Occipital epilepsies: identification of specific and newly recognized syndromes

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Summary
Occipital epilepsies often elude diagnosis as they frequently masquerade as other seizure syndromes. Visual hallucinations are the key clinical symptoms indicating an occipital focus, but may be difficult to elicit on history, especially from children, and are not always present. When visual symptoms are not prominent, the seizure semiology and scalp EEG may lead the clinician away from considering an occipital focus, as they often reflect seizure propagation rather than seizure origin. Clinical and neuroimaging advances have led to the recognition of many new occipital epilepsy syndromes, which generally present in childhood or adolescence. Major groups include malformations of cortical development [focal cortical dysplasia, periventricular heterotopia (PVH), subcortical band heterotopia (SBH)], polymicrogyria, vascular (including epilepsy with bilateral occipital calcifications often associated with coeliac disease), metabolic and the emerging idiopathic occipital epilepsies. The idiopathic occipital epilepsies now comprise three identifiable electroclinical syndromes of childhood and adolescence, the biological inter-relationships and overlap with idiopathic generalized epilepsies of which are discussed here. We emphasize the clues to recognition of specific occipital epilepsies, some of which now have specific treatments. Where medical therapy is ineffective, occipital corticectomy should be considered. Emerging evidence suggests that some syndromes have a good surgical outcome, and the consequences to visual function may be less severe than anticipated.

Keywords: cortical dysplasia; heterotopia; occipital epilepsy; polymicrogyria

Abbreviations: MELAS = mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke like episodes; MERRF = myoclonus epilepsy ragged-red fibre; PME = progressive myoclonus epilepsies; PVH = periventricular heterotopia; SBH = subcortical band heterotopia

Introduction
Occipital epilepsy, although relatively uncommon (Loiseau et al., 1991; Manford et al., 1992; Berg et al., 1999; Jallon et al., 2001), is probably under-recognized. In population studies of newly diagnosed epilepsy, occipital seizures were diagnosed in 1.2–2.6% of cases (Manford et al., 1992; Jallon et al., 2001). As occipital epilepsies are able to emulate other epilepsy syndromes and are a challenge to identify, they may remain undiagnosed. Here we highlight the clues to recognition of occipital epilepsies, and discuss a systematic approach to patients emphasizing some of the specific and newly recognized occipital syndromes. Additionally we briefly discuss the complexities of the idiopathic occipital epilepsies, including the inter-relationships between the currently defined syndromes and the idiopathic generalized epilepsies.

Electroclinical features of occipital seizures
Visual hallucinations are the hallmark of occipital seizures, but are not invariably present. Hallucinations typically
commence in the visual field contralateral to the affected visual cortex and then spread to involve the entire visual field. Elementary visual seizures are characterized by fleeting visual manifestations which may be either positive (flashes, phosphenes) or, less commonly, negative (scotoma, hemianopia, amaurosis). Positive phenomena are usually flashes of colour or light, which are simple in shape and may be static or mobile. If the occipito-temporal cortex is involved, the visual hallucinations become complex and colourful, and scenes of varying complexity may be ‘seen’. Perceptive illusions may occur, which are classified as simple or complex. Simple illusions are where objects appear distorted and seem to have changed in size (macropsia or micropsia), shape (metamorphopsia), illumination, colour or clarity. Lines may appear wavy (dysmorphopsia), objects may appear inclined (plagiopsic) and there may be a loss of colour (achromatopsia). Complex illusions are where objects appear disoriented in distance (macroproxiopia, microtelepsia), appear to be distant and minute (teleopsia), appear to have a loss or enhancement of stereoscopic vision, or are persistent or recurrent (palinopsia) (for reviews see Dreifuss, 1985; Sveinbjornsdottir and Duncan, 1993).

The major differential diagnosis is migraine. In occipital seizures, stereotyped visual hallucinations manifest as multiple bright coloured balls or circles which multiply, change in size, move horizontally, may flash, and last for seconds. In migraine, visual symptoms manifest as black and white, flickering, linear, zigzag patterns in the central field, gradually expanding and lasting for minutes (Panayiotopoulos, 1999b). Other organic causes of visual hallucinations include ocular pathology (glaucoma, retinal detachment, etc.), hallucinations in blind fields (Lance, 1976), Charles Bonnet phenomenon (visual hallucinations of the blind) (Teunisse et al., 1996), peduncular hallucinosis and narcolepsy. Visual hallucinations also occur in delirium, especially drug-induced confusion and alcohol withdrawal, and psychoses (Norton and Corbett, 2000).

Other symptoms at onset of occipital seizures include sensations of ocular movement, tinnitus and vertigo; the latter two presumably represent spread to the posterior temporal-parietal region from a ‘silent’ occipital focus (Dreifuss, 1985). Ictal vomiting, eye deviation and autonomic features are other clues of occipital seizures and are seen classically in the benign childhood seizure susceptibility syndrome described by Panayiotopoulos (1989b). The external manifestations of occipital seizures may include clonic and/or tonic contraversion of the eyes and head or eyes only, forced closure of the eyelids and palpebral jerks (Ajmone-Marsan and Ralston, 1957; Takeda et al., 1970; Ludwig and Ajmone-Marsan, 1975; Dreifuss, 1985). If the seizure spreads to involve the temporal lobe, automatisms and impaired awareness may occur (Ajmone-Marsan and Ralston, 1957; Ludwig and Ajmone-Marsan, 1975). Should the seizure focus be in the suprachiasmal area it may spread to involve the suprasylvian convexity or the mesial surface, mimicking epilepsy of parietal lobe or supplementary motor origin (Ajmone-Marsan and Ralston, 1957; Ludwig and Ajmone-Marsan, 1975). Secondarily generalized seizures may also occur. Post-ictal deficits may include blindness, which can be prolonged and often follows severe seizures or status epilepticus (Sadeh et al., 1983). Headache, sometimes indistinguishable from migraine, can occur as a premonitory or post-ictal symptom.

