Celiac crisis in an adult on immunosuppressive therapy

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BRIEF COMMUNICATION

‘Celiac crisis’ is a rare presentation of celiac disease with manifestations that include severe diarrhea, and severe metabolic and electrolyte abnormalities. It is most frequently seen in children younger than two years of age and has been rarely described in adults. A case of a 50-year-old woman who presented with diarrhea, severe dehydration, hypokalemia and metabolic acidosis is described. Based on positive serology and small bowel biopsy, she was diagnosed with celiac disease. The patient also had histological evidence of lymphocytic colitis. Microscopic colitis has not previously been described in association with celiac crisis, but it may have contributed to the presentation of celiac crisis in the current case. The patient was on corticosteroids and azathioprine for autoimmune hepatitis at the time of her presentation. The current case demonstrates that moderate immunosuppression does not prevent a celiac crisis, although previous reports have shown that patients may respond rapidly to high-dose corticosteroids.

Key Words: Acidosis; Celiac crisis; Celiac disease

With the advent of serological testing for celiac disease, it has become evident that the presentation of celiac disease can vary. The spectrum of presentation includes asymptomatic individuals with a family history of iron deficiency, individuals with symptoms of mild bloating and diarrhea, and patients with significant weight loss and malabsorption (1). One rare presentation of celiac disease is the so-called ‘celiac crisis’ (2). This syndrome includes the rapid onset of life-threatening acidosis, hypokalemia and dehydralation in association with severe diarrhea, and has been more frequently described in pediatric patients younger than two years of age (3,4). The present study describes a case of a 50-year-old woman on immunosuppressive therapy for autoimmune hepatitis who presented with ‘celiac crisis’. The patient also had evidence of associated microscopic colitis on colonoscopy. The occurrence of celiac crisis in adults, and the effects that immunosuppressive therapy and the coexistence of microscopic colitis may have had on the patient are reviewed.

CASE PRESENTATION

A 50-year-old woman presented to the hospital with ascites. Her computed tomography scan results were suggestive of cirrhosis. Based on a workup that included a positive smooth muscle antibody result, increased immunoglobulin (Ig) G level (22 g/L; normal level between 6.43 g/L and 13.92 g/L) and a liver biopsy that demonstrated chronic active hepatitis, she was diagnosed with autoimmune chronic hepatitis. She was started on prednisone 30 mg/day and azathioprine 100 mg/day. Over the next two months, her liver enzymes began to gradually improve. She was continued on the above immunosuppressive regimen because of the gradual enzyme improvement.

Her medical history was significant for hypothyroidism, and she was put on thyroid replacement therapy. There was no significant family history of gastrointestinal disorders. She was taking spironolactone 200 mg/day, which controlled her ascites. She reported no recent travel history.

She had a one- to two-year history of passing four to five loose stools per day. However, in the two weeks before hospital admission, she had developed severe watery diarrhea with more than 10 bowel movements per day and nocturnal bowel movements. She did not have significant abdominal pain and had noted no blood in her stools. She was admitted to the hospital with increasing weakness, and her blood test showed the following: sodium 127 mmol/L; potassium 2.6 mmol/L; chloride 101 mmol/L; total CO₂ 12 mmol/L; urea 17.4 mmol/L and creatinine 187 μmol/L. She was initially treated with intravenous (IV) normal saline and bicarbonate. Her weight at the time of admission was 85.7 kg and after rehydration, her weight improved to 89.1 kg. Her dehydration was corrected by normalization of her urea and creatinine levels. Her diarrhea

La crise cœliaque est une présentation rare de maladie cœliaque dont les manifestations incluent la diarrhée abondante et de graves anomalies métaboliques et électrolytiques. On l’observe surtout chez des enfants de moins de deux ans. Elle est rarement décrite chez les adultes. Est présenté le cas d’une femme de 50 ans qui a consulté à cause d’une diarrhée, d’une déshydratation marquée, d’une hypokaliémie et d’une acidose métabolique. D’après une sérologie positive et une biopsie de l’intestin grêle, on a diagnostiqué une maladie cœliaque. La femme présentait également des manifestations histologiques de colite lymphocytaire. On n’a jamais décrit de colite microscopique en association avec la crise cœliaque, mais dans le présent cas, elle peut avoir contribué à la présentation de la crise cœliaque. Le patient prenait des corticoides et de l’aza-thioprine pour soigner une hépatite auto-immune au moment de la consultation. Le présent cas démontre qu’une modeste immunosuppression ne prévient pas une crise cœliaque, même si des articles précédents ont démontré que les patients peuvent répondre rapidement à de fortes doses de corticoïdes.

