

SHORT REPORT

Visual disturbances representing occipital lobe epilepsy in patients with cerebral calcifications and coeliac disease: a case series

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Paroxysmal visual manifestations may represent epileptic seizures arising from the occipital lobe. In coeliac disease (CD) bilateral occipital calcifications and seizure semiology consistent with an occipital origin have been described, primarily in Mediterranean countries. By reporting three adult patients from an Australian outpatient clinic with visual disturbances, occipital cerebral calcifications, and CD, this study seeks to emphasise that CD should be considered even when patients of non-Mediterranean origin present with these symptoms. Seizure types included simple partial, complex-partial, and secondarily generalised seizures. The seizure semiology consisted of visual disturbances such as: blurred vision, loss of focus, seeing coloured dots, and brief stereotyped complex visual hallucinations like seeing unfamiliar faces or scenes. Symptoms of malabsorption were not always present. Neurological examination was unremarkable in two patients, impaired dexterity and mild hemiatrophy on the left was noted in one. Routine electroencephalography was unremarkable. In all cases, computed tomography demonstrated bilateral cortical calcification of the occipital-parietal regions. Magnetic resonance imaging showed no additional lesion. All patients had biopsy confirmed CD. Seizure control improved after treatment with gluten free diet and anticonvulsants. This report illustrates the association between seizures of occipital origin, cerebral calcifications, and CD even in patients not of Mediterranean origin.

Occipital lobe epilepsy is a relatively rare form of focal epilepsy, with a variety of underlying causes.^{1,2} Paroxysmal visual manifestations are the hallmark of epileptic seizures arising from the occipital lobe. Such seizure types may also be characteristic of the epilepsy related to coeliac disease (CD).³ The existence of a specific syndrome of CD, epileptic seizures, and intracranial calcifications was proposed by Sammaritano and colleagues in 1988,⁴ and was confirmed in several subsequent series.^{3,5–8} Nearly all reported cases have been described in young patients of Mediterranean origin, but the prevalence in other ethnic and age groups may be underestimated.⁹

We report three adult cases from an Australian neurology outpatient clinic to illustrate that the association between occipital lobe epilepsy, bilateral cerebral calcifications, and CD is not restricted to the Mediterranean population.

METHODS

We describe three patients who presented to an Australian neurology outpatient clinic with seizures characterised by visual disturbances. All were of Anglo Celtic ancestry (second

or third generation offspring of immigrants from the British Isles). The diagnosis of CD was based on villous atrophy on duodenal biopsy and raised anti-gliadin and/or anti-endomysial IgA and IgG antibodies.

CASE REPORT

Case 1

A 41 year old woman presented with a history of visual disturbances, consisting of blurring of vision and seeing coloured dots. These phenomena were intermittent, lasting from minutes to one hour, and were occasionally accompanied by a headache. The patient felt she was fully aware during these episodes. On occasion, the visual disturbances would be immediately followed by generalised convulsions. The seizures started at age 2 and continued until age 12. Initially treated with phenobarbital, she was seizure free for many years. She also described mild gastrointestinal complaints of recurrent epigastric pain and intermittent diarrhoea. A detailed neurological and ophthalmological examination was unremarkable. Computed tomography (CT) of her brain revealed serpentine calcification of the parietal-occipital regions bilaterally (fig 1). Magnetic resonance imaging (MRI) showed no additional abnormalities. Routine electroencephalography (EEG) was normal. Blood test screening for CD showed positive anti-endomysial IgA antibodies. The diagnosis of CD was confirmed by partial villous atrophy on small bowel biopsy. The patient was started on valproate and a gluten free diet. Three months later she continued to have seizures, although the overall seizure frequency had improved.

Case 2

This 43 year old man presented with a history of seizures since age 5. Seizures started with blurred vision, a hot feeling, and a visual hallucination, which consisted of a complex scene. He had the sensation that his eyes and head would flick to the right, accompanied by repetitive movements of one hand or foot. His father confirmed that awareness was briefly lost during these episodes. Headache was a prominent feature of the post-ictal phase. Neurological examination revealed mild left hemiatrophy, with reduced hand size and impaired dexterity on that side. CT scan and MRI of the brain showed serpentine calcification involving occipital-parietal regions bilaterally, particularly on the right. EEG was normal. Numerous anticonvulsants were tried without much effect. By the age of 20, the seizures had largely abated. About five years ago the patient was diagnosed with CD on clinical, biochemical, and histological findings and was started on a

Abbreviations: CD, coeliac disease; CT, computed tomography; EEG, electroencephalography; MRI, magnetic resonance imaging



Figure 1 Computed tomography in case 1 revealing serpentine calcification of the parietal-occipital regions bilaterally.

gluten free diet. Currently treated with lamotrigine and a gluten free diet he has approximately one simple-partial seizure each month.

Case 3

This 57 year old woman with known CD since childhood complained of episodes of visual disturbances. CD was diagnosed on the basis of raised anti-gliadin antibodies and villous atrophy on duodenal biopsy, but only recently had she modified her diet. She currently denies the presence of symptoms related to her CD apart from the inability to gain weight. The visual disturbances started at the age of 23 and consisted of loss of focus, obscured vision for a few seconds, followed by visual hallucinations, which consisted of seeing unfamiliar people. Sleep deprivation appeared to trigger these episodes. She also had several generalised tonic clonic seizures from sleep. Neurological examination was unremarkable. CT scan showed occipital calcifications bilaterally. EEG was normal. She was on phenytoin for many years but stopped the medication after being free of the major seizures for some time. However, when anticonvulsants were ceased the visual disturbances became more frequent. She was started on valproate and continued with her gluten free diet. Since then, the visual disturbances have greatly decreased.