The interictal scalp EEG in occipital epilepsy is frequently abnormal, but the apparent localization may direct the reader away from the occipital regions, or to the incorrect side if the focus is on the mesial surface. Posterior temporal activity is the most common finding, and other findings include diffuse posterior sharp or spike activity with a wide field of distribution (Ludwig et al., 1976; Williamson et al., 1992) and bilateral frontally predominant paroxysms (Williamson and Spencer, 1986). Frequent bilateral epileptiform discharges may be recorded independently from each occipital lobe, the lower voltage discharges seen in the lobe with secondary spread (Gibbs and Gibbs, 1953). The classical interictal pattern of the idiopathic occipital epilepsies comprises runs of nearly continuous high amplitude, rhythmic 2–3 Hz, unilateral or bilateral posterior sharp and slow wave complexes, with ‘fixation-off’ sensitivity. Fixation-off sensitivity is the phenomenon of activating epileptiform activity when fixation, which utilizes central vision, is lost. There is a corresponding termination of epileptiform activity when fixation is resumed (Panayiotopoulos, 1998) (Fig. 1). In total darkness, opening and closing the eyes has no effect on ongoing epileptiform activity, whereas retention of fixation in darkness by focusing on a spot of light attenuates it (Panayiotopoulos, 1981). This pattern may also be seen in symptomatic occipital epilepsies and other epilepsies (Ludwig and Ajmone-Marsan, 1975; Sadeh et al., 1983; Williamson and Spencer, 1986; Barkovich et al., 1996; Cho et al., 1999; Kurth et al., 2001). Photic activation of interictal occipital discharges occurred in 13%, and asymmetric photic driving occurred in one-quarter of occipital cases in one series selected from an EEG laboratory (Ludwig and Ajmone-Marsan, 1975).

Ictal scalp recordings do not always suggest an occipital origin of the seizure. Intracerebral recordings in proven occipital cases show rapid spread to posterior temporal, parietal and frontal regions, and scalp recordings may just reflect regions of spread (Ajmone-Marsan and Ralston, 1957; Bancaud, 1969; Takeda et al., 1970). Propagation of the seizure to the opposite occipital lobe through the corpus callosum is often a late finding in adults (Williamson and Spencer, 1986), but may be rapid on scalp EEG in children with occipital spike-slow wave abnormalities.

In making the diagnosis of occipital epilepsy, a history of visual hallucinations and the aforementioned external manifestations are critical clues, but are easily overlooked. In young children, the critical signs may be vomiting, pallor and eye deviation. Great care should be taken to try and elicit any history of occipital symptoms; asking patients to draw their hallucinations may be valuable. Diagnostic difficulty also
arises when simple partial occipital seizures evolve into complex partial, focal motor or even secondarily generalized seizures. The pathways of seizure propagation can mislead the clinician both in terms of symptomatology (Ludwig and Ajmone-Marsan, 1975) and EEG patterns (Takeda et al., 1970). Occipital lobe seizures should be suspected in any unsolved case with apparent bilateral or multifocal epileptiform discharges, especially if predominantly posterior.

Causes of occipital seizures

The occipital region is prone to involvement in a number of diffuse encephalopathies or systemic conditions (Table 1). Acute occipital seizures can be the presenting symptom of various conditions, including the reversible posterior leukoencephalopathy syndrome. This syndrome is usually characterized by altered mentation, headache, visual symptoms and multiple occipital seizures in the setting of acutely elevated blood pressure, eclampsia or immunosuppressant agents (Hinchey et al., 1996). Remarkably, occipital seizures may be the only manifesting symptom and the blood pressure may only be moderately elevated (Bakshi et al., 1998). The syndrome is caused by disruption of the posterior cerebral circulation autoregulation (MacKenzie et al., 1976; Nag et al., 1977; Dinsdale, 1983; Will et al., 1987; Trommer et al., 1988), with resulting cerebral oedema in the supratentorial white matter and cortico-medullary junction. Lesions on MRI are isointense to hypointense on T1-weighted imaging and hyperintense on T2-weighted imaging (Bakshi et al., 1998), and may be located in the occipital lobes, posterior parietal lobes, the posterior temporal lobes, pons, thalamus and cerebellum, and even the anterior hemisphere. Sparing of the calcarine and paramedian occipital lobe is usually seen, distinguishing this syndrome from bilateral posterior cerebral artery territory infarction (Hinchey et al., 1996). The posterior leukoencephalopathy syndrome is typically completely reversible with treatment of the underlying condition.

Chronic occipital epilepsies may be caused by a wide spectrum of pathologies, similar to other focal epilepsies, including tumours, vascular lesions and malformations of cortical development. The commonest group, particularly in childhood, are the idiopathic occipital epilepsies, where significant advances in understanding have occurred recently. A few rarer chronic epilepsy syndromes specifically affect the occipital region, including Sturge-Weber syndrome, adult forms of Rasmussen’s syndrome and a number of more recently defined entities (Table 1).

Occipital epilepsy syndromes

Malformations of cortical development

Malformations of cortical development are being recognized with increasing frequency as a cause of intractable epilepsy.
with the widespread use of MRI. A number of specific malformations can present as occipital epilepsy.

