JGH Open An open access journal of gastroenterology and hepatology
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JGHF Journal of Gastroenterology and Hepatology Foundation
doi:10.1002/jgh3.13117

CASE REPORT

Celiac disease with neurological manifestations mimicking stiff-person syndrome

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Key words
autoimmune disease, celiac disease, stiff person syndrome.

Accepted for publication 21 June 2024.

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Funding support: National Natural Science Foundation of China 62331025; Natural Science Foundation of Tibet Autonomous Region XZ2021ZR-ZY13(Z); National High-Level Hospital Clinical Research Funding 2022-PUMCH-B-124

Celiac disease (CD), a gluten-related disease, is a multi-system rare disorder mainly involving the gastrointestinal tract. The clinical signs of CD are exceedingly heterogeneous, which increases the difficulty of clinical differential diagnosis. Neurological manifestations are one of the non-classical CD symptoms. As some patients present only neurological symptoms at early stages, the diagnosis of CD is always delayed. Correct diagnosis and management could decrease patient morbidity and deaths. A 32-year-old male was admitted to the hospital due to progressive muscle atrophy of both lower limbs and lumbar stiffness. Based on positive gluten-sensitive enteropathy autoantibody profiles and gastroscopy foundation, the diagnosis of CD was established. The patient was instructed to gluten-free diet. The antibody titer of gluten-sensitive enteropathy autoantibodies decreased, and the patient's symptoms alleviated. We emphasize the importance of CD screening in patients with neurological disorders of unknown aetiology.

Introduction

Celiac disease (CD), known as a gluten-related disease, is a multi-system rare disorder that mainly involves the gastrointestinal tract.[1] The clinical signs of CD are exceedingly heterogeneous, which increases the difficulty of clinical differential diagnosis.[2] Neurological manifestations are one of the non-classical CD symptoms.[3] As some patients present only neurological symptoms at early stages, the diagnosis of CD is always delayed.[4] Correct diagnosis and management could decrease patient morbidity and deaths.[5] Here we report the case of a Chinese patient suspected with neurological manifestations mimicking the stiff-person syndrome (SPS).

Case report

A 32-year-old male was admitted to the hospital in 2022 with severe malnutrition, mild anemia, progressive muscle atrophy of both lower limbs, and lumbar stiffness. The patient began to develop right lumbar weakness in June 2021. He could slowly and independently go up about three floors, and walk on flat ground without restriction. He had gait changes and stiffness of the waist and limbs. In October 2021, the above symptoms progressed to bilateral waist weakness, difficulty in climbing up and down stairs, weakness and instability of both hips when going down the stairs, apparent slowness in walking speed and small stride length, feeling strained in both Achilles' tendons when walking, small dorsiflexion of both feet, gait like "duck walk", gradual atrophy of both lower limb muscles, and evident bilateral thighs. At the same time, there was stiffness in the waist and difficulty in bending; stiffness increased when the waist was strained and with emotional tension. At the end of 2021, there was dull pain at the root of both thighs, horizontal distension, and pain at both costal margins. He visited the emergency department of our hospital in February 2022 with a rash, gross hematuria, and diarrhea, and then was admitted to our hospital. Physical examination showed that the patient had a severely malnourished face, wasting body type, and systemic muscular atrophy. He walked with an abnormal, slow, stiff gait, and cautiously and carefully. The spine was physiologically curved without tenderness or deformity. Sensory and ataxic examinations were normal. Muscle tension of both lower limbs was not high, muscle

