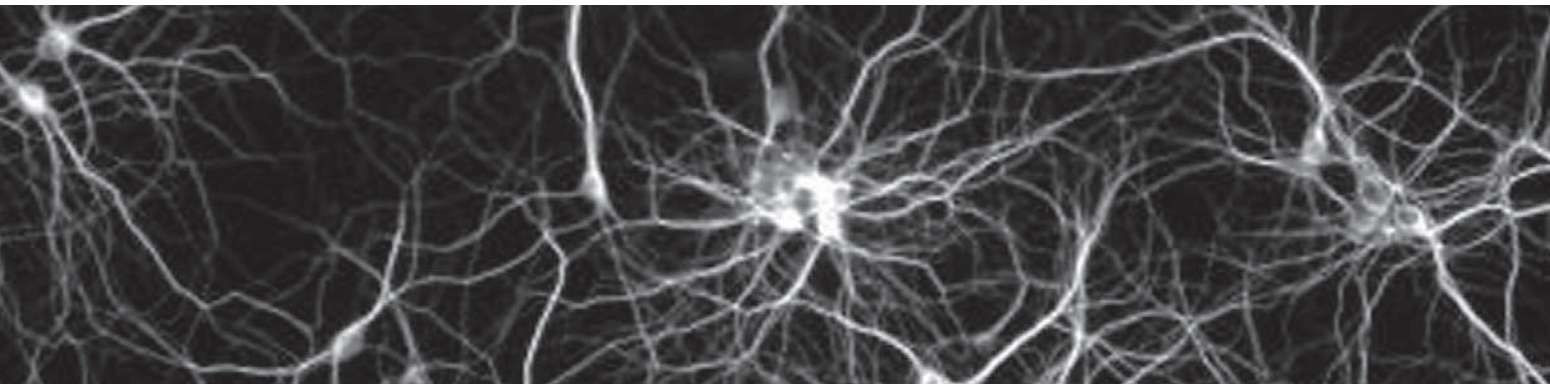

A rare neurological presentation of celiac disease

S. V. Shetab-Boushehri[1,2], R. Khodabandehlou[3]

ABSTRACT – **Background:** Celiac disease (CD) is an autoimmune disease of the small intestine due to sensitivity to gluten, a protein which is present in wheat, rye, and barley. The most common clinical findings in CD are gastrointestinal complications but neurological presentations are also seen in some patients. **Case report:** A case is described of a 40-year-old man who presented CD-related optic neuropathy, a very rare neurological manifestation of CD. He reported sudden right upper visual field blindness upon awakening in the morning without pain. He was treated with intravenous methylprednisolone for five days, followed by two-year azathioprine and methotrexate administration. His case is presented with magnetic resonance imaging, clinical history, and laboratory findings. **Conclusion:** It is reasonable that CD patients be evaluated for neurological symptoms even in the clinically stable long-term course. In addition, CD needs to be considered when making a differential diagnosis for patients presenting neurological symptoms of unknown primary cause.

Key words: celiac disease, optic neuropathy

INTRODUCTION

Celiac disease (CD) is an autoimmune disease of the small intestine due to sensitivity to gluten, a protein which is present in wheat, rye, and barley (1). The most common clinical findings in CD are gastrointestinal complications but neurological presentations are also seen in some patients (2,3). The most common gastrointestinal symptoms in symptomatic celiac patients are diarrhea, weight loss, abdominal distension, malaise, and anemia (1). Neurological manifestations in celiac patients can be seizures, dementia, or psychiatric illness but the most common manifestations are ataxia and peripheral neuropathy. Also, multifocal encephalopathy can be the neurological manifestation of CD (2). Because approximately half of adult-onset celiac patients lack prominent gastrointestinal symptoms, patients with

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neuropathy should be accurately examined regarding CD (2). The present case represents a rare neurological complication of CD.