**Occipital cortical dysplasia**

Occipital cortical dysplasia with balloon cells was first described in the seminal paper on cortical dysplasia by Taylor and colleagues (Taylor et al., 1971). Clinical onset is usually in the first two decades of life. These lesions can easily be overlooked on MRI scans unless the occipital region is carefully examined, and the reader is familiar with the complex gyral anatomy of the posterior cortex. Characteristic findings include poor delineation of the grey/white matter interface, focal cortical thickening (Kuzniecky et al., 1991; Barkovich et al., 1995; Chan et al., 1998; Lee et al., 1998; Bastos et al., 1999; Bernasconi et al., 2001; Usui et al., 2001) and subcortical white matter T2 prolongation (Chan et al., 1998; Usui et al., 2001) secondary to glial proliferation (Usui et al., 2001) (Fig. 2A and B). As is typical of cortical dysplasia in other sites, occipital dysplasia can show very active localized epileptiform patterns on EEG (Mattia et al., 1995; Palmini et al., 1995; Chan et al., 1998).

This disorder is often refractory to anti-epileptic drugs. Surgical resection often results in a good outcome (Kuzniecky et al., 1997; Aykut-Bingol et al., 1998), and complete excision of the lesion can lead to a marked reduction in seizure frequency (Palmini et al., 1995; Hong et al., 2000). Occipital surgery is associated with a risk of a significant visual field defect (Blume et al., 1991; Williamson et al., 1992). However, in occipital malformations of cortical development, the frequency of pre- and postoperative field defects is less than anticipated (Kuzniecky et al., 1997). This finding suggests that cortical visual reorganization may occur. Confirmation of visual functional reorganization can be studied pre-operatively by functional MRI and visual-evoked potential studies (Kong et al., 2000), allowing better prediction of visual outcome.
Occipital periventricular heterotopia

The occipital region is a common site for focal periventricular heterotopia (PVH) (Raymond et al., 1994). Occipital PVH is more often bilateral than unilateral and the ventricles are of normal size (Raymond et al., 1994). Unilateral cases are more commonly right-sided (Raymond et al., 1994; Battaglia et al., 1997), and may be associated with subcortical heterotopia (Dubeau et al., 1995).

Patients with occipital PVH are usually of normal intelligence and have no neurologic abnormalities. There is a female predominance and family history is unremarkable (Cho et al., 1999). Whereas many familial and some sporadic cases of contiguous PVH are associated with mutations of the X-linked filamin-1 gene (Fox et al., 1998), filamin-1 gene mutations have not been described in patients with focal occipital PVH (Poussaint et al., 2000).

Occipital seizures typically develop in the second decade, with onset ranging from early childhood to age 40 years (Raymond et al., 1994; Battaglia et al., 1997; Cho et al., 1999). The interictal EEG has a normal background with focal epileptiform activity that does not always accord with the distribution of the heterotopia. Pronounced photic driving was noted in one report that co-localized with the PVH (Battaglia et al., 1997). Ictal recordings in bilateral PVH demonstrated diffuse fast activity superimposed on focal multiple spike discharges; in unilateral heterotopia the recruiting discharges were mostly confined to the affected hemisphere.

A heterotopion is identified in MRI studies as isointense to cortical grey matter on all pulse sequences and does not enhance with gadolinium (Poussaint et al., 2000) (Fig. 3). An important differential diagnosis is tuberous sclerosis. Heterotopia may be differentiated by their isointensity to grey matter as well as their ovoid and smooth shape, whereas subependymal nodules of tuberous sclerosis are iso- or hypointense to white matter, calcified, elongated, irregular in shape, and may enhance with gadolinium (Barkovich et al., 1992).

Most patients with occipital PVH have medically refractory epilepsy, perhaps reflecting reports from specialist centres. A number of reports of temporal or occipital surgery have yielded disappointing results (Li et al., 1997; Aykut-Bingol et al., 1998). Whether removal of all the nodules, if technically possible, would alleviate the seizures remains uncertain. It may be that the epileptogenic zone is much more extensive than the nodules alone, and a more widespread removal may be required (Li et al., 1997). Presently, such cases should be regarded as poor surgical candidates. In contrast, cases with occipital dysplasia, where the abnormal tissue is completely removed, may do well (Kuzniecky et al., 1997; Hong et al., 2000).

Subcortical band heterotopia (double cortex)

Similar to PVH, subcortical band heterotopia (SBH) can be associated with mutations in a gene on the X chromosome.
Polymicrogyria

Polymicrogyria has heterogeneous causes but is regarded as an abnormality of post-migratory cortical organization (Barth, 1987; Evrard et al., 1989; Barkovich et al., 2001). It may be caused by genetic conditions such as Zellweger’s syndrome (Volpe and Adams, 1972; Evrard et al., 1978; Barth, 1987), by disorders of perfusion and hypoxia [from the 6th month in utero onwards (Barth, 1987; Evrard et al., 1989)], by infectious agents [cytomegalovirus (Marques Dias et al., 1984; Barth, 1987; Evrard et al., 1989)] and by toxic insults (Barth, 1987; Evrard et al., 1989).

Polymicrogyria should be distinguished from ulegria, which consists of small atrophic gyri with broad sulci and results from hypoxia occurring late in pregnancy or in the perinatal period (Table 1) (Barth, 1987; Barkovich et al., 1992). The MRI appearance of polymicrogyria varies; it may be hard to distinguish from pachygyria where there are broadened gyri, cortical thickening and an irregular grey–white matter interface (Barkovich et al., 1992).

