Epilepsy surgery of posterior quadrant dysplasia in the first year of life: Experience of a single Centre with long term follow-up

F. Novegno a,*, L. Massimi a, D. Chieffo a, D. Battaglia b, P. Frassanito a, L.F. Bianco b, T. Tartaglione c, G. Tamburrini a, C. Di Rocco a, F. Guzzetta b

a Pediatric Neurosurgery, Catholic University Medical School, Largo A. Gemelli 1, 00168 Rome, Italy
b Pediatric Neurology, Catholic University Medical School, Largo A. Gemelli 1, Rome, Italy
c Neuroradiology, Catholic University Medical School, Largo A. Gemelli 1, Rome, Italy

1. Introduction

A significant proportion of candidates to epilepsy surgery are affected by malformations of cortical development (MCD). Focal cortical dysplasias (FCD) currently represent up to one fifth of MCD, as result of the improved diagnosis by means of high resolution MRI in the last decade. A successful long term follow-up after surgical resection is often reported in FCD, the seizure-free rates being about 75%. On the other hand, the more diffuse forms of cortical dysplasia, which possibly extend over multiple lobes, are burdened by a worse outcome. Posterior quadrant dysplasia (PQD) involves the posterior areas of a single hemisphere, namely the occipital lobe and the posterior part of parietal and temporal lobes. Its management is particularly challenging. Actually, PQD is a rare variant of cortical dysplasia, and only a few cases have been reported in the literature so far. The experience on its surgical management during the first year of life is limited to sporadic, isolated cases.

Between 2002 and 2005, four children less than one-year-old and affected by drug-resistant epilepsy associated with PQD were admitted to our Institution and underwent surgical treatment. One patient remained seizure-free during all the follow-up (Engel I). The remaining three children showed a recurrence of the seizures, requiring subsequent surgical procedures in two cases. In one case (Engel II), the seizure control has been obtained thanks to pharmacological treatment. The other two patients respectively had only a partial (Engel III) and a less relevant reduction of the number of seizures (Engel IV).

Both the epileptic and the neuropsychological outcome of our series were significantly influenced by persistent contralateral interictal anomalies rather than by the timing of the surgical procedure. Unpredictable results should be expected in this kind of patients if there is the detection of contralateral independent epileptiform activities on the EEG at diagnosis. Parents and relatives should be aware of the results’ variability, even though a reduction of seizures may be expected, enabling an easier handling of the child’s condition.
5 to 7 months) that included at least four drugs in monotherapy or in combination. Before and after surgery, they were assessed according to the following procedures:

- detailed clinical history and physical examination;
- ictal/interictal prolonged scalp video-EEG recordings;
- high resolution MRI;
- neuropsychological tests; and
- behaviour observation.

After surgery, the patients were followed with serial assessment every 6 months during the first year and, afterwards, yearly.

2.1. Seizure classification

Epilepsy was classified according to the International League Against Epilepsy (ILAE) classification.8

Seizure outcome was assessed using the Engel’s scale.9

2.2. Video-EEG

Video polygraphic study was performed using 11 EEG electrodes according to the 10/20 international system. Deltoid surface electromyogram (EMG) also was recorded. Every patient underwent numerous recordings when awake and repeated, sometimes prolonged, sleep recordings; each patient had at least one nocturnal polysomnography video-EEG recording lasting >24 h.

2.3. Neuroimaging

All the patients were examined using a 1.5 Tesla MR system (Horizon Echospeed/Excite, General Electric, Milwaukee, USA). Angio-MRI or angio-CT scans were also performed.

2.4. Neurological evaluation

Motor function was estimated pre and post-operatively through a careful neurological examination. Visual function was assessed using a test battery that includes: ocular movements (spontaneous and in response to a target), the ability to fix and follow a target, and the visual field.

2.5. Neuropsychological examination

The developmental assessment was obtained using the Griffiths Mental Development Scales. The Griffiths’ scales10 were performed to assess the developmental quotient according to the single scales (locomotor, personal social, hearing and language scale, hand–eye coordination, performance, practical reasons) and the general developmental quotient (GQ). The Vineland Adaptive Behaviour Scales11 were administered to evaluate the adaptive behaviour. Mental development disorders were defined according to the Diagnostic and Statistical Manual of Mental Disorders (DSM V-TR).

