

Case Report

Coeliac Disease and Cystic Fibrosis: Understanding the Intersection of Two Chronic Conditions — More Than a Coincidence?

S Shameem, H Musson & RJ Bright-Thomas

Shahna Shameem¹

Helen Musson¹

Rowland J. Bright-Thomas^{1,2}

¹ Manchester Adult Cystic Fibrosis Centre, Department of Respiratory Medicine, North West Lung Centre, Wythenshawe Hospital, Manchester University NHS Foundation Trust, Manchester, UK

² Division of Immunology, Immunity to Infection & Respiratory Medicine, University of Manchester, Manchester, UK

Correspondence

Shahna Shameem
Email: shahnashameem2011@gmail.com

Abstract

Objectives: Coeliac disease (CD) and cystic fibrosis (CF) are distinct medical conditions that can share clinical features including gastrointestinal disturbances, malabsorption, and nutritional deficiencies. CD is an autoimmune disorder triggered by gluten (prolamine storage proteins found in wheat, barley, and rye) while CF is a genetic disorder affecting the CFTR gene, leading to abnormal mucus production that affects multiple organ systems. Although not directly related, there is increasing evidence that people with CF may be at a higher risk for developing CD, posing unique diagnostic and therapeutic challenges.

Methods: We reviewed all CF patients attending Manchester Adult CF centre, later diagnosed with CD and explored their clinical manifestations, laboratory results, histology results with view to understand how these two disorders affect patients individually and when they coexist.

Results: The prevalence of CD in CF patients attending Manchester Adult CF Centre was 1.3:100 which is more than the general UK population (1:100). The average lag time for diagnosing CD in CF patients was 17.25 months. The most common symptom in these patients were unintentional weight loss and laboratory feature was low transferrin saturation levels. In all cases the patient's symptoms improved after introduction of gluten free diet.

Conclusion: Given the overlapping gastrointestinal manifestations and potential for atypical clinical presentations, a high index of clinical suspicion is warranted for the diagnosis of CD in patients with CF. The observed prevalence of CD within our CF cohort exceeds that of the general UK population, consistent with previously published data. Timely and accurate identification of CD in this population is clinically significant, as institution of a gluten-free diet can mitigate gastrointestinal morbidity, optimize nutritional status, and prevent long-term complications associated with untreated CD.

Keywords

Coeliac disease, cystic fibrosis, increased prevalence, coexistence

Introduction

CD and CF are chronic conditions that both impact gastrointestinal health—CD through an autoimmune response to gluten and CF through genetic dysfunction of the CFTR protein. Though once considered rare, the coexistence of these two conditions is now reported more frequently, with CD appearing more prevalent in CF patients than in the general population. Diagnosing both in the same patient is challenging due to overlapping symptoms. This case series examines their shared pathophysiology, clinical presentation, diagnostic challenges, and management strategies.

Materials and methods

We reviewed case records of all patients attending Manchester Adult Cystic Fibrosis Centre for confirmed diagnosis of CD. 4 Cases were identified, their demographics, clinical presentation, laboratory results, investigations for diagnosing CD (serology and Gastro Intestinal histology) were reviewed.

Results

Case 1

A 42-year-old male with CF, CF Related Diabetes (CFRD), pancreatic insufficiency (PI), hypertension (HTN), CF-related liver disease (CFLD), and chronic kidney disease (CKD) due to IgA nephropathy, presented with significant weight loss (14%) over 12 months. He underwent coeliac screening due to the rapid weight loss. He reported ongoing malabsorptive symptoms and bloating. There was no family history of CD. His coeliac screen showed elevated tissue transglutaminase IgA antibodies (TTG IgA >250 kU/L), with low transferrin saturation, normal vitamins and iron levels. Duodenal biopsy revealed mild to moderate villous atrophy (Marsh 3A), confirming the diagnosis of CD. The patient was started on a gluten-free diet, and his weight stabilized.

Case 2

A 35-year-old female with CF, CFRD, and PI presented with abdominal bloating and mild weight

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loss (1.2%) over a 4-month period. The patient had no known family history of CD. Coeliac screening revealed elevated TTG IgA antibodies (138 kU/L) with low transferrin saturation, normal vitamins and iron levels. Duodenal biopsy showed partial villous flattening and increase in intraepithelial lymphocytes (Marsh 3A), consistent with CD. She was started on a gluten-free diet, with gradual improvement in her symptoms.