Polymicrogyria is categorized as focal or diffuse (Barkovich et al., 1996). This has pragmatic importance: focal cases with seizures may do well after surgery (Salanova et al., 1992; Kuzniecky et al., 1997; Aykut-Bingol et al., 1998), whereas patients with diffuse polymicrogyria are not good surgical candidates (Barkovich et al., 1996).

Chronic occipital epilepsy can be associated with unilateral or bilateral focal polymicrogyria (Kuzniecky et al., 1997). Seizures typically begin in the first or second decade in otherwise normal children, manifest as complex partial seizures with automatisms, and characteristically have a lack of primary visual ictal symptomatology (Kuzniecky et al., 1997).

Usually there is no major visual field defect (Guerrini et al., 1997b; Kuzniecky et al., 1997). The lack of field defects and the low frequency of visual auras may be because of the typical watershed location of polymicrogyria with associated sparing of the striate cortex (Kuzniecky et al., 1997). In some cases, however, polymicrogyric visual cortex may have intrinsic visual function (Innocenti et al., 2001). Surgery can improve seizure control without necessarily causing a field defect (Kuzniecky et al., 1997).

Occipital seizures in the progressive myoclonus epilepsies

The progressive myoclonus epilepsies (PME) are a group of rare heterogeneous disorders characterized by myoclonic and generalized seizures and progressive neurological deterioration. Focal, especially occipital, seizures may also occur. When occipital seizures occur early in the course of the disease, the diagnosis of PME may be easily overlooked (Berkovic et al., 1986, 1993).

Occipital seizures and posterior epileptiform activity are common to many forms of PME, but are most frequent and characteristic of Lafora disease. In Lafora disease, occipital seizures can be the presenting or dominating early clinical manifestation (Roger et al., 1983; Tinuper et al., 1983) and, in the setting of behavioural abnormalities, visual hallucinations can be misinterpreted as psychotic in origin (Acharya et al., 1995; Kuzniecky, 1998). Lafora disease is best diagnosed by skin biopsy. Lafora bodies are found in sweat gland duct cells (Carpenter and Karpati, 1981) and apocrine myoepithelial cells (Busard et al., 1987). They are spherical inclusions which are strongly positive on periodic acid Schiff stain. Eighty per cent of patients with Lafora disease have a mutation in the laforin gene on chromosome 6q (Minassian et al., 1998, 2000, 2001; Ganesh et al., 2000). Since multiple mutations in this gene occur, DNA diagnosis is not readily available at present.

Other PMEs, where occipital seizures may occur, include juvenile neuronal ceroid lipofuscinoses, myoclonus epilepsy ragged-red fibre syndrome (MERRF, see below) and Unverricht-Lundborg disease (So et al., 1989).

Mitochondrial disorders

The mitochondrial cytopathies are disorders of primary oxidative metabolism. They present as multisystem disorders with a predilection for muscle and brain. A number of clinical syndromes have been described with diverse clinical presentations and considerable clinical overlap (Kuriyama et al., 1984). MERRF (Fukuhara et al., 1980) usually presents as a typical PME. Mitochondrial myopathy, encephalopathy, lactic acidosis and stroke-like episodes (MELAS) (Pavlakis et al., 1984) is characterized by episodic vomiting, migraine, seizures and stroke-like episodes (often in the occipital regions), which may cause permanent or reversible hemiparesis, hemianopia and cortical blindness syndromes. Common characteristics of both syndromes include dementia, ataxia, short stature and sensorineural deafness. MERRF and MELAS can present with occipital lobe seizures. Some cases are best regarded as a MELAS/MERRF overlap (Serra et al., 1996).

In a patient with occipital seizures and PME, MERRF should be strongly suspected if there are associated clinical features such as myopathy, deafness, optic atrophy, lipomas or maternal inheritance (Berkovic et al., 1993).

In MELAS, focal seizures predominate, particularly occipital seizures (Dvorkin et al., 1987). These may be associated with transient or permanent visual field defects or other posterior cortical symptoms (Dvorkin et al., 1987; Aldrich et al., 1989). With disease progression, severe partial
epilepsy, recurrent episodes of epilepsy partialis continua, partial status epilepticus or secondary generalized seizures may occur (Montagna et al., 1988). In adults with MELAS, the partial seizures may have focal motor features; yet the presence of prominent posterior interictal discharges and photoparoxysmal responses suggests that the posterior/occipital areas are significantly involved (Canafoglia et al., 2001).

MRI scans in MELAS shows lesions particularly in the parieto-occipital region; these can cross vascular territories (Kuriyama et al., 1984) and are often transient. Lesions are laminar cortical, multifocal, usually spare white matter, and show increased signal intensity on T2-weighted images (Matthews et al., 1991) (Fig. 4A and B). Transient hyperintense areas are thought to be caused by reversible vasogenic oedema (Matthews et al., 1991). The MRI may be normal in the early stages of the disease despite repeated seizures (Canafoglia et al., 2001). Angiography usually does not show emboli or stenotic lesions (Hasuo et al., 1987; Ooiwa et al., 1993), and diffusion-weighted imaging changes are typically consistent with vasogenic rather than cytotoxic oedema; the apparent diffusion coefficient is increased in MELAS, whereas it is reduced in ischaemic infarction (Yoneda et al., 1999; Oppenheim et al., 2000).

Diagnosis of mitochondrial disorders can be challenging because of the protean clinical manifestations and the appreciable false-negative rate of all current diagnostic investigations. Many cases are sporadic, but a careful family history, including examination of near relatives, may reveal undiagnosed cases and provide critical diagnostic clues. When familial, both MERRF and MELAS have maternal inheritance (Chinnery et al., 1998). Clinical diagnosis is supported by the presence of ragged red fibres on muscle biopsy (DiMauro et al., 1985), which may be missed if an unaffected muscle is sampled (Berkovic et al., 1989). Other findings include lactic acidosis, elevated CSF lactate, myopathic changes on EMG, and elevated lactate on proton MRS (Castillo et al., 1995). DNA diagnosis is performed on hair, blood and muscle; the common mutations for MERRF (A8344G) and MELAS (A3243G) can be readily identified.

