Postpartum onset of adult celiac disease in identical twin sisters

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Different risk factors for the onset of celiac disease have been enumerated, with the single most important factor being a known familial history of biopsy-defined disease (1). However, estimated rates of familial celiac disease have been difficult to determine due to the important phenomenon of clinical discordance, even in genetically identical twin pairs (2). In addition, nongenetic factors have been suspected to play a role in the clinical onset of adult celiac disease, including pregnancy and the puerperium (3,4).

CASE PRESENTATIONS

In 2008, a 28-year-old woman was first evaluated for diarrhea 10 times daily and weight loss of 3 kg. Diarrhea began four weeks after delivery of her first child, a healthy female. Fecal studies revealed *Clostridium difficile*, but diarrhea persisted despite a course of metronidazole. Colonoscopy was normal, including the terminal ileum. Subsequent fecal studies for bacteria and parasites were negative, including *C difficile*, but her tissue transglutaminase antibodies (TTG) were markedly elevated (>200 U/mL [normal up to 20 U/mL]). Small bowel biopsy showed changes representative of celiac disease (Figure 1), and initiation of a gluten-free diet led to resolution of her diarrhea along with normalization of her weight and TTG levels.

In 2009, her identical twin, a 29-year-old woman also presented with postpartum diarrhea, three times daily and weight loss beginning within 10 weeks of delivery of her first child, also a healthy female. Fecal studies for bacteria and parasites were negative, but her TTG

level was also markedly elevated (>200 U/mL). A small bowel biopsy showed features of celiac disease (Figure 2). Diarrhea and weight loss resolved on a gluten-free diet and TTG levels also normalized. There was no other familial history of celiac disease in either parent of the identical twin sisters. Human leukocyte antigen (HLA) testing for both identical twin sisters revealed HLA DQ2 and DQA1 (05), while HLA DQ8 was absent.

DISCUSSION

The present report is the first of postpartum celiac disease in identical twin sisters. It has been previously hypothesized that either hormonal changes associated with pregnancy or the puerperium play a critical role in precipitating postpartum disease or, alternatively, an immunological reaction during pregnancy to fetal antigens occurs (3,4). Although the risk for eventual development of familial celiac disease in both infants is likely to be significant (1), previous reports suggest that the long-term outcome for both affected adult mothers will be positive, assuming that a strict gluten-free diet is maintained (3,4). In addition, celiac disease, if treated, will not pose a risk to future pregnancies. Most importantly, the time of onset of celiac disease in both of these identical twins provides additional strong evidence that pregnancy or the puerperium per se may be a special time of risk for the initial clinical appearance of adult celiac disease.

The present report also serves to emphasize the phenomenon of clinical discordance in the evaluation of twins, particularly identical

Figure 1) Endoscopic small bowel biopsy from first identical twin sister at 28 years of age showing features of adult celiac disease including crypt hyperplasia, chronic inflammation and loss of villi (hematoxylin and eosin stain, original magnification $\times 100$)

Figure 2) Endoscopic small bowel biopsy from second identical twin sister at 29 years of age showing features of adult celiac disease including crypt hyperplasia, chronic inflammation and loss of villi (hematoxylin and eosin stain, original magnification $\times 100$)

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monozygotic twin pairs. Although shown later to be HLA-identical, the discordance time was approximately one year before clinical changes became apparent in the second twin. This is consistent with an Italian twin study showing that in most concordant twin pairs, the discordance time was less than two years (5), with monozygotic and dizygotic twins having a 70% and 9% cumulative probability, respectively, for celiac disease within five years. Development of adult celiac disease in an identical twin should prompt screening studies for the disease in the clinically discordant identical twin.

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