighted image (2 300/100) (B), coronal turbo spin-echo FLAIR T2-weighted image (6 000/100/2 000) (C) and sagittal turbo spin-echo FLAIR T2-weighted image (D) show increased signal of the subcortical white matter tapering towards the ventricle. Smaller size of the right frontal horn in comparison to the left, with no mass effect of the lesion, is observed (A-C).
In about 50% of specimens taken from the temporal lobe, AD coexisted with hippocampal sclerosis (HS), configuring ‘dual pathology’. At visual assessment, HS was revealed by atrophy, decreased signal of the hippocampus on T1-W images and increased signal on T2-W images and by loss of definition of internal anatomy (figure 3).

The various subgroups of cortical dysplasia were not only characterised by different neuropathological and MR aspects, but also by distinctive electroclival patterns and post-operative outcome. Briefly, the patients with AD had lower seizure frequency than those with CD and TFCD, and the epileptogenic zone involved mainly the temporal lobe. In patients with TFCD, the epileptogenic zone was most frequently extratemporal, and interictal stereo-EEG was distinctive [15, 30].

Patients with TFCD had the best outcome after surgery, with 75% being seizure-free (Engel class 1a) [31] after at least one year of clinical follow-up, compared with 50% of CD and 43% of AD patients.

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Figure 3. MR images of architectural dysplasia with associated ipsilateral hippocampal sclerosis (‘dual pathology’). Coronal turbo spin-echo inversion-recovery T1-weighted image (3 000/20/400) (A), coronal turbo spin-echo FLAIR T2-weighted image (6 000/100/2 000) (B) and coronal turbo spin-echo T2-weighted image (2 300/100) (C). Reduced volume of the left temporal pole is recognisable, with mild signal changes of the white matter and poor distinction between grey and white matter.

Coronal turbo spin-echo inversion-recovery T1-weighted image (3 000/20/400) (D) and coronal turbo spin-echo FLAIR T2-weighted image (6 000/100/2 000) (E) acquired at the level of the hippocampal formation show atrophy of the left hippocampus which exhibits low signal on T1 increasing on T2, and loss of definition of the internal structure (arrows).
References