Une crise cœliaque chez un adulte prenant des immunosupresseurs

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Microscopic colitis has been associated with celiac disease. The association between microscopic colitis and celiac disease has been described (8); microscopic colitis may be one of the causes of failure to respond to a gluten-free diet (9,10). None of the other reported cases of celiac crisis in adults looked for microscopic colitis. Microscopic colitis by itself does not result in metabolic acidosis, and has not been reported to cause severe dehydration and hypokalemia in association with celiac disease. We hypothesize that it may be one factor that contributes to the development of this rare presentation. Microscopic colitis has been associated with defective active and passive absorption of sodium and chloride, and reduced chloride-bicarbonate exchange (11), although the latter seems to be more associated with collagenous colitis.

Finally, the present report is the first to describe an adult patient with celiac crisis who was receiving immunosuppressive therapy at the time of presentation. Immunosuppressive therapy may be used to treat patients with refractory celiac disease (RCD), a rare condition of nonresponse to a strict gluten-free diet (12). Initial reports described the response of celiac disease to corticosteroids (13) and, because of frequent relapse once corticosteroids are stopped, subsequent small series have reported the maintenance of remission with azathioprine (14,15). More recent case reports and small series have reported the response of RCD to cyclosporine and budesonide. In a series of 13 patients with RCD, eight responded clinically and histologically to oral cyclosporine (16). Budesonide has also been effective, with 76% of 29 patients responding clinically in one series (with no histological response) (17) and seven of nine patients responding in another series (18). Patients with RCD type 1 (normal intraepithelial lymphocytes) appear to respond better to immunosuppressive therapy than those with RCD type 2 (phenotypically immature intraepithelial lymphocytes) (14). Cytokine modulators have also been used to treat RCD. Several case reports (19-21) have shown the clinical and histological benefits of antitumour necrosis factor-alpha therapy. Interleukin-10 has an inhibitory effect on T lymphocytes, but a nonrandomized open-label study (22) in 10 patients with RCD showed little benefit associated with this therapy.

Immunosuppressive therapy decreases the inflammatory response in celiac disease (13), and we hypothesize that the
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likelihood of someone developing a ‘celiac crisis’ would be less in patients on immunosuppressive therapy. Although immunosuppressive therapy may be used to treat RCD, symptomatic celiac disease may develop in patients on immunosuppressive therapy (23). The present case demonstrates that immunosuppressive therapy is not sufficient to prevent the presentation of a celiac crisis. Immunosuppressive therapy was effective in treating a celiac crisis in four pediatric patients (24,25). The doses used were prednisone 1.5 mg/kg/day, IV hydrocortisone 10 mg/kg/day and IV hydrocortisone 20 mg/kg/day. The doses used in these reports are substantially higher than what our patient was receiving. Lloyd-Still et al (24) reported a dramatic response to high-dose corticosteroids, with significant improvement 24 h after infusion of corticosteroids. Our patient responded gradually to a gluten-free diet (over approximately three weeks) and this gradual response may have been partly due to the fact that the corticosteroid dose was not increased.

CONCLUSIONS
Celiac crisis is an uncommon presentation in adults. This diagnosis should be considered when patients present with unexplained severe diarrhea, metabolic acidosis, hypokalemia and dehydration. Microscopic colitis may be one of the factors that contribute to the development of this condition. Although modest immunosuppression does not prevent a celiac crisis, previous reports have shown that patients may respond to high-dose corticosteroids.

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