3. Results

3.1. Pre-surgical data

The details of each patient are summarized in Table 1.

3.2. Clinical history

Three patients had uncomplicated pregnancy and normal delivery; one patient (# 1) had respiratory distress at birth. Family history of epilepsy was noticed in two cases (# 1 and 4).

3.3. Epileptic findings

The mean age at epilepsy onset was 1 month (range: 4 days to 3 months). Three patients presented the first seizures within the first week of life. Seizures were partial in all cases, meanly lasting 1–4 min, and followed by clusters of asymmetrical spasms. The frequency was as high as 20–100 episodes per day, despite multiple antiepileptic drug administration (including ACTH).

The interictal EEG mainly showed asymmetrical background abnormal activity (slow waves) and repetitive paroxysmal activity of high amplitude spikes and poly-spikes on the affected hemisphere, with predominance on the posterior and temporal regions. In three cases (# 1, 3 and 4) independent contralateral abnormalities were detected; in particular, contralateral subclinical epileptic discharges were recorded in one case (# 3). In all patients a clear asymmetrical hypsarrhythmic pattern appeared 2–3 months after epilepsy onset.

In case of partial seizures, ictal EEG showed discharges of theta-rhythmic activity localized on the posterior regions of the affected side, with contralateral and anterior spreading. In case of spasms, it documented diffuse high-voltage slow waves followed by low voltage rapid activities, exclusively or predominantly on the affected hemisphere.

Corresponding clinical signs during ictal discharges were not always detectable and sometimes asymmetrical spasms were evident only at the end of the discharges.

3.4. Neurological and neuropsychological findings

Axial hypotonia, asymmetric movements with slight hemiparesis contralateral to the brain lesion, severe impairment of the visual function and strabismus were detected in all cases. The head was consistently rotated contralaterally to the affected side, as result of possible visual hemi-inattention. Two patients showed nystagmus (# 1 and 4).

A severe developmental delay was found in one case (# 1), while the remaining three children had a low average GQ. A disharmonic developmental profile with worse results in motor, performance, and hand-eye coordination scales was observed. All patients showed stereotyped movements, lack of eye contact, poor responsiveness and irritability.

3.5. Neuroimaging

Neuroradiological findings of PQD were found in all cases. PQD involved the left hemisphere in all but one patient (# 2). The affected cortex showed a hyperintense MRI signal on T1 and hypointense on T2. A dysmorphic aspect of the homo-lateral hemisphere, with predominance on the posterior and temporal regions. In three cases (# 1, 3 and 4) independent contralateral abnormalities were detected; in particular, contralateral subclinical epileptic discharges were recorded in one case (# 3). In all patients a clear asymmetrical hypsarrhythmic pattern appeared 2–3 months after epilepsy onset.

In case of partial seizures, ictal EEG showed discharges of theta-rhythmic activity localized on the posterior regions of the affected side, with contralateral and anterior spreading. In case of spasms, it documented diffuse high-voltage slow waves followed by low voltage rapid activities, exclusively or predominantly on the affected hemisphere.

Corresponding clinical signs during ictal discharges were not always detectable and sometimes asymmetrical spasms were evident only at the end of the discharges.

3.6. Surgical procedures

Age at surgery ranged from 5 to 7 months (mean: 6 months). The total excision of the PQD was obtained in one case (# 2) and a subtotal removal in another one (# 4). Because of the poor differentiation between normal and abnormal tissue, a partial excision of the dysplastic tissue was realized in the remaining two children (# 1, 3) together with functional hemispherectomy. However, these two patients required a further operation due to the persistence of clinical and subclinical ictal activities on the affected side, associated with contralateral paroxysmal discharges (# 3). The excision of the residual PQD was performed in both cases, 1 year (# 1) and 4 years (# 3) after the first operation.

Table 1
Summary of the pre-operative and post-operative findings.