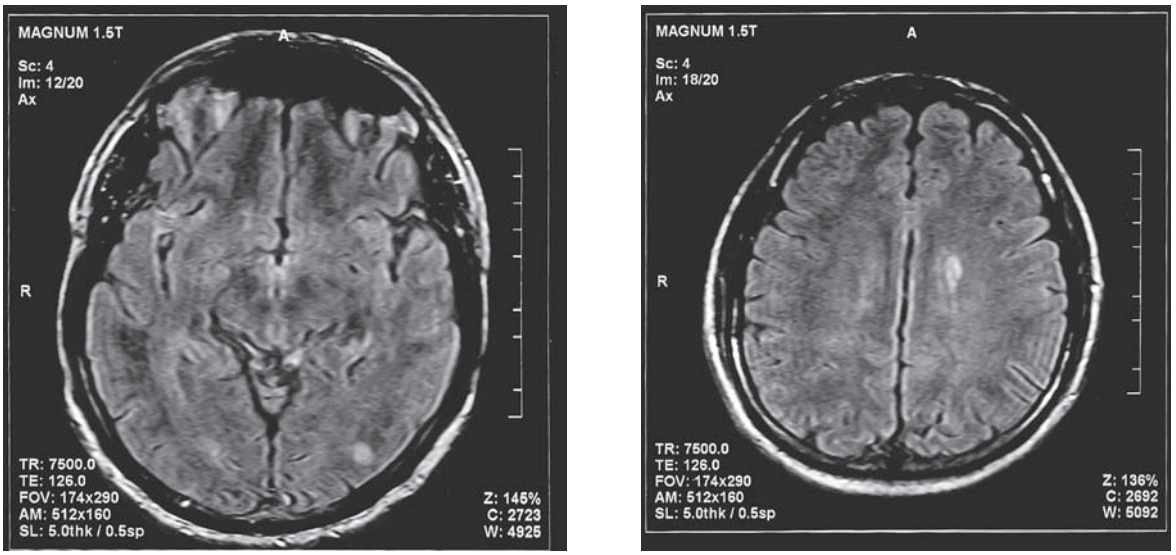
CASE REPORT

A 40-year-old male, a toxicologist, actually the first author, presented with chief complaint of right visual loss. He reported sudden loss of the upper half of the visual field on the right eye upon awakening in the morning without pain. He did not smoke cigarettes or drink alcohol, did not have high blood pressure, diabetes mellitus or hyperlipidemia. The patient had been diagnosed with CD three years before, and the disease was well controlled by simple dietary manipulation. At that time, he underwent an endoscopic (stomach and duodenum) examination by a gastroenterologist. A biopsy from the duodenum was obtained and sent for pathological examination. The results were consistent with the diagnosis of CD. His first symptoms of CD were hematochezia, intestinal cramping, refractory hiccups, anal fissure, malabsorption, heartburns and stomachache. He reported that he had stopped dietary restriction for about one year. After each meal containing wheat products, he experienced massive hematochezia accompanied with fever. His past medical history contained only properly treated brucellosis at the age 23. His two uncles had CD.

Except for Marcus Gunn's sign and loss of the upper half of the visual field on the right eye, which was detected by Goldmann visual field testing, his neurological status was normal, including funduscopy of optic discs and retinal angiography. Brain magnetic resonance imaging (MRI) showed two hyperintense lesions on T2WI and FLAIR images, one in the left periventricular region in the frontal part of lateral ventricle and another one in the left occipital juxtacortical region without enhancement.

Serologic examination revealed high titer of antigliadin Ab IgG (AGA) (39 U/mL, normal <12 U/mL) obtained by ELISA, high blood IgE (424 IU/mL, normal <100 IU/mL) and mild anemia with anisocytosis. Cerebrospinal fluid (CSF) oligoclonal bands were negative (Fig. 2), as well as serum immunologic tests (CRP, ANA, RF, ANCA, anti SSA Ab, anti SSB Ab, anti ds DNA, anti phospholipid Ab (lupus anticoagulant (LA) antibodies, cardiolipin IgG and IgM antibodies), anti-endomysial antibody (anti-EMA)). CSF protein (42 mg/dL, normal 15-45 mg/dL) and cells (WBC 2/μL, RBC 0/μL) were normal.

His CSF angiotensin-converting enzyme (6.0 IU/L) was a little above the normal value of <4.0 IU/L. Sarcoidosis was ruled out by chest computed tomography scan. We performed Goldmann visual field testing that showed loss of vision in the upper half of the visual field on the right eye. He was diagnosed as AGA induced neuropathy and treated with intravenous methylprednisolone 1 g daily for 5 days, with good recovery of his vision. Then, he was treated by azathioprine 3 mg/kg/day for 3 months but, due to diarrhea and stomachache, azathioprine was replaced by methotrexate 7.5 mg weekly for 15 months. After two-year follow up,



A B

Fig. 1. *Magnetic resonance images without contrast enhancement before treatment showing a juxtacortical plaque (A) and periventricular plaque (B).*

