Biopsy-defined adult celiac disease in Asian-Canadians

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Celiac disease is thought to be a genetically based disorder reported mainly from European countries as well as countries to which Europeans have emigrated, including North America. This report documents a clinical experience of biopsy-defined celiac disease in 14 Asians diagnosed since 1988 in a single Canadian teaching hospital. Eleven were Indo-Canadians, including 10 of Punjabi descent. Other ethnic groups were also represented, including two Japanese and one Chinese patient. Abdominal pain was the most frequent presenting symptom. Anemia, particularly associated with a deficiency of iron was common, along with diarrhea and weight loss. Endoscopic studies documented lymphocytic gastric and colonic mucosal changes in over one-third of the cases while antibodies for tissue transglutaminase were positive in all patients tested. Dermatitis herpetiformis, diabetes mellitus and autoimmune liver disease were also documented. These findings indicate for the first time that adult celiac disease occurs in Asian populations living in North America, particularly in those of Punjabi descent.

Key Words: *Celiac disease; Environmental factors in celiac disease; Genetics; Gluten-free diet; Small bowel biopsy; Tissue transglutaminase assay*

Confirmation par biopsie de la maladie cæliaque de l'adulte chez les Canadiens d'origine asiatique

On croit que la maladie cæliaque aurait une forte composante génétique et qu'elle affecterait principalement les populations d'Europe et les terres d'accueil d'émigrants d'origine européenne, y compris l'Amérique du Nord. Le présent article relate une expérience clinique menée sur la maladie cæliaque diagnostiquée au moyen de la biopsie chez 14 sujets asiatiques depuis 1988 dans un seul centre hospitalier universitaire canadien. Onze de ces patients étaient des Indo-Canadiens, dont 10 du Pendjab. D'autres groupes ethniques étaient également représentés parmi ces patients qui comptaient deux Japonais et un Chinois. Dans la plupart des cas, c'est la douleur abdominale qui avait amené les patients à consulter. L'anémie, surtout associée à une carence en fer, était également fréquente, ainsi que la diarrhée et la perte de poids. L'endoscopie a confirmé la présence d'anomalies lymphocytaires de la muqueuse de l'estomac et du côlon chez plus du tiers des sujets, tandis que tous présentaient des résultats positifs aux test de dépistage des anticorps dirigés contre la transglutaminase tissulaire. On a aussi noté des cas de dermatite herpétiforme, de diabète sucré et de maladie hépatique auto-immune. Ces observations permettent pour la première fois de conclure que la maladie cæliaque de l'adulte affecte les populations nord-américaines d'origine asiatique, et plus particulièrement les Punjabi.

Celiac disease is a genetically based disorder diagnosed mainly in Europe and in those countries to which Europeans have emigrated, including North America. Interestingly, the disorder is also relatively common in northern India, where there is a long history of wheat cultivation before 1000 BC (1) and a high frequency of specific human leukocyte antigen (HLA) marker molecules that have been associated with celiac disease (2-4). Moreover, some early studies documented celiac disease in wheat-eating areas of Bengal and Punjab, compared with the predominantly rice-eating areas of southern India (5,6), as well as in Indian and Pakistani immigrant children in England (7,8). Indeed, in the South Asian population of Leicestershire, particularly in Punjabis, the incidence of celiac disease was reported to be even higher than in Europeans (9). Others have also recorded celiac disease in Cantonese children (10) and, more recently, Japanese children (11). In addition, there are rare reports of celiac disease in natives from North and South America, thought to be descendents from Asians (12,13).

Previous studies from Vancouver have detailed clinical, pathological and serological features of different forms of inflammatory bowel diseases, including both ulcerative colitis and Crohn's disease, in both Chinese and Indo-Canadians (14-18). To date, however, there are no published studies on adult celiac disease in either Asian immigrants or individuals of Asian descent in North America. This report documents a clinical experience of biopsy-defined adult celiac disease in Asians diagnosed during the past two decades at a single teaching hospital in Vancouver, British Columbia. These findings indicate that adult celiac disease can occur in different Asian-Canadian populations, particularly in Indo-Canadians that have descended from the Punjab region of Northern India.

PATIENTS AND METHODS

During a 21-year period from January 1982 to December 2002 inclusive, 214 patients with adult celiac disease were seen by the investigator; of these, 14 were of Asian descent and all of these were diagnosed at the University of British Columbia Hospital, Vancouver, British Columbia. Complete office and hospital records were reviewed for details of clinical presentation and laboratory studies (hemogram, liver chemistry tests, immunoglobulins, carotene, iron and iron binding capacity, ferritin, folic acid, vitamin B_{12}, calcium, magnesium, glucose, proteins, including albumin, and thyroid function studies). Fecal specimens for bacterial

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and parasitic studies were negative. After small intestinal biopsies were done, all patients were seen by a clinical dietitian to provide specific instructions on the gluten-free diet. Patients were periodically evaluated, as required, to address concerns regarding diet treatment. Compliance and response to a prescribed gluten-free diet were repeatedly assessed. For some patients, another family member or interpreter was also instructed on the gluten-free diet. None of the Asian patients reported here had a familial history of celiac disease.