DISCUSSION

An association between epilepsy and CD has been recognised since the 1960s, when Cooke and Smith described “unexplained attacks of unconsciousness” in five patients with CD.¹⁰ Since then, a higher prevalence of epilepsy among patients with CD¹¹ and an increased frequency of CD in epileptic patients has been found.^{12–13} “Episodes of blindness” were reported by Banerji and Hurwitz¹⁴ in a study of neurological manifestations in adults with CD. Subsequently, others have proposed that paroxysmal visual manifestation and ictal EEG discharges arising from the occipital lobe may be characteristic of the epilepsy related to CD.^{3–6} Our patients developed seizures in their early childhood and adolescence manifested by visual symptoms and elementary and complex visual hallucinations. The correlation of elementary hallucinations, such as coloured dots or blobs described by one patient, and ictal blurred vision reported by all patients with occipital seizure onset, has been described.^{1–15} Although ictal EEG recordings were not made,

the visual disturbances closely preceded loss of awareness or convulsions, and appear to be the initiating symptom of seizure propagation, providing strong supporting evidence that the seizures were arising from the occipital lobes.

All our patients had bilateral occipital calcifications, epilepsy, and biopsy confirmed CD, similar to those described in the young Mediterranean population series.^{3–4, 6–8, 16–17} The calcifications seen in these cases are typically bilateral, corticosubcortical, and flocculonodular, without cerebral atrophy. The calcifications resemble those found in Sturge-Weber syndrome and in the past have led to a diagnosis of Sturge-Weber syndrome without naevus flammeus.^{17–19} Some of these reported cases might be undiagnosed cases of CD. A high prevalence of CD was found in patients with epilepsy and bilateral occipital calcifications. In two Italian studies of epilepsy and cerebral calcifications of unknown origin, eight of 16 and 24 of 31 patients had biopsy confirmed CD.^{5–7, 16} In contrast, the prevalence of bilateral occipital calcifications in patients with epilepsy and CD is relatively low, ranging between none of 16 and five of 12 in an Irish and Italian study, respectively.^{5, 12} Our case series, encountered outside the Mediterranean population, further emphasises this interesting syndromic association, and suggests that it may not be an ethnically or geographically restricted finding.

A genetic predisposition has been suggested to play a role in the pathogenesis.^{12–20} Nearly all patients with CD carry the HLA-DQ2 (95%) or HLA-DQ8 (5%) haplotypes.¹⁹ Data from Mantovani indicate that the HLA genotype and phenotype predisposing to CD are the same as those predisposing to epilepsy and bilateral occipital calcifications.²⁰ It is conceivable that in individuals with the same immunogenetic background, additional genetic and environmental factors are specifically related to the onset of CD induced dysfunction of the occipital lobe. It has been proposed that calcifications might be related to reduced central nervous folate concentrations, secondary to malabsorption and impairment of folic acid transport across the blood-brain barrier.^{5, 18–21} However, the actual pathophysiology has not yet been determined. In addition, folic acid deficiency is not always demonstrable in subjects affected by epilepsy, cerebral calcifications, and CD.^{5–6} The lack of a high prevalence of bilateral occipital calcifications in patients with CD, even in those with a long exposure to gluten, also seems to be contrary to the hypothesis of a nutritional deficiency as a cause of the calcifications. Another possibility is that the cerebral calcifications are caused by an autoimmune or immune complex related endothelial inflammation.^{5–9} Further studies need to be undertaken to clarify the pathophysiology of occipital calcifications and epileptogenicity of the surrounding cortex.

The epilepsy associated with bilateral occipital calcification can be difficult to treat.² Some of these patients develop drug resistant seizures.¹⁶ There is no correlation between the severity of epilepsy and the age of seizure onset or extent of cerebral calcifications.⁷ As noted in our patients, seizure control was improved in some cases after the institution of a gluten free diet with folic acid supplements^{5–6, 8}; however, others reported no effect.³ The success of the diet in improving seizure control appears to be potentiated by its institution soon after the onset of the epilepsy and at an early age.^{5–6, 8}

Of note, our patients had none or only mild gastrointestinal symptoms. Often CD is asymptomatic and detected only by serological screening.^{5–7} Screening for anti-endomysial or anti-tissue transglutaminase IgA antibodies is currently the method of choice for suspected occult CD.^{22–23} Although small bowel biopsy is the diagnostic gold standard, and confirmed the diagnosis in our three patients, these serological markers can be useful in helping to select patients for invasive diagnosis.

In summary, we described three adult patients with visual disturbances, bilateral occipital-parietal calcifications, and CD, who presented to an Australian neurology outpatient clinic, illustrating this described association outside the typical young Mediterranean population. Visual symptoms representing occipital lobe epilepsy and cerebral calcifications may be the first clue to the presence of otherwise asymptomatic CD. We conclude that patients with epilepsy who have seizures suggestive of occipital semiology and cerebral calcifications of unexplained aetiology should be carefully investigated for CD, even in the absence of gastrointestinal symptoms.

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