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

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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 diarrhea. 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 complaint of recurrent epigastric pain and intermittent diarrhea. 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 gluten free diet.

Abbreviations: CD, coeliac disease; CT, computed tomography; EEG, electroencephalography; MRI, magnetic resonance imaging.
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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 unremark-
able. 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 “un-
explained 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.4–6 “Episodes of blindness” 
were reported by Banerji and Hurwitz4 in a study of 
neurological manifestations in adults with CD. Subsequent-
ly, 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 child-
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elementary and complex visual hallucinations. The correla-
tion 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 5 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.1 3 4 6–8 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 naevoid flammeus.10–15 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 14 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 11 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 conceiv-
able 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 concen-
trations, secondary to malabsorption and impairment of folic 
acid transport across the blood–brain barrier.5 14 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.12 24 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 calcifi-
cations are caused by an autoimmune or immune complex 
related endothelial inflammation.5 14 24 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.7 Some of these patients develop drug 
resistant seizures.14 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 supplements5 6; however, 
others reported no effect.1 Several cases after the institution of 
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 
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**Figure 1** Computed tomography in case 1 revealing serpentine calcification of the parietal-occipital regions bilaterally.

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

References