**Epilepsy with bilateral occipital calcifications**

Epilepsy with bilateral occipital calcifications was initially confused with Sturge-Weber syndrome, but has now emerged as a distinct entity often associated with coeliac disease. The largest series of cases has been reported from Italy; this may indicate a racial or geographic predilection (Gobbi et al., 1998). Clinical diagnosis is supported by the presence of ragged red fibres on muscle biopsy (DiMauro et al., 1985), which may be missed if an unaffected muscle is sampled (Berkovic et al., 1989). Other findings include lactic acidosis, elevated CSF lactate, myopathic changes on EMG, and elevated lactate on proton MRS (Castillo et al., 1995). DNA diagnosis is performed on hair, blood and muscle; the common mutations for MERRF (A8344G) and MELAS (A3243G) can be readily identified.

Seizure onset in ‘epilepsy with bilateral occipital calcifications’ is usually in the first decade of life. Initially the epilepsy is mild, comprising partial seizures with visual and/or motor adverse signs with or without secondary generalization (Gobbi et al., 1992b). In some cases, an epileptic encephalopathy evolves with partial, tonic clonic or hemiconic seizures, which evolve into atypical absence, atonic and tonic seizures. Intellectual deterioration may occur (Gobbi et al., 1988; Magaudda et al., 1993). It is not clear which factors determine such an evolution; there is no correlation with age at onset or severity of epilepsy, or extent of cerebral calcifications (Magaudda et al., 1993).

Interictal posterior uni- or bioccipital spike-wave discharges suppressed by eye opening are seen. The discharges may also be seen in the occipito-parietal regions and even the temporal regions. The background is usually normal although in some patients, as the disease progresses, background activity slows. During sleep, posterior polyspike bursts may occur more frequently than in wakefulness (Gobbi et al., 1992a; Sveinbjornsdottir and Duncan, 1993; Hernandez et al., 1998). Although the occipital calcifications are bilateral, interictal and ictal discharges may be confined to the posterior quadrant of one hemisphere (Bernasconi et al., 1998).

The occipital calcifications are seen best on CT scan (Fig. 5A). They are usually bilateral, symmetrical, linear,
occulo-nodular, and in the cortical and subcortical layers. The calcifications are situated mainly in the posterior regions but may be seen in the temporal, parietal and frontal lobes. Contrast enhancement does not alter the CT scan. There is no atrophy in the cortical areas adjacent to the calcifications. MRI is either unremarkable, or demonstrates reduced signal in the calcified areas (Magaudda et al., 1993) (Fig. 5B). It is not clear at what stage of the disease the calcifications appear as in most published series they were already present at time of diagnosis. In one case, the calcifications appeared years after diagnosis (Hernandez et al., 1998).

The occipital calcifications seen in cases with combined bilateral occipital calcifications, coeliac disease and epilepsy are similar to those found in Sturge-Weber syndrome. Clinical and neuroradiological features aid in distinguishing these two syndromes. Clinically, the former does not have the cutaneous signs, glaucoma or neurological deficit seen in Sturge-Weber syndrome. Neuroimaging in Sturge-Weber syndrome shows lobar or hemispheric atrophy (Dieber and Dulac, 1987), cortical calcifications are unilateral and ipsilateral to the naevus flammeus (bilateral in 15–19%) (Bolshauser et al., 1976), and contrast enhancement is always seen (Dieber and Dulac, 1987). In contrast, in coeliac disease with epilepsy there is no atrophy, no contrast enhancement, and the calcifications are bilateral and subcortical (Gobbi et al., 1992b; Magaudda et al., 1993). Intracranial serpentine double-contoured calcifications may also be seen following methotrexate, radiotherapy (Young et al., 1977) and administration of certain antiepileptic drugs (Reynolds, 1973) such as phenytoin, and also with folic acid deficiency (Lanzkowsky, 1970; Corbeel et al., 1985).

Coeliac disease is often asymptomatic at diagnosis. Frequently there is a history of anaemia or malabsorption in the first 3 years of life (Gobbi et al., 1992a, b; Hernandez et al., 1998; Kuzniecky, 1998). A family history of coeliac disease may provide a clue to the diagnosis (Hernandez et al., 1998; Kuzniecky, 1998). Folic acid levels are often below normal (Ventura et al., 1991; Gobbi et al., 1992b) and anticonvulsant levels may be within the normal range. After commencement of a gluten-free diet, the intestinal mucosa should return to normal. A gluten-free diet may result in a clear reduction in seizure frequency and even seizure freedom without requiring any change in antiepileptic treatment (Ventura et al., 1991). The chance of seizure freedom after a gluten-free diet is not related to the age of onset of epilepsy; rather, it is significantly related to the age of commencement of a gluten-free diet and compliance, and inversely related to the duration of epilepsy. Hence it is important to begin early therapy even in those without symptoms of malabsorption (Gobbi et al., 1992a, b; Hernandez et al., 1998).

