Acta Scientific MEDICAL SCIENCES (ISSN: 2582-0931)

Volume 7 Issue 8 August 2023

Case Report

White-Matter Lesions in the Central Nervous System in Biopsy-Defined Adult Celiac Disease

Hugh James Freeman*

Department of Medicine (Gastroenterology), University of British Columbia, Vancouver, BC, Canada

***Corresponding Author:** Hugh James Freeman, Department of Medicine (Gastroenterology), University of British Columbia, Vancouver, BC, Canada.

DOI: 10.31080/ASMS.2023.07.1631

Received: July 03, 2023

Published: July 17, 2023

Abstract

Brain white-matter lesions may be detected late in the clinical course of different disorders thought to have an autoimmune pathogenesis, particularly in the pediatric population. Here, a 42 year old male with diarrhea and weight loss was discovered to have adult onset celiac disease. After institution of a gluten-free diet, he responded with resolution of his diarrhea, weight gain and histological improvement. Over a decade later, he was observed to have incidental white-matter lesions in his central nervous system detected with MRI and thought to have resulted from microvascular changes or inflammatory demyelination. This report describes an adult with brain white-matter lesions in well-established celiac disease and failure of a long-term gluten-free diet to prevent their development.

Keywords: Celiac Disease; Gluten-free Diet; Brain White-Matter Lesions; Demyelination; Vascular Disease; Autoimmune Disease

Introduction

A wide variety of neurological changes have been described in adults with celiac disease [1]. Celiac disease is an immune-mediated small bowel disorder characterized by impaired nutrient absorption including a multitude of vitamins that may, in themselves, lead to neurological impairments. In addition, other neurological changes may occur that may be attributed to alterations in microvasculature or autoimmune changes (including antibody cross-reactivity, immune-complex deposition and direct neurotoxic effects of gluten-containing peptides). An altered intestinal microbiome may also be critical, possibly due to molecular mimicry [2,3]. Most important, it is far from clear whether a gluten-free diet can reliably or effectively revert any of these reported neurological changes to normal.

White matter lesions may present in a number of neurological diseases, sometimes suggesting the presence of ischemia due to a vasculitis or caused by inflammatory demyelination, particularly in an immune-mediated disorders, such as multiple sclerosis or amyotrophic lateral sclerosis.

Indeed, a large prospective German study noted the presence of white-matter lesions in children and young adults with "biopsy-proven" celiac disease with or without intestinal symptoms [4]. However, a direct correlation of neurological findings with gluten exposure could not be established. In the present case, the purpose was to define this association between brain white-matter lesions in an older adult with biopsy-defined celiac disease, and demonstrate that, despite celiac disease resolution with a long-term gluten-free diet, no effect on brain MRI white-matter lesions could be defined.

Case Report

A 42-yr old male was referred with diarrhea for at least 10 years with weight loss of 15 kg. A duodenal biopsy in November 1997 showed typical histopathological features of adult celiac disease with crypt hyperplastic villous atrophy and intra-epithelial lymphocytosis (Marsh 3). Treatment consisted of a gluten-free diet alone leading to resolution of his diarrhea and weight gain. About 1 year later, repeat duodenal biopsies showed improvement with reappearance of villi [5]. Subsequently, he followed a strict gluten-free diet except for occasional rare periods of dietary noncompliance during vacations to foreign countries. Of note, his father reportedly had biopsy-defined celiac disease diagnosed in his forties and a sister was diagnosed with celiac disease in her thirties in Australia.

In May 2007, he developed a mild bilateral resting tremor. There was no weakness, change in balance, gait or posture. There were no cognitive complaints, alterations in handwriting or postural dizziness. There was no history of diplopia, vertigo, ataxia, dysarthria, dysphasia, numbness or paralysis. There was no prior history of optic neuritis, Lhermitte's sign, Bell's palsy or trigeminal neuralgia. Because of the clinical suspicion of Parkinson's disease, neurological studies were done through the UBC Brain Research Center. A brain MRI and MR angiogram of the Circle of Willis revealed extensive bilateral and symmetric T2 hyper-intense (white-matter) foci in the subcortical area and periventricular areas of the cerebral hemispheres. No mass or lesions were identified in the basal ganglia. Midline was central with unremarkable ventricles. Generalized atrophy was present. No evidence of enhancement or micro-hemorrhage was seen. The angiogram showed no evidence of large or medium vessel stenosis or vasculitis. Features were believed to be consistent with extensive bilateral and symmetric white-matter disease, typical of small vessel ischemia. Blood studies including a hemogram, glucose, ceruloplasmin, blood urea nitrogen (BUN), creatinine, low density lipoproteins, anti-neutrophilic cytoplasmic antibodies (ANCA), extractable nuclear antigen test (ENA), angiotensin-converting enzyme (ACE) level, anti-nuclear antibodies, lupus anticoagulant, anti-cardiolipin antbodies, rheumatoid factor were all normal or negative. Lumbar puncture including cell count, protein and glucose were normal. There was no oligoclonal banding.

