

A Case of Celiac Disease, Epilepsy, and Cerebral Calcifications With Temporal Lobe Epilepsy

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ABSTRACT

This is a case report of a 55-year-old man with medication refractory right temporal lobe epilepsy since adolescence. He was found to have bilateral posterior cerebral calcifications on routine head computed tomography with confirmation on magnetic resonance imaging. He also had elevated antibody markers for celiac disease. He was diagnosed with the rare, but well-described syndrome of celiac disease, epilepsy, and cerebral calcifications (CEC). He failed a brief trial of gluten-free diet and went on to have a right temporal lobectomy with sustained freedom from disabling seizures. This case is an example of the growing recognition of neurologic disorders associated with celiac disease. It also provides an example of the characteristic radiographic sign associated with CEC.

He declined further workup and treatment for celiac disease. Serum folate levels were checked on 3 occasions with all results within laboratory reference standards. The patient underwent right anterior temporal lobectomy with pathology confirming hippocampal sclerosis with severe cell loss and gliosis in CA1/CA3/CA4. He continues to have daily auras, and remains on an antiseizure medication, but has been free of disabling seizures for greater than 2 years.

CASE REPORT

A 55-year-old man with a 40-year history of medication-refractory localization-related epilepsy was admitted for epilepsy surgery workup. Review of his imaging found bilateral occipital/parietal/temporal cerebral calcifications on noncontrast head computed tomography (CT) (Figure). Magnetic resonance imaging (MRI) confirmed the presence of calcifications and found right hippocampal atrophy. Video electroencephalogram (EEG) monitoring captured several of his habitual seizures. They were localized to the right mesial temporal lobe by seizure semiology and scalp EEG. The patient denied symptoms of celiac disease, but reported a brother with a history of gluten intolerance. He was found to have a markedly elevated Tissue Transglutaminase IgA blood level at 134 (normal range 0-19). The patient did not improve with a brief attempt at a gluten-free diet.

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DISCUSSION

Celiac disease is an autoimmune condition with growing prevalence and an expanding list of associated diseases including several neurologic disorders such as neuropathy, cerebellar degeneration, and epilepsy.^{1,2} Celiac disease, epilepsy, and cerebral calcifications (CEC) is a rare, but well described syndrome of celiac disease, epilepsy, and cerebral calcifications.³ Originally there were reports of several cases of patients with bilateral occipital calcifications. The appearance of the calcifications was similar to “tram-track” radiographic sign of Sturge-Weber syndrome, with the important exemption of bilaterality. In investigating these patients an association of epilepsy and celiac disease was uncovered. These findings were codified by the Italian Working Group on Coeliac Disease and Epilepsy as the syndrome of CEC in 1992.⁴ The syndrome was originally thought to have a geographic and ethnic predilection to the Mediterranean region, particularly Italy, but subsequent case reports from Europe, South America, and Australia have been published.^{5,6,7} This patient is of North European (Germanic) ancestry with the country of origin being the United States, but he lacked more specific ancestral knowledge.

The underlying cause for the association of CEC has not been fully determined. There was speculation that the calcifications were secondary to folate dysmetabolism because similar imaging findings have been described in patients treated with methotrexate.⁸ Others believe that folate is an unlikely mediator,⁹ with more recent investigation suggesting that the mineralization is secondary to direct autoimmune affects from a specific antibody to neuronal trans-

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glutaminase isoenzyme (TG6).^{5,10} The role of the calcifications in the etiology of the seizures is not entirely straightforward, either. It appears in some cases there may be an association of the epileptogenic region and the calcifications, as surgical removal of the calcifications has rendered a patient seizure free.¹¹ But other cases do not support the epileptogenicity of the calcifications. Calcifications have been reported to occur after the onset of epilepsy, and in some cases surgical removal of them did not affect the seizure frequency.¹⁰ The use of temporal lobectomy in patients with CEC and temporal lobe epilepsy been undertaken at another center with satisfactory results similar to this case.¹²

This case highlights an important topic for neurologists, gastroenterologists, radiologists, and primary care physicians. Celiac disease has protean manifestations including progressive neurologic diseases like neuropathy, cerebellar atrophy, and epilepsy. These conditions may be the sole symptom of the disease with absence of gastrointestinal complaints. It can be argued that this case did not have pathologic confirmation of celiac disease as the patient declined intestinal biopsy, but, according to the leading researchers on this topic, CEC is felt to be a spectrum of disease. It does not require active intestinal celiac disease to make the diagnosis. At the time of presentation many patients have silent or latent celiac disease.⁴ CEC could be looked at as an autoimmune disease that affects different organ systems to varying extents. The compelling radiographic findings and elevated antibody titers and a history of epilepsy are sufficient to qualify our patient for at least an incomplete form of CEC.

There are still a number of unexplained elements of the CEC association. While there is anecdotal evidence that a gluten-free diet is helpful, it remains to be proven.⁷ In this case the patient did not respond to the diet. However, he did endorse substantial diet non-compliance. It is also unclear why there is an association between epilepsy and celiac disease if the calcifications themselves are not the mediators.¹³

CONCLUSION

Initially CEC was felt to only be in the Mediterranean population, but after recognition of the disease within the larger European community, cases started to be reported from several regions. Likewise, it is not unexpected that there would be patients with CEC in the United States. The lack of other reports is more likely related to under-recognition than absence of the disease. This case can serve to increase the awareness of neurologic disease associated with celiac disease, as well as provide an example of the near pathognomonic imaging finding of CEC.

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Figure. Head Computed Tomography of 55-year-old Man With Right Temporal Lobe Epilepsy Demonstrates Bilateral Occipital/Temporal Cerebral Calcifications



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