<table>
<thead>
<tr>
<th>Pre-surgery</th>
<th>Post-surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Case #/sex</strong></td>
<td><strong>Age at seizure onset</strong></td>
</tr>
<tr>
<td>1/M</td>
<td>4 days</td>
</tr>
<tr>
<td>2/F</td>
<td>3 months</td>
</tr>
<tr>
<td>3/M</td>
<td>7 days</td>
</tr>
<tr>
<td>4/F</td>
<td>3 days</td>
</tr>
</tbody>
</table>

Post-surgery

<table>
<thead>
<tr>
<th>Case #</th>
<th>Age at surgery and follow-up duration</th>
<th>Epileptic findings (Engel)</th>
<th>EEG</th>
<th>Motor abilities</th>
<th>Griffiths</th>
<th>Visual function</th>
<th>VABS (adaptive level)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7 months and 17 months FU: 6 years</td>
<td>III AED at the follow-up end: TPM, CLB</td>
<td>Interictal: asymmetrical BA; no hypersynchrony patterns. After 3 months left FCT 5 and SW; after 9 months interictal right focal spikes.</td>
<td>Improved, still not able to walk</td>
<td>DQ: 29 (MA 17 months)</td>
<td>Fixation, visual attention and OKN: improved. Acuity: unchanged</td>
<td>Communication, daily living skills and socialization: improved</td>
</tr>
<tr>
<td>2</td>
<td>7 months FU: 5 years</td>
<td>I AED at the follow-up end: TPM</td>
<td>Interictal: asymmetrical BA; no hypersynchrony patterns. After 8 months right FCT 5 and SW</td>
<td>Improved, able to walk without support at 2 years</td>
<td>DQ: 97</td>
<td>Fixation, visual attention and OKN: improved. Acuity: borderline</td>
<td>Communication, daily living skills and socialization: improved</td>
</tr>
<tr>
<td>3</td>
<td>5 months and 4 years 5 months FU: 7 years</td>
<td>IV AED at the follow-up end: DPA, CLB</td>
<td>Interictal: asymmetrical BA; no hypersynchrony patterns. After 2 months left FCT 5 and SW; (at 9 months) right interictal focal spikes. Ictal (at 16 months): left fast activity predominant on FCT, spreading on the right side. Subclinical theta/rhythmic discharges on the right posterior regions.</td>
<td>Improved, still not able to walk</td>
<td>DQ: 39 (MA: 11 months)</td>
<td>Fixation: improved. Visual attention, acuity and OKN: unchanged</td>
<td>Communication, daily living skills and socialization: improved</td>
</tr>
<tr>
<td>4</td>
<td>5 months FU: 8 years</td>
<td>II AED at the follow-up end: DPA, TPM, CLB</td>
<td>Interictal asymmetrical BA; no hypersynchrony patterns. After 12 months left FCT SW; 21 months independent right PTO 5 and SW</td>
<td>Improved, able to walk without support at 4 years</td>
<td>DQ: 53</td>
<td>Visual attention: unchanged. Fixation and acuity: improved</td>
<td>Communication, daily living skills and socialization: improved</td>
</tr>
</tbody>
</table>

Fig. 1. Preoperative (a, c and e) and postoperative (b, d and f) axial T2w MR images of cases 1 (a and b), 2 (c and d) and 3 (e and f) showing volume reduction of the affected occipital and temporo-parietal lobes, associated with diffuse irregular cortical thickening with prevalent polymicrogyric pattern in cases 1 and 3, and pachygryic pattern in case 2; the altered cortex is characterized by mildly hypointensity if compared to unmyelinated subcortical white matter. The post-operative images show the temporo-parieto-occipital CSF-filled surgical cavities.
The postoperative course was uneventful since no major complications were observed after all the procedures. Patient #1 required the endoscopic marsupialisation of a left periventricular cyst that developed 2 years after the second operation and caused the recurrence of left fronto-central seizures.