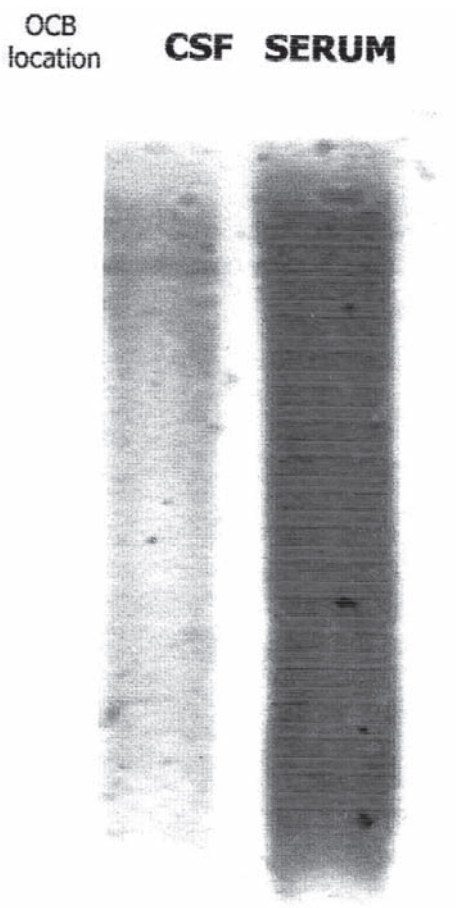


Fig. 2. *Cerebrospinal fluid oligoclonal bands.*

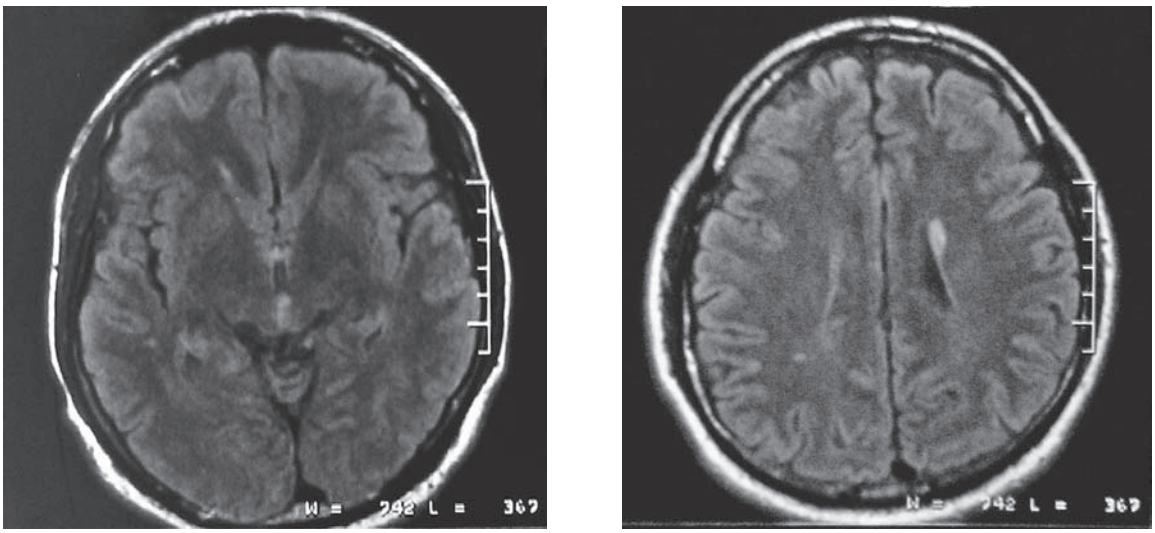
there were no new plaques or contrast enhancement on MRI images (Fig. 3).

Juxtacortical plaque disappeared completely and his AGA returned to the normal value. During two-year follow up, he had a gluten-free diet and experienced no hematochezia and his gastrointestinal symptoms relieved as well.

DISCUSSION

Celiac disease is a common condition that affects up to 1% of the population worldwide (2). It is an autoimmune disorder of the small intestine that occurs in genetically predisposed people of all ages, from middle infancy onward (1). Several case reports have highlighted the occurrence of various neurological disorders, including neuropathy, ataxia, dementia, chorea, and epilepsy, in patients with established CD but optic neuropathy mimicking first attack of multiple sclerosis is rare. The mechanism of neuronal damage is unclear and may be immune or related to trace vitamin deficiency, especially vitamin E and some elements like copper (1).