The diagnosis of celiac disease for each patient was based on small intestinal biopsies, done before and after the institution of a gluten-free diet (19). Severely abnormal 'flat' small intestinal biopsies (so-called 'crypt hyperplastic villous atrophy') were reported before the institution of a gluten-free diet (19). Dietary treatment was started within two weeks. In all patients, a second small intestinal biopsy was done at least three months after the initiation of the gluten-free diet to demonstrate normalization of the abnormal structural changes (19). In some patients, additional small intestinal biopsies were required to ensure persisting histological improvement. Endoscopic studies of the stomach and colon were also done and biopsies were obtained from both the gastric and the colonic mucosa to exclude other previously reported microscopic inflammatory diseases seen in celiac disease (ie, lymphocytic and/or collagenous gastritis and/or lymphocytic and/or collagenous colitis) (20-23). In addition, results of special stains for *Helicobacter pylori*, done in each patient, were recorded. After serum assays for tissue transglutaminase antibodies were developed for research purposes in the University of British Columbia Hospital laboratory (24), separate clinical assays were developed in the hospital. For the patients in the present study, all four that were tested had positive tissue transglutaminase antibody results using this clinical assay, but only after initial biopsy results were known, and before the institution of a gluten-free diet.

RESULTS

In the present series, there were 14 patients of Asian descent with biopsy-defined celiac disease. Of these, two were Japanese-Canadians, one was Chinese-Canadian and 11 were Indo-Canadians. Most (eight or 57.1%) had emigrated from Asia, but five (35.7%) were born in Canada, including one Japanese-Canadian female (Richmond, British Columbia in 1931) and four Indo-Canadians (two males, two females), all with parents born in Northern India (Punjab region). Finally, one Indo-Canadian male, born in Malawi, emigrated to Canada in 1975; both of his parents were also born in Northern India (Punjab). Table 1 shows epidemiological data for the 14 patients, diagnosed from 1988 to 2002. There were seven male patients and seven females, with 13 diagnosed in the past decade. Of the 11 Indo-Canadians, 10 were either born or direct descendents from parents born in the Punjab region; only one Indo-Canadian female, recently diagnosed, was born east of Bombay. For this Indo-Canadian group, all had resided in Canada for prolonged periods of time, ranging from 17 to 32 years before a diagnosis of celiac disease was established (mean of 24 years). Interestingly, the oldest patient in this study, a Chinese-Canadian woman, was born in Northern China. She came to Vancouver in 1973. Historically, her diet was primarily wheat-based, rather than rice-based, even in Northern China.

Table 2 details clinical features of the 14 patients of Asian descent with biopsy-defined celiac disease. There were seven females and seven males. For this group of Asians with celiac disease, three of 14 (or 21.4%) were over the age of 60 years at the time of their initial diagnosis and all of these patients were women. This is consistent with the increasing recognition of celiac disease in the elderly reported elsewhere from this hospital (25). Before 1993, only one patient was diagnosed with celiac disease. During the next decade, diagnoses of celiac disease were made sporadically with no more than three new patients detected in any specific calendar year. Although not used as a clinical screening tool in these patients, it is of interest that sera obtained for tissue transglutaminase (from the year 2000 when the assay was first established in this hospital clinical laboratory) in all four patients with a biopsy-defined diagnosis were positive. To date, no patient with Immunoglobulin A deficiency has been detected in this Asian group.

TABLE 1
Epidemiological data on Asians with biopsy-defined celiac disease

Age/Sex	Ethnic group	Year of birth	Place of birth	Year of diagnosis	Years† in Canada
18/M	Japanese	1970	Japan	1988	10
69/F	Chinese	1924	Northern China	1993	20
61/F	Japanese	1931	Canada	1993	61
36/M	Indian	1959	Malawi*	1996	21
44/M	Indian	1957	Punjab, India	2002	22
17/F	Indian	1978	Canada*	1995	17
19/M	Indian	1978	Canada*	1998	19
19/F	Indian	1979	Canada*	1998	19
41/F	Indian	1958	Punjab, India	2000	32
44/M	Indian	1952	Punjab, India	1996	24
51/M	Indian	1945	Punjab, India	1997	20
31/M	Indian	1966	Canada*	1997	31
53/F	Indian	1950	Punjab, India	2002	32
64/F	Indian	1938	Eastern India	2002	27

**Parents born in Punjab, India; †Before diagnosis*

Clinical symptoms were also recorded. Abdominal pain (71.4%), diarrhea (35.7%) and weight loss (57.1%) were common, usually for less than two years. Anemia (42.8%) and deficiencies of various nutrients, particularly iron, were common. Endoscopic studies are also detailed in Table 2. To date, no esophageal inflammatory or neoplastic disease were detected. Lymphocytic gastritis, lymphocytic colitis, or both, were present in five patients (35.7%). Collagenous inflammatory diseases were not detected in the stomach, small intestine or colon. Only one patient had gastritis associated with *H pylori*. To date, no neoplastic disorder has developed in any of these 14 patients.