The mechanism of epilepsy in this syndrome is not known. It has not been established whether a gluten-free diet is able to change cerebral calcifications (Hernandez et al., 1998). Surgical resection when lateralization can be established can lead to good seizure control in those in whom a gluten-free diet and/or folic acid replacement has not been effective (Bye et al., 1993; Bernasconi et al., 1998). Pathological specimens of resected tissue demonstrate cortical vascular abnormality with patchy pial angiomatosis, venous haemangiomas in deep cortical layers, fibrosed veins, subcortical calcification of vessel walls, gliosis without leptomeningeal involvement, and large jagged microcalcifications. The abnormalities are similar although not identical to those found in Sturge-Weber syndrome (Bye et al., 1993; Cronin et al., 1998; Kuzniecky, 1998). The evolution of epilepsy is independent of the existence of occipital lesions, and the calcifications may be an epiphenomenon of the underlying disease process (Ambrosetto et al., 1992).

Idiopathic occipital epilepsies

Gastaut first reported that occipital epilepsy could present as a benign, idiopathic syndrome in middle childhood (Gastaut, 1982). This disorder was not as easily identified as benign rolandic epilepsy for a number of reasons. First, there are now three forms of idiopathic occipital
epilepsy recognized. Description of the common early childhood form by Panayiotopoulos (1989) was a major advance (Panayiotopoulos, 1989a, 2000). Subsequently, Guerrini and colleagues described idiopathic photosensitive epilepsy, a condition that can be confused with both late-onset occipital epilepsy and idiopathic generalized epilepsy (Guerrini et al., 1995). Secondly, the electroclinical similarities between the idiopathic and symptomatic occipital epilepsies hindered acceptance of the idiopathic group prior to better recognition of the latter with neuroimaging advances. Thirdly, idiopathic occipital epilepsies are less common than benign rolandic epilepsy, and account for 20–30% of the benign childhood partial epilepsies (Panayiotopoulos, 1989a, 2000).

The aetiology is currently unknown, although an increasing number of partial epilepsy syndromes with a genetic basis are being recognized (Berkovic et al., 1996; Berkovic and Scheffer, 1999). Support for a genetic basis can be drawn from rare cases with multiple affected family members (Nagendran et al., 1990). These syndromes are similar with respect to normal development and examination, equal sex distribution, and normal laboratory and imaging findings, yet differ with regard to age of onset, seizure frequency and duration, circadian rhythm, clinical characteristics, ictal EEG patterns, and prognosis.

### Early onset childhood epilepsy with occipital spikes

Children present at 3–6 years of age (mean 4.7 years, range 1–14 years), typically with prolonged nocturnal seizures. Seizures often begin with prominent autonomic and behavioural features, such as pallor, sweating and irritability. Vomiting and tonic eye deviation are the hallmarks of these seizures, but are not invariable (Panayiotopoulos, 1989a, b, 1993, 1999a, 2000; Ferrie et al., 1997; Andermann and Zifkin, 1998; Oguni et al., 1999; Berg and Panayiotopoulos, 2000; Caraballo et al., 2000; Kivity et al., 2000).

The interictal EEG characteristically shows runs of bilateral high amplitude, rhythmic, 2–3 Hz, sharp and slow wave complexes emanating from the posterior quadrants with fixation-off sensitivity (Panayiotopoulos, 1981, 1993, 1999a, 2000; Ferrie et al., 1997). Epileptiform discharges may be synchronous or independent, and are morphologically similar to centrotemporal spikes; sometimes only a spike component is seen (Panayiotopoulos, 1989b, 1993, 1999a, 2000). One-third of children may also have centrotemporal or frontal spikes; more frequently these occur at a later age (Ferrie et al., 1997; Panayiotopoulos, 1993, 1999a, 2000). Other interictal findings in 15% of cases include brief, generalized spike and slow wave discharges (Panayiotopoulos, 1989a, b; Yalcin et al., 1997). Photic stimulation is usually unremarkable. EEG recordings may be normal early in the clinical course, show transient abnormalities, abnormalities confined to sleep, or have persisting abnormalities years after seizures are controlled (Panayiotopoulos, 2002). The ictal EEG demonstrates posteriorly dominant rhythmic slow wave activity admixed with spikes (Beaumanoir, 1993; Panayiotopoulos, 2000). The variability of interictal EEG findings has led to a debate about the best way to conceptualize this syndrome. Panayiotopoulos (2002) now prefers to regard it as benign childhood seizure susceptibility syndrome, as one-third of cases do not have occipital discharges, and one-third have a single seizure only that does not fulfill the diagnostic criteria of ‘epilepsy’.

The first presentation of early onset benign occipital epilepsy, with prolonged loss of consciousness, can mimic an acute cerebral insult and cause considerable alarm. Interictal EEG abnormality and tonic head or eye deviation should prompt the diagnosis, although interictal epileptiform activity may be absent on early post-ictal EEGs, only to appear a day later (Verrotti et al., 2000).

As seizures are usually infrequent, treatment is often not indicated (Panayiotopoulos, 1993, 1999a, 2000). Should treatment be required, carbamazepine, sodium valproate and phenobarbitone are equally efficacious (Ferrie et al., 1997). Drug withdrawal should be considered after 1–2 years (Ferrie and Grunewald, 2001). Partial status epilepticus can be managed with rectal diazepam. Despite multiple episodes of partial status epilepticus, there is no evidence of a long-term detrimental effect.

