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Occipital ulegyria causing epilepsy and visual impairment: an easily overlooked epilepsy syndrome*

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ABSTRACT – Ulegyria refers to scarring of the cerebral cortex usually arising from perinatal ischaemia. The scarring has a specific configuration in which small atrophic circumvolutions at the bottom of a sulcus underlie an intact spared gyral apex. This disconnection of overlying cortex may allow an "epileptogenic" island of cortex to generate seizures. Ulegyria is often associated with epilepsy and developmental delay, however, the syndromic association of visual impairment with epilepsy due to occipital ulegyria may not be recognised as a specific entity. Here, we report a series of five patients with occipital ulegyria who presented with widely variable seizure semiology and an array of visual deficits. In some patients, the link between the epilepsy and the visual impairment was not appreciated until they attended an epilepsy clinic.

Key words: ulegyria, cortical blindness, drug-resistant epilepsy

"Ulegyria" is a term used to describe a pattern of focal cortical injury in which gyri appear as small circumvolutions with relatively well preserved apical parts and thinning of sulcal portions (*figure 1*) (Kuchukhidze *et al*., 2008) This characteristic morphological pattern is attributed to the unique vasculature of sulci in neonates who display dominant apical perfusion (Kuchukhidze *et al*., 2008). This results in tissue at the base of gyri being more susceptible to hypoxic injury. Watershed zones of the major cerebral arteries, *i.e*. frontoparietal, occipital, and perisylvian areas, are particularly vulnerable (Kuchukhidze *et al*., 2008). Despite ulegyria being first described in 1899, it is rarely reported in the literature (Kuchukhidze *et al*., 2008). The exact incidence is unknown. A retrospective review at a tertiary referral centre reported a frequency of 0.5% amongst attending epilepsy

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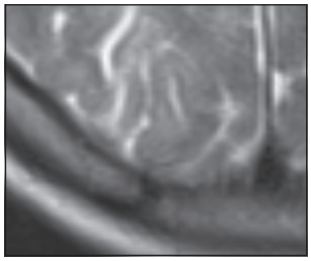

Figure 1. The characteristic morphological appearance of ulegyria in which small atrophic circumvolutions at the bottom of a sulcus underlie an intact spared gyral apex.

patients (Kuchukhidze *et al*., 2008). Improvements in neonatal care, and consequent improving survival from perinatal asphyxia, suggest that the prevalence of ulegyria is likely to grow (Ozturk *et al*., 2016). Thus, ulegyria is a condition that neurologists are likely to encounter with increasing frequency and need to become familiar with. We describe five adults with occipital ulegyria who were referred to a tertiary care epilepsy clinic due to poorly controlled epilepsy.

Case 1

Case 1 is a 49-year-old, right-handed female with drug-resistant epilepsy. She had her first febrile convulsion at age 18 months. At 2 years of age, she developed frequent focal seizures manifesting with behavioural arrest associated with oral automatisms (lip smacking), sometimes with a convulsive phase. Her perinatal history was remarkable for perinatal asphyxia. She was noted to have significant visual impairment in early childhood. She also experienced delayed attainment of speech and language milestones. Profound blindness, initially attributed to neonatal oxygen toxicity in spite of an unremarkable slit lamp examination, prevented her from completing normal mainstream schooling.

In adulthood, her visual acuity was less than 3/60 bilaterally. Her pupillary light reflexes were preserved. An EEG performed at the age of 2 showed frequent bursts of bihemispheric spike-and-slow-wave activity with highest amplitudes over bilateral parietal regions. Brain MRI performed at age 47 revealed small, atrophic gyri with relatively spared apex and broad sulci, and associated subcortical white matter volume loss, in both occipital lobes (*figure 2*).

Case 2

Case 2 is a 32-year-old female who was referred to an epilepsy clinic due to drug-resistant epilepsy. Her epilepsy began at age 5 with events characterised by ictal fear, motor arrest, and mutism. She was born at term but the neonatal period was complicated by hypoxic ischaemic encephalopathy. She experienced speech and motor delay, and presently has moderate intellectual disability.

Her clinical examination revealed microcephaly and a coarse sensory strabismus resulting from failure of visual fixation due to profound visual loss. An EEG during childhood showed generalised slow-spike-and-wave activity, while two EEGs performed in adulthood did not show any definite epileptiform activity. Brain MRI revealed bilateral occipital ulegyria (*figure 2*).

