CASE REPORT

Case of coeliac disease presenting in the psychiatry ward

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SUMMARY

We describe a case of coeliac disease that was diagnosed in the psychiatry inpatient unit of a general hospital. The patient was admitted due to suicidal behaviours and developed an agitated catatonic state while in the inpatient psychiatry unit. An extensive diagnostic study allowed for the diagnosis of coeliac disease and while her state was unresponsive to antidepressants, anxiolytics, antipsychotics and electroconvulsive therapy, the patient improved significantly when a gluten-free diet was started. While it is well known that, occasionally, gluten sensitivity and coeliac disease can present as brain gluten sensitivity, such cases are typically characterised by motor and/or cognitive symptoms and by white matter abnormalities. Psychiatric presentations of these conditions have only rarely been reported.

(escitalopram 20 mg/day, pregabalin 150 mg/day and quetiapine 200 mg/day) and was discharged with the diagnoses of borderline personality disorder and factitious disorder. In the course of her third admission, the patient developed an agitated catatonic state, characterised by extreme psychomotor agitation, verbal stereotypies, bizarre behaviours (such as coprophagia) and total insomnia. This state of agitated catatonia did not respond or was aggravated by pregabalin (600 mg/day), olanzapine (20 mg/day), escitalopram (20 mg/day) and haloperidol (5–15 mg/day) and responded only partially to lorazepam (up to 30 mg/day) and to electroconvulsive treatment. On this occasion, due to the fluctuating course of the disease and the lack of response to treatment, a more extensive diagnostic investigation was performed.

BACKGROUND

Gluten sensitivity is a systemic autoimmune disease occurring in response to ingested gluten, with high titres of serum antigliadin and antitransglutaminase antibodies, all of which improve after removal of gluten from the diet. Gluten-sensitive enteropathy, or coeliac disease, is one aspect of gluten sensitivity. However, the skin and the central and peripheral nervous systems can also be affected by gluten sensitivity, independently of the presence of enteropathy. Manifestations of brain gluten sensitivity are very diverse. Clinical presentations are mostly motor or cognitive, and the occurrence of white matter abnormalities has also been described. Contrary to the skin and gut, lesions are generally inaccessible for histological confirmation, and diagnosis relies on serological tests and/or the possibility of concomitant enteropathy.¹

CASE PRESENTATION

A 47-year-old white woman, with a prior history of irritable bowel syndrome and iron deficiency anaemia, was admitted consecutively, on three occasions, to the acute inpatient psychiatry unit of Centro Hospitalar de Lisboa Ocidental (CHLO). Previously, she had been followed irregularly at the outpatient unit of a private psychiatric hospital, due to generalised anxiety disorder, and was treated, also irregularly, with benzodiazepines. Of her admissions to the acute inpatient psychiatry unit of CHLO, two were due to suicide attempts, and in another she presented with severe depression with transient psychotic symptoms (paranoid delusions). During the first two admissions, she responded poorly to psychotropic medication

INVESTIGATIONS

Physical, including full neurological, examination was unimpressive. Mild anaemia (haemoglobin: 11.5 g/dL; normal: 12–15 g/dL) with mild macrocytosis (mean cell volume: 97.1 fL; normal: 80–96.1 fL), low folate (3.2 nmol/L; normal: >6.25 nmol/L) and elevated sedimentation rate (48 mm/hour; normal <20 mm/hour) were found on routine blood testing. Vitamin B₁₂, serum iron and total iron-binding capacity were normal, but reticulocyte count (18×10^9 ; normal: $20\text{--}100 \times 10^9$), ferritin (9.8 ng/mL; normal: 12–137 ng/mL) and transferrin saturation (14%; normal: 20–55%) were low. In additional serial blood testing, low albumin (3.2 g/dL; normal: 3.5–5 g/dL) and low calcium (7.8 mg/dL; normal: 8.4–10.2 mg/dL) were also found. A head CT suggested abnormal cortico-subcortical differentiation, leading to brain MRI, which demonstrated unspecific focal white matter hyperintensities in the frontal and left parietal lobes (figure 1). EEG, while unspecific, was suggestive of encephalopathy. Investigation of cardiac and carotid causes for frontal and parietal brain lesions was negative. While analysis of cerebrospinal fluid was not suggestive of infection or inflammation, cerebral vasculitis was suspected due to high titres of antinuclear antibodies in the serum (1:320, granular pattern). Soluble antinuclear antibody subtypes (Ro, La, Sm, RNP, Scl70, Jo1, CENP-B), antineuronal antibodies (Hu, Ri, Yo, CV2/CRMP5, MA/Ta, amphiphysin) and other more specific autoantibodies (anti-dsDNA, antihistone, antinucleosome, antiribosomal P protein, MPO-ANCA, PR3-ANCA, anticardiolipin, anti- β_2 -glycoprotein), as well as lupus anticoagulant, were negative.

