PAMJ Clinical Medicine
Pan African Medical Journals

Case report

Autism and celiac disease: a case in Marrakech and review of the literature

Asma Helyaich[1,2,&], Karima El Fakiri[1,2], Aicha Bourrahouat[2,3], Imane Ait Sab[2,3], Nourreddine Rada[1,2], Ghizlane Draiss[1,2], Mohammed Bouskraoui[1,2]

[1]Pediatric A Department, Mother-Child Pole, Mohammed VI University Hospital, Marrakech, Morocco, [2]Team for Childhood, Health and Development, Marrakech School of Medicine, Cadi Ayyad University, Marrakech, Morocco, [3]Pediatric B Department, Mother-Child Pole, Mohammed VI University Hospital, Marrakech, Morocco

[&]Corresponding author: Asma Helyaich, Pediatric A Department, Mother-Child Pole, Mohammed VI University Hospital, Marrakech, Morocco

Received: 10 Oct 2019 - Accepted: 05 Dec 2019 - Published: 10 Dec 2019

Domain: Pediatric gastroenterology, Pediatric neurology

Keywords: Autism, autistic spectrum disorder, celiac disease, gluten sensitivity, malabsorption, nutrition

Abstract

Celiac disease is a gastrointestinal disorder affecting approximately 1% of the population. Autism spectrum disorder (ASD) describes a range of developmental disorders that affects communication and behavior with no known cause. Several epidemiological studies have explored a possible connection between celiac disease and ASD. Aims: to evaluate the association between celiac disease and ASD. The following case report reviews the history of a child with autism who after limited response to other interventions was placed on a gluten-free casein-free diet with marked improvement in autistic and medical symptoms. The screening for CD is recommended in all children with autism, even if no gastrointestinal symptoms are present.

Case report | Volume 1, Article 52, 10 Dec 2019 | 10.11604/pamj-cm.2019.1.52.20603

Available online at: https://www.clinical-medicine.panafrican-med-journal.com/content/article/1/52/full

Introduction

Celiac disease (CD) has long been associated with neurologic and psychiatric disorders, notably cerebellar ataxia, peripheral neuropathy, epilepsy, dementia, and depression. A wider spectrum of neurologic syndromes increasingly are recognized both as complications of prediagnosed CD and as initial manifestation of CD [1]. Diagnosis of autism is based on the presence of various behavioral symptoms. No single cause exists for the autistic spectrum of disorders. Because the cause of autism is unknown, many hypotheses have been suggested. One of the most popular interventions for ASD is the gluten-free casein free (GFCF) diet. In this article, we present the case of a child diagnosed with autism whose illness resolved after diagnosing underlying celiac disease and assorted nutritional deficiencies were addressed.

Patient and observation

We received a 3-year-old boy with autistic disorder on hospital of pediatric ward A at university hospital Mohammed VI of Marrakech. He has no family history of illness or autistic spectrum disorder. The history revealed that at 2 years of age. The child was diagnosed with a "severe communication disorder", with social interaction difficulties and sensory processing delay. A composite follow-up of all previous assessments and investigations was undertaken. Blood work was normal (thyroid-stimulating hormone (TSH), hemoglobin, mean corpuscular volume (MCV), and ferritin). Genetic testing was unremarkable (normal karyotype, negative for fragile X) and the magnetic resonance imaging (MRI) in search of a demyelinating attack of the white matter, electroencephalography (EEG), optometry assessment were also normal. At the conclusion of this composite assessment, the boy was given a primary diagnosis of autistic spectrum disorder. A plan was instituted including speech-language therapy, intensive individualized educational programming, and contact was encouraged with the Autism Society. For that purpose, the parents moved to morocco to be surrounded by family without any huge improvement. Upon a thorough questioning, the parents reported that their child presents unexplained fatigue, gastrointestinal symptoms included bloating, constipation and diarrhea. Psychiatric symptoms included a frequently depressed mood, disproportionate anger, and emotional lability.