Other studies included: red cell folate, vitamin B12 and syphilis serology, all normal. IgA tissue transglutaminase antibodies measurement, done on a gluten-free diet, was 16 U (normal < 20 U). Neurological consultation concluded that results were consistent with Parkinson's disease and treatment with Sinemet was provided. White-matter changes were considered to be incidental, not causing symptoms and not requiring added treatment. A repeat MRI scan in December 2007 was unchanged.

Sinemet improved his Parkinsonian symptoms.

In summary, a young man with established biopsy-defined celiac disease had symptomatic and histopathologic improvement on a glutenfree diet. After this diagnosis in 1997, he remained well, but was evaluated a decade later for tremor from Parkinson's disease. He was free of intestinal symptoms on a gluten-free diet for more than a decade and tissue transglutaminase serological assays were normal. Repeat MRI scanning showed no change with numerous white-matter lesions over a year, unchanged on a gluten-free diet.

Discussion

This report records central nervous system white-matter MRI lesions in biopsy-defined adult celiac disease despite prolonged treatment with a prescribed gluten-free diet. Identical white-matter changes in the brain were previously described in 75 diet-treated patients with celiac disease, but primarily in a pediatric-based population, ages 2.8 to 24.2 years [4]. Although only 10 of these 75 prospectively-studied patients were neurologically symptomatic, no correlation between these MRI-detected lesions, diet compliance or neurologic changes were detected after a mean gluten exposure of 2.4 years. These findings were similar to the observations in our patient, diagnosed after years of symptomatic celiac disease, but only after more than a decade on a gluten-free diet resulting in symptomatic and histopathologic resolution. Similar to this earlier pediatric report [4], no cerebral MRI-calcifications were noted in our adult patient. The present results are consistent with the prior suggestion of an extraintestinal manifestation of celiac disease, possibly due to ischemia from autoimmune small vessel disease or vasculitis or, alternatively, an inflammatory form of demyelination. Indeed, in an Oxford study [7], younger-onset autoimmune diseases (less than 30 years), including an increased risk of celiac disease (i.e., 57%), were also increased in adults with later development of another neurodegenerative disease with white-matter lesions, amyotrophic lateral sclerosis.

Similarly, white-matter lesions were also reported in other adults with celiac disease causing amyotrophic lateral sclerosis [7-9]. In one, MRI findings were significantly improved after institution of a gluten-free diet [7]. In another with familial celiac disease and amyotrophic lateral sclerosis, no gluten-free diet effects were reported. Finally, in a third case, a gluten-free diet failed to improve symptoms, but progression of the neurologic disease did not occur [9]. In all of these cases [7-9], an association between the 2 disorders was suggested. These contrasted with a Swedish study using patients thought to have evidence of celiac disease but no definitive association with amyotrophic lateral sclerosis, although biopsies were not systematically repeated after gluten-free diet treatment to document a histopathological response [10]. In a further Dutch study [11], an association could not be defined, although biopsies to define celiac disease were not done.

Because of the possible association of celiac disease with white-matter lesions on MRI, white-matter lesions may be a clinical clue to underlying celiac disease. Added studies in patients with both disorders are needed to determine if long-term treatment with a gluten-free diet could have an ameliorating effect on the neurological disease.

Bibliography

1. Freeman HJ. "Neurological disorders in adult celiac disease". *Canadian Journal of Gastroenterology* 22 (2008): 909-911.

2. Therrien A., *et al*. "Celiac disease: extra intestinal manifestations and associated conditions". *Journal of Clinical Gastroenterology* 54 (2020): 8-21.

3. Giuffre M., *et al*. "Celiac disease and neurological manifestations: from gluten to neuroinflammation". *International Journal of Molecular Sciences* 23 (2022): 15564.

4. Kieslich M., *et al*. "Brain white-matter lesions in celiac disease: a prospective study of 75 diet-treated patients". *Pediatrics* 108 (2001): E21.

5. Freeman HJ. "Mucosal recovery and mucosal healing in biopsy defined adult celiac disease". *International Journal of Celiac Disease* 5 (2017): 40-42.

6. Turner MR., *et al*. "Autoimmune disease preceding amyotrophic lateral sclerosis". *Neurology* 81 (2013): 1222-1225.

7. Brown KJ., *et al*. "White matter lesions suggestive of amyotrophic lateral sclerosis attributed to celiac disease". *AJNR American Journal of Neuroradiology* 31 (2010): 880-881.

8. Turner M.R., *et al*. "A case of celiac disease mimicking amyotrophic lateral sclerosis". *Nature Clinical Practice Neurology* 3 (2007): 581-584.

9. Ham H., *et al*. "A case of celiac disease with neurologic manifestations misdiagnosed as amyotrophic lateral sclerosis". *Intestinal Research* 15 (2017): 540-542.

10. Ludvigsson JF., *et al*. "No association between biopsy-verified celiac disease and subsequent amyotrophic lateral sclerosis—a population based cohort study". *European Journal of Neurology* 21 (2014): 976-982.

11. Visser AE., *et al*. "No association between gluten sensitivity and amyotrophic lateral sclerosis". *Journal of Neurology* 264 (2017): 694-700.