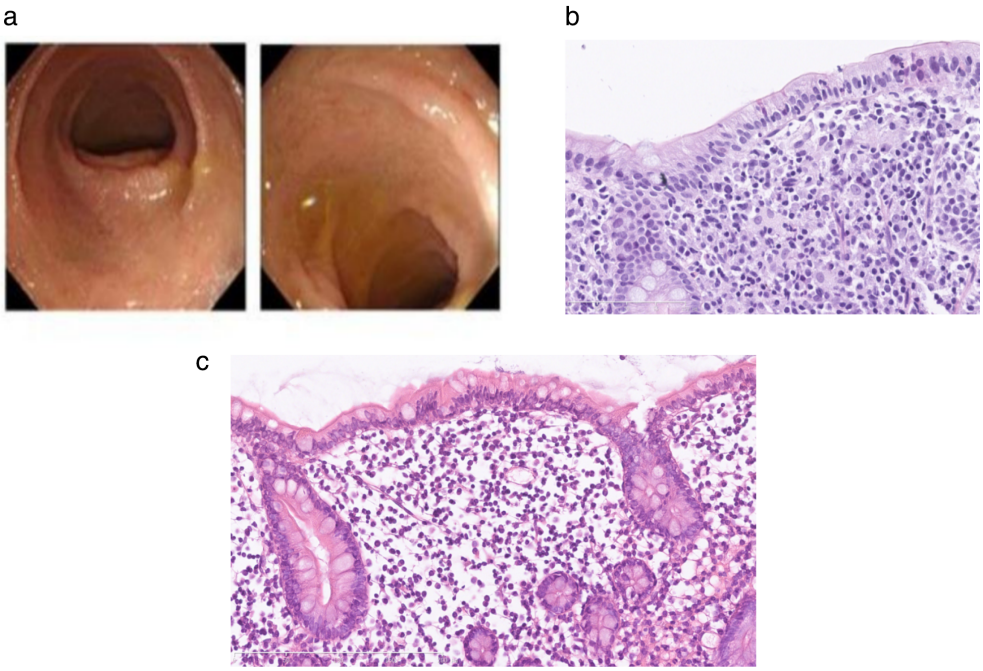

Figure 1 (a) Colonoscopy findings:The mucosa of the distal ileum was thinner and the villi of the small intestine was shortened. (b) Pathology of descending part of duodenum (HE stain ×400): Small intestinal mucosal villi were low and flat, there was more lymphocyte infiltration in the proper membrane, and focal intraepithelial lymphocytosis and goblet cells were present. (c) Pathology of the terminal ileum tissue (HE stain ×400): At the end of the ileum, the villi in the small intestine mucosa were thick and blunt, with more lymphocytes infiltrating the lamina propria, and plasma cells were visible. There was no significant increase in intraepithelial lymphocytes, and no granulomas or goblet cells were present.

strength of the lower limbs was grade 5, paresis test was not suitable, knee reflexes of lower limbs were hyperactive on the right side compared to the left side, right Achilles tendon reflexes were lower than on the left side, and bilateral pathological signs were negative. Abdominal muscle tension fluctuated and was sometimes stiff, especially in sitting and standing positions. The initial diagnosis of SPS was considered at admission, but electromyography and the negative results of glutamic acid decarboxylase (GAD) antibodies did not support it. Even after the treatment with intravenous immunoglobulin, clonazepam, baclofen, and celebrex, muscle stiffness and spasm did not improve. Since he had a family history of lumbar weakness and abnormal walking, hereditary myopathy was suspected, but whole exon sequencing did not detect pathogenic/suspected pathogenic variants associated with clinical phenotypes. Meanwhile, the patient also had a 20-year history of intermittent diarrhea, yellow-brown soft stool, or thin mushy stool 3–4 times/day, 200–400 mL each time. There was no mucous pus or blood in the stool, and it could be improved after 1–2 days of fasting and taking floxacin. He had experienced a weight loss of 20 kg in the past 6 months, and had a weight of 40 kg and a BMI of 13.2 kg/m^2 at admission. Laboratory tests showed normocytic normochromic anemia, normal VitB12 results, decreased absorption of xylose, positive staining for Sudan III in stool, and positive gluten-sensitive enteropathy autoantibody profiles: anti-tissue transglutaminase (tTG) IgG antibody 39 CU (<20 CU), deamidated gliadin peptide (DGP) IgG antibody 67 CU (<20 CU), and tTG IgA antibody 20 CU (<20 CU). The patient's genotype and serotype of HLA were reported as HLA-DQB1*02 and HLA DQ2. Short, flat villi and increased intraepithelial lymphocytes in the small intestine were observed with gastroscopy and colonoscopy with histopathologic examination (Fig. 1a–c). The symptoms did not improve significantly after VitB, VitAD, and VitK supplementation. After the patient was instructed to have a gluten-free diet (GFD) for 4 months, the antibody titer of gluten-sensitive enteropathy autoantibodies decreased: tTG IgG antibody 20 CU and DGP IgG antibody 25 CU. The patient's weight increased by 1 kg, and the yellow-brown soft stool kept eluting 1–3 times/day. The final diagnosis of suspected CD was made.

Discussion

SPS is a rare autoimmune disease typically manifesting as axial stiffness and episodic painful spasms. Other diagnosis criteria include electrophysiological indications suggesting simultaneous contraction of active and antagonistic muscles, and positive GAD antibodies present. Although this patient had lumbar stiffness, it did not meet the other diagnostic criteria. Atypical digestive symptoms and positive gluten-sensitive enteropathy autoantibody profile gave the clue to CD.

The diagnosis of CD relies on a combination of clinical, serological, and histopathological findings. A positive HLA DQ2 was helpful in suspecting CD. A very high concordance (99%) between anti-TG IgA and CD had been found, with sensitivity and specificity of 99%. The decrease in the level of antibodies after GFD treatment could clinically validate the gluten-related disease. Digestive symptoms, villi atrophy in endoscopic findings, and focal intraepithelial lymphocytosis in histopathology reports confirmed the diagnosis of CD.[6]

The global prevalence of CD is about 1%. About 6–10% of CD patients with neurologic manifestations have been reported in the literature, and more than 40% are in untreated CD.[7] Neurologic manifestations vary with CD patients in different reports, including neuromuscular disorders. SPS has been reported to overlap with CD; 95% of patients with SPS have evidence of gluten sensitivity or CD and have been reported to benefit from a strict GFD.[8] Notably, less than 10% of patients with gluten-related neurologic disorder have gastro-internal symptoms, yet over 40% have gastroscopic findings.[9] Delayed diagnosis for gluten-related neurologic disorder will cause irreversible loss of cerebellar cells. As a result, GFD treatment cannot effectively improve the disease status.

Although sporadic cases of CD are reported, the epidemiologic data for CD in China are currently scarce. The estimated gene and antibody-carrying rates are higher than expected in the Chinese population.[10] We report this case to highlight the need to increase clinical awareness of CD and to conduct screening tests in patients with unknown neurologic symptoms.

Acknowledgments

We would like to thank Dr.Tsoi Man Fung, Simon, for English language editing. The authors declare that they have no conflict of interest.

Informed consent statement

Written informed consent has been obtained from the patient to publish this report.

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