### 3.7. Pathology

The pathologic analysis of surgical specimens revealed structural abnormalities consistent with severe cortical dysplasia. Typical disorganization of the laminar architecture was observed,

---

Fig. 2. Case 4: (a) axial CT scan image, (b and c) axial T2w and T1w images, (d) sagittal T2w image and (e and f) coronal T1w and T2w images. CT and MR images show volume reduction of left temporal and occipital lobes, associated with marked cortical thickening, with prevalent pachygyric pattern; the occipital cortex is smooth, with few cerebral gyri and sulci, characterized by mildly hyperdensity on CT scan image, hyperintensity on T1w images and hypointensity on T2w images, if compared to unmyelinated subcortical white matter. The left lateral ventricle is abnormally dilated. (g) Axial T2w image, (h) coronal T2w image and (i) sagittal T1w image. MR images show temporo-parieto-occipital CSF-filled surgical cavity with complete removal of the lesion.
respectively.

A significant (Engel III) and a less relevant reduction of seizure severity (Engel IV) has been achieved, patients #1 and 3 only a significant (Engel III) and a less relevant reduction of seizure severity (Engel IV) has been achieved, respectively.

Contralateral interictal focal abnormalities (spikes) were observed in three cases (#1, 3 and 4).

Fig. 3. Representative histopathological images: (a) cortical dysplasia with abnormal cortical architecture (H&E stain), (b) balloon cells with glassy eosinophilic cytoplasm lacking cellular processes are visible on higher magnification (H&E stain) and (c) abundant pericellular immunostaining for synaptophysin is observed over the ectopic neurons in the subcortical white matter.

with sparse balloon cells inside the cerebral cortex and the subjacent white matter.

3.8. Post-surgical follow-up

The follow-up ranged from 5 to 8 years (average: 6.5 years).

3.9. Epileptic outcome

One patient (# 2) remained seizure-free during all the follow-up (Engel I). The remaining three children showed a recurrence of the seizures respectively by 3, 6 and 30 months from the first surgical procedure. They mainly presented with partial motor seizures, gelastic and autonomic seizures. Patients # 1 and 3 had showed independent paroxysmal activities (spikes) contralateral to the lesion on preoperative EEG assessment (patient # 1 also presented subclinical epileptic discharges on the unaffected side).

Early postoperative EEG recordings showed an asymmetrical background activity without paroxysmal abnormalities or hipsarrhythmic patterns. In all cases, interictal paroxysmal activities (spikes and spike-wave complex) were detected on the residual regions of the affected hemisphere three months after the first operation. During the follow up, clinical and subclinical ictal activities were detected on the affected side in two cases (# 1 and 4), and contralaterally in one (# 3). Contralateral interictal focal abnormalities (spikes) were observed in three cases (#1, 3 and 4).

Patient #4 currently maintains a seizure control (Engel II) thanks to the pharmacological treatment (VPA, TMP and CLB). In patients #1 and 3 only a significant (Engel III) and a less relevant reduction of seizure severity (Engel IV) has been achieved, respectively.

3.10. Neurological and neuropsychological outcome

Hemi-paresis and strabismus still persist in all cases. Axial hypotonia disappeared in one case (# 2), who started walking alone at two years of age; it was significantly reduced in the other three patients even though only one of them was able to begin walking at the age of 4 (case # 4). Nystagmus improved in all patients. A significant improvement of visual attention was observed in all patients.

Two patients show a severe mental retardation (cases # 1 and 3) and one a moderate grade of mental delay (case # 4). Only one child has a borderline cognitive development (case # 2). Adaptive behaviour is better in the two children with minor emotional disorders and without a motor impairment (cases # 2 and 4).

The quality of life as experienced by the parents has improved in all cases.