On exploring his history, the child was born from Yemenite father and Moroccan mother in Germany at-term weighing 3500g with an Apgar score of 9 at 1 minute and 10 at 5 minutes after an uneventful pregnancy and delivery. No concerns were present in the neonatal period. Development in the first 24 months of life appeared fine according to the parents-his motor skills seemed to progress normally and he achieved expected milestones. After 2 years of age, his language skills slowly began to regress. He also demonstrated a change in temperament as he started to whine repeatedly and to scream without provocation. Physical examination revealed a height and weight normal for age. He was uncommunicative, restless, and somewhat agitated. General examination was unremarkable other than dark rings around the eyes. There were no dysmorphic features evident. He had difficulty maintaining eye contact, and he appeared disinterested in what was taking place. No abnormality was found on abdominal assessment. Anti-tissue transglutaminase antibodies levels were 76 U (normal < 10). The patient underwent upper endoscopy as duodenal biopsy to confirm a celiac disease diagnosis. It shows a total villous atrophy corresponding to a stage 4 of Marsh classification. Given the positive screen for celiac disease (positive anti-tissue transglutaminase antibodies and results of duodenal biopsy), dietary intervention was immediately commenced. All gluten was eliminated from the boy´s diet. Within 1 month, the boy´s gastrointestinal symptoms were relieved and his behavior had changed. The mother reported that her boy became

progressively more communicative. The child has continued on the gluten-free diet and has progressed well and remained healthy over the following 6 months.

Discussion

Autism is a common (1 in 1000) developmental disorder of early childhood characterized by impairment in social interaction and communication with absence of speech in about 50% of cases. Eighty four autistic children also display various behaviors that typically include stereotyped motor behaviors (hand flapping, body rocking), insistence on sameness, and resistance to change. The underlying cause of autism remains unclear; however, it is believed to be a genetic disorder based on studies showing high concordance in monozygotic twins [2]. Autism can be a manifestation of genetic disorders such as fragile X syndrome and tuberous sclerosis; however, the majority of cases are idiopathic. The available data suggest involvement of multiple interacting genes and environmental modifiers in the pathogenesis of autism [3]. Autism Spectrum Disorders (ASDs) have been linked with GI symptoms in several studies. One of the most popular interventions for ASD is the gluten-free casein free (GFCF) diet. The implication of gluten sensitivity in autism was based mostly on the leaky-gut hypothesis: that abnormal intestinal mucosa permits absorption of digestion products of dietary proteins such as gluten and casein [4]. This results in excessive intake of short peptides that provoke an immune reaction or act as exorphins that directly affect the nervous system. Excess peptides in autism from abnormal intestinal mucosa and/or a defective peptidase activity is also the basis for the opioid excess hypothesis [5]. Marcason *et al.* hypothesized that some symptoms may be caused in the ASD patients by opioid peptides formed from the incomplete breakdown of foods containing gluten and casein [6]. Increased intestinal permeability which occurs in children with ASD allows these peptides to cross the intestinal membrane, enter the blood, and cross the blood-brain barrier, affecting the endogenous opiate system and neurotransmission within the nervous system. The resulting excess of opioids is thought to lead to behaviours noted in ASD. Removal of these substances from the diet could determine a change in autistic behaviours. The hypothesis between the association of CD and autism could be genetic or related to autoimmunity, as evidence based on the existence of an association between HLA DQ2 and autism has been reported by some authors [7,8].

In the fact, only a small group of children affected by ASD may benefit from a GFCF diet indicating that autism may be part of the spectrum of NCGS, at least in some cases. In the other hand, despite its popularity, the efficacy of this diet in improving autistic behaviour remains not proven [9]. However, there is little evidence to support these hypotheses. Whether urinary peptides and activity of certain peptidases are altered in autism continues to be a controversial issue [10]. It also is controversial whether the intestinal mucosa in autism is abnormal. D´Eufemia *et al.* [11] reported abnormal intestinal permeability in 9 of 21 autistic children but none of 40 controls. Horvath *et al.* found a high prevalence of reflux esophagitis, gastritis, chronic duodenitis, low intestinal disaccharidase activity, and higher pancreatobiliary response to intravenous secretin, suggesting up-regulation of hepatic and pancreatic secretin receptors. The same group reported improvement of autistic symptoms for weeks after a single intravenous secretin injection; Asperger discussed a possible link between Asperger Syndrome and CD more than a half century ago. Subsequently, Goodwin and Goodwin hypothesized a possible association between autism and gluten in their case report of child with autism who demonstrated improvement following the initiation of a gluten free diet. Return to a normal diet resulted in an exacerbation of autistic symptoms [12]. There are studies which indicate that higher coincidence of celiac disease and autistic disorders is possible. Such conclusions were drawn by Barcia *et al.* who

showed that in a group of children with autistic disorders, celiac disease was more than 3-times more frequent than in the overall population (1:106 vs 1:30, p=0.014). After 6 months of a gluten-free diet they achieved some improvement as regards gastrological symptoms in patients who suffered from them, but no behavioral improvement was observed [13].