Approximately 1 month after the start of this last admission, despite supplementation for nutritional

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Figure 1 Brain MRI demonstrated unspecific focal white matter hyperintensities in the frontal and left parietal lobes (white arrow).

Figure 2 Abdominal and pelvic CT revealed target pattern images in the small intestine (white arrow).

deficiencies, the patient had lost ~10% of her weight at admission and developed diarrhoea. Faecal microbiology was negative, but a faecal occult blood test was positive. Abdominal and pelvic CT scan revealed target pattern images in the small intestine (figure 2), suggesting intussusception of the small intestine leading to further investigation of intestinal diseases. Antigliadin (IgG; 41U/mL) and antitransglutaminase (IgA; 35 U/mL) antibodies were positive, prompting upper gastrointestinal

Figure 3 In upper gastrointestinal endoscopy, complete villous atrophy was found in the second part of the duodenum.

Figure 4 Histology of duodenal biopsies (H&E staining, ×40) demonstrated complete villous atrophy and crypt hyperplasia, as well as marked intraepithelial lymphocytosis (*inset—H&E staining, ×400). H&E, haematoxylin and eosin stain.

endoscopy, which was suggestive of coeliac disease: the duodenal mucosa had a mosaic appearance in the bulb (not shown) and complete villous atrophy was found in the second part of the duodenum (figure 3). Histology of duodenal biopsies confirmed the diagnosis, with complete villous atrophy and crypt hyperplasia, as well as marked intraepithelial lymphocytosis (figure 4), suggesting stage 3c mucosal damage (Marsh-Oberhuber classification).

OUTCOME AND FOLLOW-UP

After 2 months of gluten-free diet, with significant improvement of psychiatric and gastrointestinal symptoms, all laboratory parameters had normalised, and the patient was discharged, treated only with clonazepam (1 mg/day) and zolpidem (10 mg/day). In the 4 years following discharge from the inpatient unit, the patient has remained under regular care of our outpatient community psychiatry team and similar to a significant proportion of coeliac disease patients, reports close to complete adherence to gluten-free diet.² Given the biopsy-confirmed diagnosis of coeliac disease, a gluten challenge has not been recommended.

The patient has remained stable, with no gastrointestinal symptoms, weight-loss or other signs of malnutrition. Laboratory findings on follow-up have also been unimpressive, with the exception of low folate, treated with folic acid supplementation. Similarly, the patient has not reported psychiatric symptomatology, with the exception of mild anxiety on clonazepam discontinuation, meriting introduction of a selective serotonin reuptake inhibitor. Currently, the patient is medicated with paroxetine (20 mg/day) and zolpidem (10 mg/day) and has achieved a full psychosocial recovery, maintaining a full-time job and living autonomously with her only child. In this respect, it is noteworthy that despite the exuberance of the presenting behavioural changes, the patient has remained well under only minimal pharmacological interventions, once the baseline disorder was diagnosed and treated.

DISCUSSION

Psychological and psychiatric symptoms in patients with known coeliac disease have been extensively described,^{3–5} and several mechanisms, including immunemediated central nervous system lesions and altered absorption processes in the gut, have been proposed to underlie this association.^{3–6–8} In fact, patients with coeliac disease or non-coeliac gluten sensitivity are more frequently positive for antinuclear antibodies and also have a higher risk for development of autoimmune diseases.⁹ Furthermore, among these patients, there are many cases of nutritional deficiency, commonly involving vitamin D, calcium, iron, folic acid and vitamin B₁₂,⁴ that could impact brain function, directly or indirectly. In the case described here, there is evidence that immune and nutritional mechanisms may have partially contributed to the clinical presentation. Sedimentation rate was elevated and positive antinuclear antibodies were found, but other more specific markers of autoimmunity were negative, and analysis of cerebrospinal fluid was not suggestive of inflammation. Furthermore, while vitamin B₁₂ levels were normal, folate, iron and calcium deficiencies were also found. However, supplementation for these deficiencies had no clinical effect, prior to diagnosis of coeliac disease and introduction of a gluten-free diet. Further research is thus fundamental to better clarify the nature of the pathophysiological mechanisms underlying gluten-induced neuropsychiatric syndromes, particularly considering the evidence that gastrointestinal inflammation and the gut-brain axis may contribute for the development of mental disorders.^{10–12}