### Late onset childhood epilepsy with occipital spikes

This syndrome presents at a mean age of 8 years with a range (3–16 years) that overlaps that of the early-onset form (Gastaut, 1982; Panayiotopoulos, 2000). Diurnal
simple partial seizures are characterized by visual hallucinations, which may be the sole feature in 30% of patients (Panayiotopoulos, 1993, 1999a; Ferrie et al., 1997; Kivity et al., 2000). Hallucinations occur in the peripheral field and move horizontally (Panayiotopoulos, 2000), and comprise evolving multi-coloured circular patterns that multiply and enlarge during seizure progression (Panayiotopoulos, 1993, 1999a; Ferrie et al., 1997; Kivity et al., 2000). Ictal blindness is common and lasts up to 5 min (Panayiotopoulos, 1993, 1999a; Ferrie et al., 1997; Kivity et al., 2000). Other visual disturbances such as amaurosis (65%), phosphenes (58%), illusions (12%) and tonic deviation of the eyes may occur (Gastaut, 1982). Ictal headache is rare, although a post-ictal migrainous headache occurs in up to 50% of cases. Behavioural, autonomic disturbances and ictal vomiting are exceptional (Panayiotopoulos, 1993, 1999a, 2000; Ferrie et al., 1997; Kivity et al., 2000).

Impairment of consciousness is rare unless associated with hemi- or generalized convulsions. Seizure duration is brief, lasting seconds to a minute, and there are often frequent daily seizures. Partial status epilepticus is rare (Panayiotopoulos, 1993, 1999a; Ferrie et al., 1997; Kivity et al., 2000). Hemiclonic seizures occur in 44% of cases, complex partial in 19%, and generalized tonic-clonic seizures in 8% (Gastaut, 1982). Seizures remit in 50–60% cases within 2–5 years from onset (Panayiotopoulos, 2000). The interictal EEG in the late-onset variant is similar to that of the early onset type (see above), whereas the ictal EEG displays fast occipital spikes (Beaumanoir, 1993; Panayiotopoulos, 2000).

As seizures are frequent with the late-onset variant, the treatment of choice is carbamazepine (Panayiotopoulos, 1993, 1999a, 2000). In the majority, seizures remit within 2–5 years although, as in the early variant, this is not universal (Newton and Aicardi, 1983).

An important differential diagnosis of both early- and late-onset childhood epilepsy with occipital spikes is basilar migraine. Basilar migraine shares many features of both syndromes, including visual loss or disturbance, brainstem symptoms, loss of consciousness and headache (Panayiotopoulos, 1999b). Interictal epileptiform activity is not seen in basilar migraine. In the period following an attack, bilateral posterior slowing may continue for hours to days (Anderman and Zifkin, 1998). Many of the manifestations of classical migraine emanate from the occipital lobes (Camfield et al., 1978), and there is a recognized association between epilepsy and migraine such that one may precipitate the other (Marks and Ehrenberg, 1993; Ottman and Lipton, 1994).

**Idiopathic photosensitive occipital epilepsy**

Idiopathic photosensitive occipital epilepsy begins between 5 and 17 years of age, and is more common in girls. Patients have normal intelligence, neurological examination, structural brain imaging and EEG background. Seizures are classically induced by television and video games, and are less frequently induced by abrupt changes in light, flickering sunlight or computer screens. Seizures begin with colourful, moving spots in the peripheral vision, followed by conscious tonic head and eye version which may be associated with blurred vision, nausea, vomiting, headache, sharp pain in the head or orbit, and unresponsiveness (Guerrini et al., 1995; Yalcin et al., 2000). These subsequent symptoms may develop even when the patient is removed from the photic stimulus (Guerrini et al., 1995). Diurnal seizures usually last minutes, although they may continue for 2 h and secondarily generalize (Guerrini et al., 1995; Yalcin et al., 2000). Whilst most diurnal seizures are related directly to light stimulation, seizures may infrequently arise from sleep (Yalcin et al., 2000).

The interictal EEG is characterized by bilateral spontaneous synchronous or asynchronous occipital spikes, or spike and wave complexes of negative polarity, which are at times associated with isolated generalized bursts (Guerrini et al., 1995). Contralateral occipital spikes correlate with head or eye version (Yalcin et al., 2000). Rolandic spikes independent of the occipital spikes may be seen or the recording may be normal (Guerrini et al., 1995, 1997a). Epileptiform activity is enhanced by eye closure and eyes closed, and may only be obvious with an Oz electrode (Guerrini et al., 1995). Intermittent photic stimulation induces an occipital photoparoxysmal response at a wide range of flash frequencies (5–40 Hz) and may also induce generalized discharges (Guerrini et al., 1995; Yalcin et al., 2000). The ictal EEG demonstrates occipital epileptiform activity which may switch sides, spread to the temporal regions or secondarily generalize as the seizure evolves (Guerrini et al., 1995).

Management of idiopathic photosensitive occipital epilepsy includes avoiding provocative factors and administering antiepileptic drugs if necessary; monotherapy with valproate is usually adequate. The prognosis is good and most patients only experience a few seizures (Guerrini et al., 1995; Yalcin et al., 2000). Rarely, control may be difficult in patients who cannot or will not avoid triggering situations.

**Relationship of the idiopathic occipital epilepsies to the idiopathic generalized epilepsies**

The three currently recognized forms of idiopathic occipital epilepsy may resemble the idiopathic generalized epilepsies. This may pose dilemmas in diagnosis and understanding of their neurobiology. The similarities between these syndromes include their onset in childhood or early adolescence, photosensitivity, and their presumed genetic aetiology.