Based on a questionnaire, Valicenti-McDermott *et al*. observed that in a group of 100 children with autistic disorders, patients with speech regression more frequently had positive family history of celiac disease and non-specific inflammatory diseases of the intestine than children with no speech regression (24% vs 0%; p=0.001) [14]. A possible link between ASD and antibodies commonly found in CD has been reported. Individuals with serological markers for CD but normal mucosa were found to be three times more likely to develop autism in the future [15]. The authors of this study suggested these individuals might suffer from non-celiac gluten sensitivity (NCGS) rather than CD. Levels of anti-gliadin IgG and anti deamidated gliadin IgG have been reported to be elevated in individuals with ASD compared with controls [16,17]. Anti-gliadin IgG levels were significantly higher in children with ASD who also reported GI symptoms than in those without GI symptoms. The levels of antibodies to deamidated gliadin and tTG2 did not differ between individuals with CD and controls [17]. According to the recommendations of the American Academy of Pediatrics, every child with an autistic disorder and gastrointestinal symptoms should be tested for celiac disease with an assessment of the total concentration of tTG-IgA antibodies with or without anti-endomysial antibodies. If gluten-free diet is applied without diagnostic examinations, the patient should undergo a gluten challenge test. Genetical tests for haplotypes HLA-DQ2 and HLA-DQ8 can be useful in exclusion of celiac disease [18]. Although the profusion of studies reporting clinical and, especially, behavioral improvement with gluten-exclusion diets in patients with autism cannot be simply ignored, it is at present difficult to statistically demonstrate that there is an association between ASD and CD or between ASD and gluten sensitivity. The reported deleterious effects on brain function, the behavior of children with ASD, consequent to gluten intake, and the frequently reported clinical improvement with restriction diets, if present, are possibly due to other and not completely clarified mechanisms. In the case of gluten sensitivity, in the absence of reliable biomarkers, the diagnosis is still dependent on establishing an exclusion diet in patients who experience distress when eating gluten-containing products [19]. With the present data, we are forced to agree with the previous work by Pavone *et al*. [20], who concluded that concomitant occurrences of autism and CD in the same individuals are most likely due to pure coincidence.

Conclusion

The gastrointestinal tract has many abnormalities in patients with autism. Further research is necessary to clarify whether the digestive manifestations are a secondary consequence of the CNS dysfunctions or part of the same pathogenic process involving both organs. From a clinical point of view, we are able to treat most of the gastrointestinal symptoms of children with autism, and these treatments often have beneficial effects on their behavior. In fact, gastroenterologists evaluating these children should be aware of the fact that various gastrointestinal therapies are used in patients with autism, but without scientific evidence of their efficacy. Further studies, especially in the field of genetics, are needed in order to prove our hypothesis about the relation between genetic characteristics and the efficiency of GFCF diet in ASD patients.

Competing interests

The authors declare no competing interests.

Authors' contributions

All the authors have read and agreed to the final manuscript.

References

1. Khalafalla O bushara. Neurologic Presentation of Celiac disease. Gastroenterology. 2005 Apr;128(4 Suppl 1):S92-7. **PubMed** | **Google Scholar**

2. Bailey A, Le Couteur A, Gottesman I, Bolton P, Simonoff E, Yuzda E *et al*. Autism as a strongly genetic disorder: evidence from a British twin study. Psychol Med. 1995 Jan;25(1):63-77. **PubMed** | **Google Scholar**

3. Muhle R, Trentacoste SV, Rapin I. The genetics of autism. Pediatrics. 2004 May;113(5):e472-86. **PubMed** | **Google Scholar**