DISCUSSION

The present report documents the detection of biopsy-defined adult celiac disease in Asian immigrants and those of Asian descent born in Canada, and represents new information on celiac disease in North America. Most of the patients in the present study were Indo-Canadian, either born in the Punjab region of Northern India or of Punjabi descent. This finding in adults is consistent with previously recorded evidence for celiac disease, notably in children, in the Punjab region as well as in children of Punjabi descent in the United Kingdom (6-9).

TABLE 2
Clinical features in Asians with celiac disease

Age/Sex	Ethnic group	Year of diagnosis	Symptoms	Complications
18/M	Japanese	1988	Abdominal pain, 4 kg weight loss	
69/F	Chinese	1993	Abdominal pain, 10 kg weght loss	Iron deficiency anemia, folate and B12 deficiency hypomagnesemia
61/F	Japanese	1993	Diarrhea	*Helicobacter pylori*-associated gastritis
36/M	Indian	1996	Abdominal pain, diarrhea, 10 kg weight loss	Iron deficiency anemia, Low serum albumin elevated AST, lymphocytic gastritis
44/M	Indian	2002	Abdominal pain	Tissue transglutaminase antibody-positive
17/F	Indian	1996	Abdominal pain, diarrhea 8 kg weight loss	Gallstones, lymphocytic colitis, dermatitis herpetiformis, lymphocytic gastritis, iron deficiency anemia, low serum albumin
19/M	Indian	1998	Abdominal pain	
19/F	Indian	1998	Abdominal pain	Lymphocytic colitis
41/F	Indian	2000	Abdominal pain	Lymphocytic gastritis, tissue transglutaminase antibody-positive
44/M	Indian	1997	Diarrhea, 20 kg weight loss	Gallstones, CAH with fibrosis (autoimmune), Iron deficiency anemia
51/M	Indian	1996	6 kg weight loss	Iron deficiency anemia, lymphocytic gastritis
31/M	Indian	1997	Abdominal pain, 4 kg weight loss	Epilepsy, iron deficiency anemia
53/F	Indian	2002	Abdominal pain, diarrhea	Tissue transglutaminase antibody-positive
64/F	Indian	2002	8 kg weight loss	Tissue transglutaminase antibody-positive, diabetes

AST Aspartate aminotransferase; CAH Chronic active hepatitis

In addition, the present report documents the histological definition of celiac disease in other Asian ethnic groups residing in North America, including Chinese and Japanese immigrants and those of Asian descent born in Canada. Similar observations were previously recorded in natives among the Coast Salish (12) who were thought to be descended from populations that historically migrated from Asia to North America over the Alaskan land bridge. Previous studies, using HLA markers (2-4), have suggested that celiac disease in these ethnic groups is largely, but not solely, genetically based, requiring an environmental factor (ie, wheat) for the expression of the disease. Wheat cultivation methods were recorded in the Punjabi region of India before 1000 BC. This was hypothesized elsewhere to be important in the appearance of celiac disease in this particular geographic area of Asia (1). In addition, as suggested by the sole Chinese patient in this report, wheat cultivation may be as important a staple as rice in Northern China. Finally, the relatively late introduction of wheat cultivation methods in the past century to North American native groups, such as the Coast Salish, may be important in the limited, but relatively recent recognition of celiac disease in these groups (12).

The clinical features of adult celiac disease were also detailed. Abdominal pain, a less common symptom in most celiac disease series (26), was the most frequently defined symptom leading to investigation, along with weight loss and diarrhea. In part, this may have reflected the adult age of the patients studied, because abdominal pain appears also to be a less commonly reported symptom in Indian children with celiac disease (27). Anemia was also commonly detected, particularly iron deficiency anemia, similar to the experience with adult celiac disease reported from India (28). Serological studies were not systematically done in our patients before the more recent development of a clinical assay in our hospital. However, since becoming available, the serum assay for tissue transglutaminase was positive in all patients with biopsy-defined celiac disease. In a previous study, tissue transglutaminase autoantibodies had been reported in an Indian population with diabetes (29). Further studies are needed to determine the value of this assay as a screening tool for celiac disease in selected immigrant populations. Finally, this investigation documented concomitant lymphocytic inflammatory changes in gastric and colonic mucosa in over one-third of the patients. This was similar to the previously recorded prevalence figures in celiac disease (30) as well as the presence of other 'autoimmune' features of celiac disease, including dermatitis herpetiformis, diabetes and chronic liver disease.

CONCLUSIONS

The present report documents an experience with celiac disease in Asian immigrants as well as in those of Asian descent born in Canada, from differing ethnic backgrounds. These findings from a single teaching hospital suggest that this occurs far more frequently than is currently appreciated, particularly in those of Punjabi descent.

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