Case 3

Case 3 is a 40-year-old, right-handed female with drug-resistant epilepsy. She currently experiences approximately ten seizures per day despite treatment with a vagal nerve stimulator and five AEDs. Her seizures involve an aura in which the visual scene "fades away", followed by a loss of consciousness for up to 30 seconds. Her first seizure occurred at 2 months of age. Her birth history is notable for perinatal hypoxia. She has mild-to-moderate intellectual disability. On examination she also had a coarse sensory strabismus due to failure of visual fixation from profound visual loss. MRI performed at age 27 showed bilateral signal abnormality within the occipito-parietal regions with loss of white matter (*figure 2*).

Case 4

Case 4 is a 19-year-old, right-handed female with intractable epilepsy. She first experienced seizures as a neonate. Her seizures are characterised by transient disorientation and behavioural arrest without major motor activity. She was born at term but sustained a hypoxic injury during delivery. She experienced motor and speech delay, and presently has moderate intellectual disability.

Notable findings on examination included microcephaly, right-sided hemiplegia, and visual acuity of less than 3/60 bilaterally. An EEG during adulthood showed background slowing over the left central region. MRI performed at age 4 showed bilateral occipital gliosis and porencephaly with *ex vacuo* ventricular dilatation (*figure 2*).

Case 5

Case 5 is a 63-year-old man with medically refractory epilepsy. His seizures consist of an aura of nausea followed by confusion, coughing and non-sensical speech. His first seizure occurred at age 12. His birth