4. Dohan FC. Is celiac disease a clue to the pathogenesis of schizophrenia. Ment Hyg. 1969 Oct;53(4):525-9. **PubMed** | **Google Scholar**

5. Panksepp J. A neurochemical theory of autism. Trends Neurosci. 1979;2:174-177. **Google Scholar**

6. Marcason W. What is the current status of research concerning use of a gluten-free, casein-free diet for children diagnosed with autism. J Am Diet Assoc. 2009 Mar;109(3):572. **PubMed** | **Google Scholar**

7. Alessandria C, Caviglia GP, Campion D, Nalbone F, Sanna C, Musso A *et al*. HLA-DQ Genotyping, Duodenal Histology, and Response to Exclusion Diet in Autistic Children With Gastrointestinal Symptoms. J Pediatr Gastroenterol Nutr. 2019 Jul;69(1):39-44. **PubMed** | **Google Scholar**

8. Rahmoune H, Boutrid N. Autism and gluten: the proof by regression! Pediatr Neurol Briefs. 2018 Sep;14;32:9. **PubMed**| **Google Scholar**

9. Juneja M, Venkatakrishnan A, Kapoor S, Jain R. Autism Spectrum Disorders and Celiac Disease: Is there an Association. Indian Pediatr. 2018 Oct;15;55(10):912-914. **PubMed** | **Google Scholar**

10. Shattock P, Hooper M, Waring R. Opioid peptides and dipeptidyl peptidase in autism. Dev Med Child Neurol. 2004 May;46(5):357. **PubMed** | **Google Scholar**

11. D´Eufemia P, Celli M, Finocchiaro R, Pacifico L, Viozzi L, Zaccagnini M *et al*. Abnormal intestinal permeability in children with autism. Acta Paediatr. 1996 Sep;85(9):1076-9. **PubMed** | **Google Scholar**

12. Liester MB, Liester MG. A Review of Psychiatric Disorders Associated with Celiac Disease. Dual Diagn Open. 2018;(2)2:1. **Google Scholar**

13. Barcia G, Posar A, Santucci M, Parmeggiani A. Autism and coeliac disease. J Autism Dev Disord. 2008 Feb;38(2):407-8. Epub 2007 Nov 6. **PubMed** | **Google Scholar**

14. Valicenti-McDermott MD, McVicar K, Cohen HJ, Wershil BK, Shinnar S. Gastrointestinal symptoms in children with an autism spectrum disorders and language regression. Pediatr Neurol. 2008 Dec;39(6):392-8. **PubMed** | **Google Scholar**

15. Ricca V, Mannucci E, Calabro A, Bernardo MD, Cabras PL, Rotella CM. Anorexia nervosa and celiac disease: two case reports. Int J Eat Disord. 2000 Jan;27(1):119-22. **PubMed** | **Google Scholar**

16. Hsu CL, Lin CY, Chen CL, Wang CM, Wong MK. The effects of a gluten and casein-free diet in children with autism: a case report. Chang Gung Med J. 2009 Jul-Aug;32(4):459-65. **PubMed** | **Google Scholar**

17. Wright K, Smith MS, Mitchell J. Organic diseases mimicking atypical eating disorders. Clin Pediatr (Phila). 1990 Jun;29(6):325-8. **PubMed** | **Google Scholar**

18. Buie T, Fuchs GJ, Furuta GT, Kooros K, Levy J, Lewis JD *et al*. Recommendations for evaluation and treatment of common gastrointestinal problems in children with ASDs. Pediatrics. 2010 Jan;125 Suppl 1:S19-29. **PubMed** | **Google Scholar**

19. Sapone A, Lammers KM, Casolaro V, Cammarota M, Giuliano MT, De Rosa M *et al*. Divergence of gut permeability and mucosal immune gene expression in two gluten-associated conditions: celiac disease and gluten sensitivity. BMC Med. 2011;9:23. **PubMed** | **Google Scholar**

20. Pavone L, Fiumara A, Bottaro G, Mazzone D, Coleman M. Autism and celiac disease: failure to validade the hypothesis that a link might exist. Biol Psychiatry. 1997 Jul 1;42(1):72-5. **PubMed** | **Google Scholar**