Atypical forms of CD, i.e. without prominent gastrointestinal symptoms and with frequent extra-intestinal manifestations, are being increasingly recognized, especially over the past decade, both in adult and pediatric patients (3). CD is around 10 times more frequent than multiple sclerosis. CD and multiple sclerosis are considered as T-cell-mediated autoimmune diseases. An immune-mediated pathogenesis, initiated by gluten, is considered in patients affected by neurologic disorders, with positive AGA and immune abnormalities of the central and peripheral nervous systems, especially if some have a favorable response to gluten-free diet with lower AGA titers (4).



A B

Fig. 3. *Magnetic resonance images without contrast enhancement after treatment: the juxtacortical plaque had healed (A); the periventricular plaque was still present (B).*

In the patient presented, MRI showed two plaques, which had some resemblance to multiple sclerosis plaques, but they were not ovoid lesions perpendicular to the ventricles (Dawson fingers) and did not completely fulfill the revised McDonald criteria (5) for dissemination in time even after 2-year follow up.

Although MS lesion plaques can be found throughout the brain, they have a predilection for periventricular white matter and juxtacortical region; they tend to have an ovoid configuration with the major axis perpendicular to the ventricular surface. At the initial stage, the lesions are typically thin and appear to be linear (Dawson fingers), which is probably associated with the inflammatory changes around the long axis of the medullary vein that create the dilated perivenular space (6).

In our patient, one of the plaques that was juxtacortical disappeared completely on T1W and T2W images after 2-year follow up, indicating remyelination without axonal loss, but the persistent periventricular one showed black hole on T1W images indicating axonal loss (both inflammatory and neurodegenerative nature of the plaques).

This case had some characteristics of optic neuritis (which is painful, subacute and central or cecocentral, or total visual field loss that improves completely or near completely) and some characteristics of ischemic optic neuropathy (which is sudden, painless, usually altitudinal field defect and not improving completely) (7). The patient was diagnosed with AGA induced demyelinating optic neuropathy. Gluten-free diet has been the most important treatment for CD, but it could be potentially useful for both CD and its neurological manifestations in our patient (8). The main difficulty for these patients is to follow a strict gluten-free diet for the rest of their lives.

The early detection of CD neurological manifestations caused by neuronal demyelination and their subsequent treatment with gluten-free diet and immunosuppressive drugs could be beneficial for patients who suffer from it.

CONCLUSION

Anti-gliadin antibodies may be directly or indirectly neurotoxic or a marker of neurotoxic autoimmune process. Neurological complications of CD presenting to gastroenterologists have been considered rare, but the findings of a high incidence of CD in patients with neurological disease of unknown cause emphasize that clinicians need to be vigilant for the atypical presentation and complications of CD (9). Therefore, it is reasonable that celiac patients should be evaluated for neurological symptoms even in the clinically stable long-term course. In addition, CD needs to be considered when making a differential diagnosis for patients presenting neurological symptoms of unknown primary cause, especially when revised McDonald criteria are not completely fulfilled and even in the absence of gastrointestinal symptoms (10).

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Rijetka neurološka prezentacija celijakije

SAŽETAK – **Uvod:** Celijakija je autoimuna bolest tankog crijeva koja nastaje kao posljedica osjetljivosti na gluten, protein koji je prisutan u pšenici, raži i ječmu. Celijakija se najčešće manifestira simptomima probavnog sustava, ali se u određenom postotku bolesnika mogu javiti i neurološki simptomi. **Prikaz slučaja:** U ovom prikazu opisuje se slučaj muškarca starog 40 godina koji se prezentirao vrlo rijetkom manifestacijom celijakije, optičkom neuropatijom. Prvi simptom bolesti je bio nagli ispad desne gornje polovice vidnog polja koji nije bio praćen bolovima. Liječen je intravenskim metilprednizolom tijekom 5 dana uz dobar klinički oporavak, a zatim azatioprinom i metotreksatom. U ovom radu prikazani su klinički simptomi, nalazi magnetske rezonancije te laboratorijski nalazi bolesnika. **Zaključak:** Iz prikazanog slučaja te podataka iz literature kod bolesnika s celijakijom bi trebalo aktivno tražiti neurološke simptome. Također na celijakiju treba misliti u diferencijalnoj dijagnostici bolesnika s neurološkim simptomima nepoznatog uzroka.

Ključne riječi: celijakija, optička neuropatija