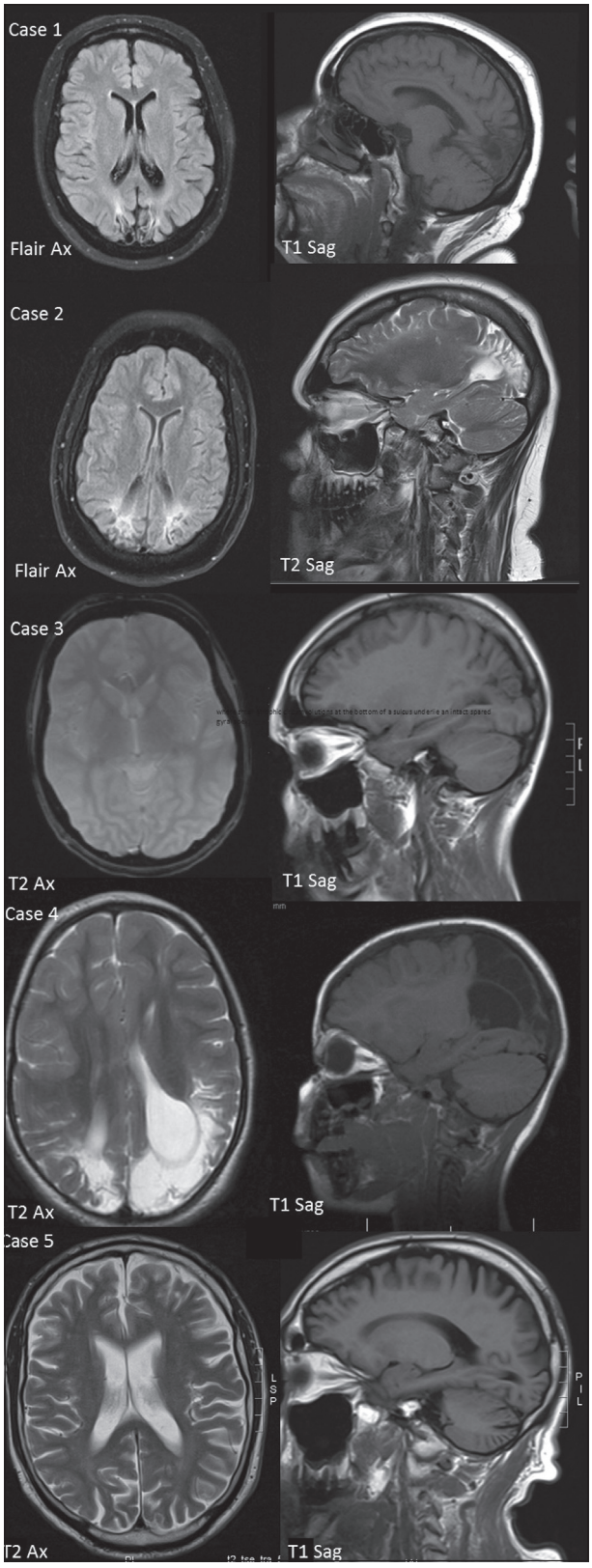

Figure 2. MRI features of occipital ulegyria: gyri appear as small circumvolutions with relatively well preserved apical parts and thinning of sulcal portions, accompanied by subcortical white matter volume loss and signal abnormalities on T2 and Flair sequences.

history was unremarkable and he was developmentally appropriate. He was not aware of any perinatal complications. He completed third-level education and is of normal intelligence. His clinical examination revealed right esophoria and visual acuity of less than 3/60, bilaterally. An EEG performed at age 35 showed left temporal sharp waves. His MRI showed bilateral medial occipital gliosis (*figure 2*).

Discussion

We describe a series of five adults with intractable epilepsy in the context of severe binocular visual impairment. The detection of ulegria on brain imaging provided the proof that each patient's visual loss and drug-resistant epilepsy had a common tissue substrate and cause. In some patients, the visiual loss was attributed to perinatal retinal injury rather than being of central/brain origin. In addition, rapid ictal propagation to more anterior brain regions, along with normal and non-specific interictal EEG abnormalities, complicated the interpretation of the seizure-onset zone. The recognition that the epilepsy and visiual loss had a common substrate was not appreciated until adulthood.

Ulegyria is a relatively common consequence of hypoxic-ischaemic encephalopathy. Watershed zones between the major cerebral arteries in the term newborn are vulnerable to reduced perfusion. Thus, ischaemic injury typically involves tissue in the frontoparietal, occipital, and peisylvian areas. Interestingly, ulegyria is thought to most commonly involve the occipital lobes (Kuchukhidze *et al*., 2008). Previous series investigating the impact of neonatal hypoglycaemia have demonstrated a posterior predilection of cortical injury, suggesting that there is a high metabolic rate in the occipital lobes during the perinatal period (Burns *et al*., 2008). This high energy demand results in occipital tissue in the border territory between the middle and posterior cerebral arteries being particularly susceptible to ischaemic insult.

Ulegyria is associated with epilepsy and developmental delay, while localising features reflect the function of the affected region of cerebral cortex. Speech and swallowing difficulty have been previously described in perisylvian ulegyria. However, the visual symptomatology of occipital ulegyria is less well characterised in the literature (Schilling *et al*., 2013). All patients in our series displayed signs of occipito-parietal dysfunction. Two patients had visual tracking problems. Three suffered from cortical blindness, and in one case, this visual impairment was misattributed to oxygen toxicity causing retinal injury as a neonate for over 40 years in spite of having an unremarkable slit lamp examination. The lack of compensation for these visual deficits by cerebral plasticity is consistent with previous findings that altered inhibitory neuronal development and cortical activation result in impaired plasticity in early brain injury (Failor *et al*., 2010). Our series demonstrates an array of often overlooked visual deficits which can be found in occipital ulegyria.

In this case series, despite clear injury to the visual cortex, only one patient experienced an aura with visual phenomenology. Previous series of occipital lobe epilepsy have reported visual seizure symptomatology in 40% of cases (Appel *et al*., 2015). Our series emphasises that a visual aura is not mandatory in occipital lobe epilepsy, and suggests that it may be less common in ulegyria compared to other causes of occipital lobe epilepsy. Drug-resistant epilepsy occurs frequently in ulegyria. All patients in our series had intractable epilepsy. However, their seizure semiology was quite variable. Interpretion of seizure semiology in occipital lobe epilepsy is complicated by the rapid ictal propogation. In previous series of posterior-onset epilepsy secondary to ulegyria, ictal semiology, characteristic of temporal, frontal, and parietal cortical regions, has been demonstrated (Kuchukhidze *et al*., 2008). This can result in difficulty defining the epileptogenic zone and can lead to clinicians concluding that this is a multi-focal epilepsy syndrome. Rapid ictal spread is not unique to ulegyria and has been demonstrated in cases of occipital lobe epilepsy due to underlying cortical dysplasia and neoplasms (Caicoya *et al*., 2007). Interictal and ictal EEG monitoring does not always result in diagnositic clarity. None of our patients had interictal epileptiform activity on EEG. While this rate is lower than the 33% frequency of occipital lobe spikes reported in other series of posterior-onset epilepsy, it does emphasise that interictal epileptiform activitiy in the occipital lobe is not a consistent feature (Appel *et al*., 2015). Furthermore the rapid spread of depolarising activity can result in EEG abnormalites being misleading. Multifocal interictal spikes and early ictal depolarisation of the medial temporal lobes have been recorded in cases of surgically responsive occipital lobe epilepsy (Caicoya *et al*., 2007). These clinical and electrographic characteristics conspire to make it difficult to recognise that patients with occiptial lobe epilepsy may have a unifying clinical syndrome associated with a specific underlying physical substrate, *i.e*. ulegyria.