While there is consensus regarding gluten-induced neurological presentations,^{1–8} psychiatric presentations of coeliac disease or gluten sensitivity are less consensual^{3–7–13} and only rarely reported.^{14–16} In this patient, it is unquestionable that the symptoms leading to an investigation of coeliac disease were psychiatric in nature, and the temporal association between gastrointestinal and psychiatric symptoms, as well as improvement of the latter on a gluten-free diet, are suggestive of causal associations between the two. In retrospect, while several elements were suggestive of coeliac disease, namely the prior history and evidence for malabsorption, awareness of the potential for such association would have certainly allowed

Learning points

- ▶ Psychiatric symptoms should be taken into account when considering the diagnoses of coeliac disease or coeliac sensitivity.
- ▶ Such diagnoses should be of particular concern whenever psychiatric symptoms are atypical, unresponsive to treatment and/or accompanied by white matter abnormalities.
- ▶ The possibility that gluten sensitivity, and even coeliac disease, can manifest as a psychiatric syndrome should be of more common knowledge among physicians specialised in psychiatric disorders, as well as those who most frequently diagnose the several forms of gluten sensitivity.

for a more timely diagnosis, sparing the patient unnecessary treatments.

Contributors AO-M, IA and BBC were responsible for clinical care delivered to the patient. AO-M wrote the case report that was critically reviewed and approved by all authors.

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REFERENCES

- 1 Hadjivassiliou M, Sanders DS, Grunewald RA, *et al.* Gluten sensitivity: from gut to brain. *Lancet Neurol* 2010;9:318–30.
- 2 Barratt SM, Leeds JS, Sanders DS. Quality of life in Coeliac Disease is determined by perceived degree of difficulty adhering to a gluten-free diet, not the level of dietary adherence ultimately achieved. *J Gastrointest Liver Dis* 2011;20:241–5.
- 3 Bressan P, Kramer P. Bread and other edible agents of mental disease. *Front Hum Neurosci* 2016;10:130.
- 4 Hallert C. Psychiatric illness, gluten, and celiac disease. *Biol Psychiatry* 1982;17:959–61.
- 5 Hallert C, Derefeldt T. Psychic disturbances in adult coeliac disease. I. Clinical observations. *Scand J Gastroenterol* 1982;17:17–19.
- 6 Abenavoli L, Delibasic M, Peta V, *et al.* Nutritional profile of adult patients with celiac disease. *Eur Rev Med Pharmacol Sci* 2015;19:4285–92.
- 7 Kalaydjian AE, Eaton W, Cascella N, *et al.* The gluten connection: the association between schizophrenia and celiac disease. *Acta Psychiatr Scand* 2006;113:82–90.
- 8 McKeon A, Lennon VA, Pittcock SJ, *et al.* The neurologic significance of celiac disease biomarkers. *Neurology* 2014;83:1789–96.
- 9 Carroccio A, D'Alcamo A, Cavataio F, *et al.* High proportions of people with nonceliac wheat sensitivity have autoimmune disease or antinuclear antibodies. *Gastroenterology* 2015;149:596–603.e1.
- 10 Cryan JF, Dinan TG. Mind-altering microorganisms: the impact of the gut microbiota on brain and behaviour. *Nat Rev Neurosci* 2012;13:701–12.
- 11 Severance EG, Alaedini A, Yang S, *et al.* Gastrointestinal inflammation and associated immune activation in schizophrenia. *Schizophr Res* 2012;138:48–53.
- 12 Wang Y, Kasper LH. The role of microbiome in central nervous system disorders. *Brain Behav Immun* 2014;38:1–12.
- 13 Ciacci C, Iavarone A, Mazzacca G, *et al.* Depressive symptoms in adult coeliac disease. *Scand J Gastroenterol* 1998;33:247–50.
- 14 Corvaglia L, Catamo R, Pepe G, *et al.* Depression in adult untreated celiac subjects: diagnosis by the pediatrician. *Am J Gastroenterol* 1999;94:839–43.
- 15 Lionetti E, Leonardi S, Franzonello C, *et al.* Gluten psychosis: confirmation of a new clinical entity. *Nutrients* 2015;7:5532–9.
- 16 Poloni N, Vender S, Bolla E, *et al.* Gluten encephalopathy with psychiatric onset: case report. *Clin Pract Epidemiol Ment Health* 2009;5:16.

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