Case 3

A 46-year-old female with CF, PI, and comorbidities of osteoarthritis and depression presented with chronic symptoms of abdominal bloating and abdominal pain. She was referred to gastroenterology due to ongoing GI symptoms and investigated for small intestinal bacterial overgrowth (SIBO) and CD. Coeliac screening showed elevated TTG IgA antibodies (>128 kU/L), and the glucose hydrogen breath test for SIBO was negative. Duodenal biopsy revealed moderate villous atrophy (Marsh 3B), confirming CD. The patient also had iron deficiency anaemia with low iron stores but normal vitamin levels. She had been receiving intermittent intravenous iron therapy prior to the CD diagnosis. Following a gluten-free diet, her symptoms improved significantly, and iron deficiency anaemia resolved.

Case 4

A 47-year-old female with CF, CFRD, PI, CFLD, and comorbidities of GERD, CF related arthropathy, and hypercholesterolemia, presented with iron deficiency anaemia requiring frequent intravenous iron infusions and weight loss with chronic GI symptoms of loose stools, abdominal bloating over two years. Blood investigations revealed iron deficiency anaemia and low iron stores, along with deficiencies in all vitamins. Coeliac screening revealed elevated TTG IgA antibodies (>250 kU/L), and duodenal biopsy confirmed florid intraepithelial lymphocytosis and subtotal villous atrophy (Marsh 3B) confirming diagnosis of CD. The patient was started on a gluten-free diet, leading to significant improvement in both her abdominal symptoms and resolution of iron deficiency anaemia.

Discussion

Recent meta-analytic data indicate that the pooled prevalence of CD in individuals with CF is more than twice that of the global prevalence observed in the general population.¹ Despite this, a significant proportion of CD cases in CF patients remain clinically unrecognized, due to overlapping symptoms that complicate the diagnostic process. Given the proposed mechanisms of immune

dysregulation in CF, which may contribute to the development of CD,² these findings highlight the need for heightened clinical vigilance and further investigation into the underlying pathophysiological links between the two conditions.

Pathophysiology of CD and CF

The pathophysiology of CD involves 3 major series of events: luminal and early mucosal events, activation of pathogenic CD4+ T cells, and subsequent tissue damage. During the luminal and early mucosal events, key features include the ingestion of “gluten” by a genetically susceptible individual. Gluten is not fully digested because of its high proline content, and this gives rise to several large undigested gluten peptides. The peptides gain access across the epithelial barrier to the lamina propria where they encounter tissue transglutaminase and antigen-presenting cells that express DQ2 or DQ8 that are ideally suited to bind those deamidated proline-rich peptides. In a further series of events this leads to activation of CD4+ T cells, and release mediators that ultimately lead to tissue damage.^{3,4,5} CF is caused by mutations in the CFTR gene, that is located on the long arm of chromosome 7 leading to a dysfunctional or absent CFTR protein.⁶ The pancreas in CF patients is one of the earliest and most affected organs. Abnormal ion transport across the pancreatic ductal epithelial cells causes obstruction of ducts with thick mucus causes epithelial injury and destruction accompanied by inflammation, fibrosis and fatty infiltration / replacement.^{7,8} This leads to exocrine pancreatic insufficiency which results in maldigestion and malabsorption, contributing to gastrointestinal symptoms.

Co-existence of CD and CF

Research in animal models revealed mechanisms through which gluten component of gliadin protein triggering epithelial stress in the intestine and then eliciting local inflammation and innate immune activation suggesting a proposed mechanism for CD. The in vitro- studies also revealed one component of gliadin protein(P31-43) can interact with an important functional domain of CFTR protein and can reduce chloride channel function of CFTR. This gliadin-mediated acquired downregulation of CFTR function is a possible mechanism for development of CD in CF patients.²

Clinical Features and Overlap

Both CD and CF share gastrointestinal symptoms, including diarrhea, bloating, weight loss. Malnutrition and failure to

Table 1. Baseline Demographics and Clinical Characteristics

Case	Gender	Age	CF Related Diabetes	Pancreatic Sufficiency	Osteoporosis	tTG IgA	GI Histology	Serum Iron	Transferrin Levels	Time To CD diagnosis since onset of symptoms
1	M	42	Y	N	Y	>250	Marsh 3A	Normal	Low	10 months
2	F	37	Y	N	N	138	Marsh 3A	Normal	Low	6 months
3	F	46	N	N	N	>128	Marsh 3B	Low	Low	25 months
4	F	47	Y	N	N	>250	Marsh 3B	Low	Low	28 months

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thrive are common in both conditions, though the underlying pathophysiological mechanisms differ. Nutritional deficiencies are common in both CD and CF, with deficiencies in fat-soluble vitamins (A, D, E, K) being particularly prominent in CF. Vitamin D deficiency is particularly notable in both diseases, in some cases CF patients with accelerated decline in bone density or presenting with CF related bone disease investigating for CD has resulted in new diagnosis of CD.⁹ In patients with CD, adherence to a gluten-free diet may lead to improvements in bone density, whereas undiagnosed CD can result in progressive bone loss and secondary osteoporosis. For this reason, the diagnosis of CD may have important implications on the management of patients with CF-related bone disease.¹⁰

In our case series, the GI symptoms were mainly weight loss and nutritional deficiencies, especially iron deficiency in most cases without anaemia led to suspicion of other malabsorptive cause and led to investigation of CD and diagnosed with coexistent CD and CF. Also, one patient had accelerated decline in bone mineral density even though their Vitamin D levels were within expected range and adequate calcium intake.