4. Discussion

PQD, also addressed as hemi-hemimegalencephaly, represents a challenging problem. This malformation actually involves the occipital, parietal and temporal lobes of one hemisphere, and is always associated with early onset, refractory epilepsy often characterized by a “catastrophic” evolution. Consequently, the patient’s psychomotor development is progressively impaired and the quality of life definitely poor. This condition advises the epilepsy specialists to consider the surgical treatment as early as possible to avoid such a clinical deterioration. Only a few data from the literature are currently available with regards of children affected by PQD and operated on early, that is within the first year of age. Indeed, infants are sporadically described, usually as part of series including older children and adults, so that only anecdotic cases are reported.4,5,12

In this subset of children, as demonstrated by our experience, the EEG at onset is often characterized by a focal pattern that tends to evolve into a hypsarrhythmic pattern within 2 or 3 months. Due to the refractory epilepsy and the progressive cognitive worsening, early surgical treatment is indicated, as well as in other cases of hypsarrhythmia associated with focal cortical injuries, as suggested by other authors.13–15

In our series, all patients presented with infantile spasms associated with partial seizures. Despite being a generalized epilepsy frequently associated with multiple epileptogenic zones, the occurrence of infantile spasms should not be considered as a contraindication for surgery, in particular when focal features are observed, namely focal lesion, focal neurological signs, history of prior or ongoing focal seizure and focal interictal EEG findings.13–16 Moreover, patients with infantile epileptic encephalopathy may have a better post-surgery outcome, especially in terms of developmental gains. Indeed, they often undergo surgical procedures at an earlier age, with a consequent shorter duration of epilepsy.14,15 On the other hand, the surgical outcome seems to be mostly influenced by the duration of the clinical history. A significant difference of outcome has been actually observed in patients with infantile spasm depending on whether they had been controlled by drugs or they were medically refractory from the beginning.15

The patients affected by infantile spasms often present increased contralateral interictal spikes, contralateral background slowing and ipsilateral and contralateral paroxysmal fast activity (PFA), as we observed in all our patients. Precocious contralateral epileptic abnormalities are usually considered as unfavourable prognostic factor. In contrast, Wyllie et al.13 recently reported a study on a series of patients affected by refractory symptomatic epilepsy presenting generalized or bilateral findings on pre-operative EEG; post-surgical outcome (72% rate of seizure-free patients) was similar to that of a
comparison group of patients with similar MRI findings and only ipsilateral electrical abnormalities. They supposed that the contra-
lateral epileptiform discharges may come from a potentially
reversible secondary epileptogenesis resulting from an interaction
between the early lesion and the developing brain. These findings
were not confirmed in our experience: 3 out of the 4 patients with
pre-operative independent contralateral interictal abnormalities
showed recurrent seizures respectively 3, 6 and 30 months after the
first surgical procedure. Accordingly, unpredictable results should
be expected in patients affected by posterior quadrant dysplasia
with the detection of contralateral independent activities. Parents
and relatives should be aware of the results’ variability, even though
a reduction of seizures may be expected, enabling an easier handling
of the child’s condition.

As for the epileptic outcome, also the neuropsychological
outcome of our series was significantly influenced by persistent
contralateral interictal anomalies rather than by the timing of
surgical procedure (see Table 1). Anyway, an overall improvement
of the quality of life was observed in all cases with a better daily
management of these patients.

As far as commonly reported, the more extensive the excision of
the PQD, better the outcome.18–20 In our small sample, the worse
results were obtained for those patients (# 1 and 3) who underwent
partial lesionectomy as first surgical step and who showed an abundance of pre-operative independent contralateral interictal
EEG abnormalities.

One of the possible mechanisms concurring to the variability of
the results is the difficulty in differentiating the borders of the
abnormal tissue from the normal cortex which makes it difficult to
obtain a complete removal of the lesion. Moreover, even with the aid
of intra-operative electrophysiological monitoring, the surgical
attitude should be to tailor the excision considering the high risk of
damaging functional areas, and to limit to selected cases the
complete removal of the lesion as first surgical step. On these
grounds, some authors1,12 advocated the association of functional
posterior disconnection procedures with lesion excision. In the
multicentric study of D’Agostino et al.,4 surgical treatment was
tailed on the single patient, 4 patients undergoing primary posterior
disconnection beyond the removal of the dysplastic lesion
at the last follow-up (range, 1.5–7 years; mean, 4 years). Such an
attitude resulted in complete seizure control in one patient, Engel
Class II in another one and Class III in the remaining two patients.
According to these authors, even a class III outcome with rare
seizures has to be considered worthwhile, allowing the resumption of
neurocognitive developmental progress and an improvement of
behaviour. Better results were obtained by Daniel et al. who
operated on two infants who showed an optimal epileptic outcome
(Engel I). No patients in both studies presented pre-operative
independent contralateral interictal abnormalities.