Diagnostic confusion may arise because idiopathic occipital epilepsies of childhood can show generalized spike-wave discharges, in addition to occipital epileptiform activity (Gastaut, 1982; Panayiotopoulos, 1989b; Yalcin et al., 1997). Care must be taken to distinguish
true generalized spike-wave discharges from bilateral posterior quadrant discharges; the latter are quite common in idiopathic occipital epilepsies. Conversely, patients with idiopathic generalized epilepsies may have bisynchronous spike-wave which coexists with focal epileptiform activity and is typically frontal, although occipital

<table>
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Table 2 Occipital epilepsy: identification of specific and newly recognized syndromes
discharges may occur (Grunewald and Panayiotopoulos, 1993; Niedermeyer, 1996). Pragmatically, the distinction is made by careful electroclinical analysis. In a series of 134 patients with occipital epilepsies of childhood, Kivity and colleagues found no overlap with the idiopathic generalized epilepsies (Kivity et al., 2000). The presence of a clear occipital aura or other features typical of the idiopathic occipital epilepsies, together with a predominance of occipital epileptiform activity, will usually allow distinction from the idiopathic generalized epilepsies. Sometimes patients report brief ‘blackout’ of vision with absences or even myoclonus, raising the possibility of an occipital focus; this is distinguished from occipital epilepsy by the brevity of the symptom, the unstructured nature of the illusion and the associated electroclinical features.

In photosensitive subjects, the distinction between idiopathic photosensitive occipital epilepsy and idiopathic generalized epilepsies with photosensitivity is made using the same principles. Photosensitivity characteristically occurs in juvenile myoclonic epilepsy and may be a feature of childhood absence epilepsy; however, absences and myoclonus are not seen in idiopathic photosensitive occipital epilepsy. Photosensitivity itself has a genetic aetiology. Rare families with multiple individuals with photosensitive epilepsy are reported (Harding et al., 1997), but it is unclear whether they have idiopathic photosensitive occipital epilepsy or other photosensitive epilepsies.

The neurobiological relationships between these epilepsies remain to be fully explored. Idiopathic generalized epilepsies are genetic disorders determined by more than one gene. The idiopathic occipital epilepsies do not have any known acquired causes and are presumably also genetic in origin. Family history data have not been extensively reported; there are a few small families described with idiopathic occipital epilepsies, as well as families with a mixture of benign partial epilepsies of childhood (Nagendran et al., 1990; Ferrie et al., 1997). In the better known overlap of benign rolandic epilepsy and idiopathic generalized epilepsy, there are observations of both syndromes in one family and of both EEG traits in single individuals. Systematic family studies of idiopathic occipital epilepsies are needed to clarify this relationship.

Management

Once the question of occipital epilepsy has been raised, the syndromes listed above need to be considered (Table 1). The clinician should carefully review the neuroimaging data; high quality MRI is needed to identify subtle malformations of cortical development and CT may highlight calcification not apparent on MRI. Metabolic investigations, including a screen for coeliac disease, should be considered. Knowledge of the emerging idiopathic occipital epilepsies is needed for optimizing advice regarding treatment and prognosis (Table 2). No differences in anti-epileptic drug efficacy in occipital epilepsies are recognized. If photosensitivity is present, valproate should be considered.

Surgery is increasingly considered in those with medically refractory occipital epilepsy and the majority benefit from it (Blume et al., 1991; Salanova et al., 1992; Williamson et al., 1992; Kuzniecky et al., 1997). A total excision of the lesion has a more favourable outcome than a partial one (Wyllie et al., 1987), although the surgical approach, whether total lesionectomy or occipital lobectomy, does not predict outcome (Aykut-Bingol et al., 1998). The focal nature of an occipital lesion (Salanova et al., 1992; Williamson et al., 1992), rather than the location of the lesion, has been shown to predict outcome, tumours faring significantly better than developmental malformations (Aykut-Bingol et al., 1998).

In patients undergoing characterization for surgical resection, functional neuroimaging, in particular ictal SPECT (single photon emission computed tomography), may aid in confirming an occipital epileptogenic focus. It is especially valuable in those without a structural abnormality on neuroimaging. Brief occipital and/or prolonged temporal hyperperfusion is seen, the temporal hyperperfusion being indicative of seizure spread. Ictal SPECT may also assist in directing intracerebral electrode placement when the scalp EEG is ambiguous or deceptive. Intercital SPECT assists in interpreting the ictal study but does not provide any unique localizing information, whereas interictal PET demonstrating occipital hypometabolism provides additional localizing assistance (Sturm et al., 2000).

EEG may also help in predicting surgical outcome. Epileptiform discharges restricted to the occipital lobe are associated with a better outcome. Unlike the temporal lobe epilepsies, an ictal discharge terminating at a distant site from seizure origin is not predictive of ongoing postoperative occipital seizures (Spencer and Spencer, 1996; Aykut-Bingol et al., 1998). Inactive postoperative scalp EEG and electrocorticography predict a better surgical outcome (Salanova et al., 1992).

The majority of reported operated cases have preoperative field defects that are often subclinical, whether complete or incomplete (Blume et al., 1991; Salanova et al., 1992; Williamson et al., 1992; Kuzniecky et al., 1997). Postsurgical visual field defects have been reported on formal testing in 20–76% of patients. Intra-operative monitoring of photic driving can be useful in minimizing postoperative defects of central vision (Curatolo et al., 2000). As both pre- and postoperative visual field defects occur less frequently than predicted (Blume et al., 1991; Kuzniecky et al., 1997), it is possible that cortical reorganization occurs in some patients, particularly those with developmental lesions (Kuzniecky et al., 1997).

Acknowledgements

We are indebted to Dr Anne Mitchell of the Austin and Repatriation Medical Centre, Department of Radiology and Ms Bronwyn Grinton of the Epilepsy Research Institute for their assistance with the neuroimaging.
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Sturm JW, Newton MR, Chinvarun Y, Berlangieri SU, Berkovic


Received June 24, 2002. Revised October 29, 2002. Accepted November 6, 2002