Diagnostic Approaches

CD is primarily diagnosed through a combination of clinical suspicion (symptoms, family history, risk factors, clinical features or associated autoimmune conditions), serological tests (anti-tissue transglutaminase antibodies, anti-endomysial antibodies), and biopsy of the small intestine.^{11,12,13} A definitive diagnosis requires the presence of villous atrophy on histological examination of duodenal biopsies, along with an improvement in symptoms on gluten free diet.

CF is diagnosed when an individual has both clinical presentation of the disease and evidence of CFTR dysfunction. The sweat chloride test remains the diagnostic gold standard for CF. A sweat chloride of ≥ 60 mmol/L is consistent with CF and < 30 mmol/L makes CF unlikely. A sweat chloride of 30–59 mmol/L should trigger further evaluation including *CFTR* gene mutation analysis. Additional measures of CFTR activity may be informative when there is clinical concern and diagnostic testing is inconclusive.^{14,15}

Co-management of CD and CF

In patients diagnosed with both CD and CF, treatment of CD through a gluten-free diet is crucial, but it must be carefully integrated with the management of CF. This allows for healing of the intestinal mucosa, alleviation of symptoms, and prevention of long-term complications such as nutritional deficiencies, osteopenia, osteoporosis, and malignancies (e.g., intestinal lymphoma).¹⁶ Enzyme replacement therapy must be initiated as soon as pancreatic insufficiency is diagnosed in CF.^{17,18} Vitamin supplementation (particularly vitamins A, D, E, and K) is essential in CF patients to correct deficiencies resulting from malabsorption. Also, other causes of GI symptoms like small intestinal bacterial overgrowth, gastric motility disorders, intussusception, constipation, gastro-esophageal reflux disease, and complications like distal intestinal obstruction

syndrome should be investigated and managed accordingly.¹⁹ Collaboration between gastroenterologists, respiratory specialists, and dietitians is vital to ensure optimal care.

Further considerations

Recently, the care of patients with CF has been revolutionized with new therapeutic agents that modulate function of CFTR. These agents have been shown to improve lung function and weight gain but their effect on the GI tract, especially as it relates to intestinal inflammation, is less well known. Preliminary in vitro human intestinal epithelial cell and in vivo mouse model data have demonstrated that ivacaftor prevented gliadin-induced pathology, which may suggest a potential therapeutic role in CD.² One case report suggested continued diligence in evaluation for additional GI pathology in patients with CF on CFTR modulator therapy with incomplete resolution of GI symptoms.²⁰ They also highlight the need for further research into CFTR modulators' effects on other GI outcomes including absorption and inflammation. Also, further research is needed focusing on the increasing incidence of CD in individuals with CF could reflect ageing in the CF population, as the median age of CD diagnosis in the general population falls within the 40s to 60s.

Conclusion

The coexistence of CD and CF is increasingly reported, with the pooled prevalence of CD in CF more than twice as high compared to the global prevalence. This presents unique diagnostic challenges. Clinicians must be aware of the potential overlap in gastrointestinal symptoms and the difficulty in distinguishing between the two conditions. If a CF patient has appropriate symptoms and does not respond to conventional CF therapy screening for CD should be considered. Early recognition and appropriate treatment are crucial to prevent long-term complications. The multidisciplinary approach to manage both conditions is essential to provide patients with optimal care, focusing on both symptom relief and nutritional support. Further research into the pathophysiological mechanisms underlying the overlap between these two disorders may improve our understanding of their co-occurrence and lead to more effective strategies for screening, diagnosis and treatment.

Biography

Dr. Shahna Shameem is a dedicated physician specializing in respiratory medicine. She holds an MBBS, DNB (Respiratory Medicine), and MRCP (UK), and has international experience across the UK, UAE, and India. She has broad knowledge in the management of complex respiratory conditions, including cystic fibrosis, long-term ventilation and sleep with excellent communication skills and commitment to multidisciplinary teamwork.

Conflicts of interest

none

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