Major early postoperative complications have been reported in
5% of the cases following hemispherotomy, including significant
intraoperative blood loss, electrolyte imbalance, and hypothermia;
moreover, late complications, namely hydrocephalus and postop-
erative haemorrhages, have been observed.21 No major early or
late complications were observed in our series, even in the two
patients who underwent hemispheric disconnection procedures at
first surgery.

5. Conclusions

Early surgical treatment represents the mainstay in the
management of children with cortical dysplasia and refractory
epilepsy, also when multiple lobes are involved as in quadran
tic forms. Though on a relatively small number of patients, our series

confirms that, even in children operated on in the first months of
life, the most important negative prognostic factor for the seizures
outcome is represented by the persistence of contralateral slowing
and paroxysmal fast abnormal EEG activity after surgery. Persist-
tant abnormal contralateral EEG findings, as expected, also
negatively influence the neurocognitive outcome, independently
from the age at surgery. On the contrary, the final extent of surgical
excision of the dysplastic tissue did not seem to relate with the
final prognosis.

Conflict of interest statement

The authors report no conflict of interest.

Acknowledgement

The authors thank the association “AREF onlus”, www.arefon-
lus.it, for its support.

References

Seizure outcome after surgery for epilepsy due to malformation of cortical
101(Jul (1)):55–62.
Focal cortical dysplasia: long term seizure outcome after surgical treatment. J
Neural Neurosurg Psychiatry 2007;78(Aug (8)):853–6. [Epub 2007 Feb 7].
Posterior quadranctic dysplasia or hemi-hemimegalencephaly: a characteristic brain
5. Daniel RT, Meagher-Villemure K, Roullet E, Villemure JG. Surgical treatment of
temporoparietoeoccipital cortical dysplasia in infants: report of two cases.
Epilepsia 2004;45[Jul (7)]:872–6.
Pediart Neurosurg 2003;39[Jul (1)]:44–9.
Epilepsia 1996;37[Jul (1)]:625–37.
8. Commission on Classification and Terminology of the International League
Against Epilepsy. Proposal for revised classification of epilepsies and epileptic
9. Engel J Jr. A proposed diagnostic scheme for people with epileptic seizures and
with epilepsy: report of the ILAE Task Force on Classification and Terminology.
10. Griffiths R. The Griffiths mental development scores from birth to 2 years.
11. Sparrow SS, Cicchetti DV. Diagnostic use of the Vineland Adaptive Behavior
Posterior quadranctic epilepsy surgery: technical variants, surgical anatomy, and
13. Asano E, Chugani DC, Juhász C, Muzik O, Chugani HT. Surgical treatment of West
syndrome. Brain Dev 2001;23[Nov (7)]:678–86.
symptomatic infant-onset epileptic encephalopathy with and without infantile
16. Obeid M, Wyllie E, Rahu AC, Mikati MA. Approach to pediatric epilepsy surgery:
state of the art. Part II: Approach to specific epilepsy syndromes andetiologies.
surgery for epilepsy due to early brain lesions despite generalized EEG findings.
dysplastic lesions in children with intractable epilepsy: role of complete
19. Hong SC, Kang KS, Seo DW, Hong SB, Lee M, Nam DH, et al. Surgical treatment of
intractable epilepsy accompanying cortical dysplasia. J Neurosurg 2000;93[Nov
(5)]:766–73.
20. Leiplath JW, Peacock WJ, Mathern GW. Lobar and multilobar resections for
medically intractable pediatric epilepsy. Pediatr Neurosurg 2001;34[Jun
(6)]:311–8.
surgery in the first three years of life. Epilepsia 1998;39[Jul (7)]:737–43.

Please cite this article in press as: Novegno F, et al. Epilepsy surgery of posterior quadrant dysplasia in the first year of life: Experience of