Identification of epilepsy secondary to ulegyria is important as there are an increasing number of reports of an improvement in seizure frequency following surgical resection. The optimal surgical approach is at present unclear. Extensive unilateral resection in bilateral perisylvian ulegyria resulted in an Engel Class I/II response in all four patients reported by Schilling *et al*. (Schilling *et al*., 2013). The one patient with a poor response in this series had a left anterior temporal

lobectomy with right cortical subpial transections. Failure was attributed to underlying dual pathology with multifocal seizure onset. In a more recent case of a patient with bilateral parietooccipital ulegyria, a dramatic reduction in seizure frequency was reported following a right parietooccipital lobe disconnection with a tailored resection of cortex at the temporo-occipito-parietal junction (Wang *et al*., 2016). These reports suggest that ulegyria may be a surgically remediable epilepsy syndrome, however, further research is required to determine the optimal surgical technique. This case series highlights the easily recognisable, but sometimes overlooked, clinical syndrome of occipital ulegyria which causes intractable epilepsy and congenital visual impairment. □

Disclosures.
None of the authors have any conflict of interest to declare.

References

Appel S, Sharan AD, Tracy JI, Evans J, Sperling MR. A comparison of occipital and temporal lobe epilepsies. *Acta Neurologica Scand* 2015; 132: 284-90.

Burns CM, Rutherford MA, Boardman JP, Cowan FM, Satodia P, Moore AM. Patterns of cerebral injury and neurodevelopmental outcomes after symptomatic neonatal hypoglycemia. *Pediatrics* 2008; 122: 65-74.

Caicoya AG, Macarrón J, Albísua J, Serratosa JM. Tailored resections in occipital lobe epilepsy surgery guided by monitoring with subdural electrodes: characteristics and outcome. *Epilepsy Res* 2007; 77: 1-10.

Failor S, Nguyen V, Darcy DP, *et al*. Neonatal cerebral hypoxia-ischemia impairs plasticity in rat visual cortex. *J Neuroscience* 2010; 30: 81-92.

Kuchukhidze G, Unterberger I, Dobesberger J, *et al*. Electroclinical and imaging findings in ulegyria and epilepsy: a study on 25 patients. *J Neurol Neurosurg Psychiatry* 2008; 79: 547-52.

Ozturk T, Er D, Yaman A, Berk AT. Changing trends over the last decade in the aetiology of childhood blindness: a study from a tertiary referral centre. *British Journal of Ophthalmology* 2016 ; 100(2) : 166-71.

Schilling LP, Kieling RR, Pascoal TA, *et al*. Bilateral perisylvian ulegyria: an under-recognized, surgically remediable epileptic syndrome. *Epilepsia* 2013; 54: 1360-7.

Wang F, Zheng H, Zhang X, *et al*. Successful surgery in lesional epilepsy secondary to posterior quandrant ulegyria coexisting with benign childhood focal epilepsy: a case report. *Clin Neurol Neurosurg* 2016; 149: 94-7.

TEST YOURSELF

(1) What imaging feature differentiates ulegyria from encephalomalacia?

(2) What is the commonest cause of ulegyria?

(3) Occipital ulegyria presents with visual failure, in addition to epilepsy; what does perisylvian ulegyria present with?

Note: Reading the manuscript provides an answer to all questions. Correct answers may be accessed on the website, www.epilepticdisorders.com, under the section "The EpiCentre".