

DDW Meet the Professor Lunch
“Celiac Disease”
Monday, May 19, 2008, 12:30 – 1:45 P.M.

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FACTS

Celiac disease (CD) is an autoimmune enteropathy triggered by the ingestion of gluten-containing grains in susceptible individuals. It is the gliadin fraction of wheat gluten, and similar alcohol-soluble proteins in other grains, that are the environmental stimuli responsible for the development of intestinal damage associated with CD. The disease is associated with HLA alleles DQA1*0501/DQB1*0201, and in the continued presence of gluten, the disease is self-perpetuating. The typical intestinal damage in CD is characterized by loss of absorptive villi and hyperplasia of the crypts which completely resolves upon elimination of gluten-containing grains from the patients' diet.

Epidemiological studies conducted during the past decade, using specific and sensitive blood tests, have revealed that CD is one of the most common chronic diseases worldwide, affecting approximately 1% of the general population. Until recently the geographical distribution of CD was mostly restricted to Europe. New epidemiological studies indicate that CD is common in other industrialized countries, such as the United States, Canada, and Australia as well as in many developing countries, suggesting that the “global village of CD” has a worldwide distribution. It appears that no continent on the planet is spared by the disease.

We now also know that in addition to the typical malabsorption symptoms (e.g., chronic diarrhea, weight loss, abdominal distension), CD can manifest itself in a previously unappreciated spectrum of symptoms that potentially can affect any organ system. Indeed, because it is more widely recognized, we now appreciate that fewer patients present with typical gastrointestinal symptoms. More prominent are patients with non-intestinal symptoms, such as anemia, joint pain, chronic fatigue, short stature, skin lesions, and neurological and behavioral problems (including peripheral neuropathy, epilepsy, dementia, schizophrenia, and seizure with intracranial calcifications).

Because CD often presents in an atypical or even “silent” manner, many cases remain undiagnosed. Such cases carry the risk of long-term complications in adolescence and adulthood, including osteoporosis, infertility, miscarriages, cancer, or the onset of other autoimmune diseases, such as type 1 diabetes, Hashimoto's thyroiditis, autoimmune hepatitis, or Sjogren's syndrome.

Given the undisputable role of gluten in causing inflammation and immune-mediated tissue damage, CD represents a unique model for studying autoimmunity. In contrast to most other autoimmune diseases in which many contributing factors are unknown, in CD there is a close association with two HLA genes, a highly specific autoimmune response (i.e., self-directed autoantibodies to the transglutaminase in intestinal cells), and, most importantly, the triggering environmental factor (gluten) are known. Therefore, the cornerstone of treatment of CD is a lifelong adherence to a strict GFD devoid of proteins from wheat, rye, barley, and related cereals. Gluten is, however, a common (and in many countries unlabeled) ingredient in the human diet, presenting a big challenge for CD patients.

Case #1

J.D. is a 32 years old white male with a long history of recurrent fractures. Since his first fracture that occurred when he was 5 years old, he experienced a total of 13 fractures, some of which not justified by the micro-trauma that caused them. Family history revealed that the maternal grandmother suffers of severe osteoporosis. He has two siblings, one of which has been diagnosed with type 1 diabetes 3 years ago when she was 24 years old.

PHYSICAL EXAMINATION: GENERAL: J.D. is a pleasant man who is in no acute distress. Weight: 79 Kg; height: 183 cm. **HEENT:** Sclerae anicteric. Moist mucous membranes. No oropharyngeal lesions. **NECK:** Supple. No adenopathy or thyromegaly. **LUNGS:** Clear to auscultation bilaterally. **HEART:** S1 and S2. Regular rate and rhythm. No murmur, gallop or rub. **ABDOMEN:** Soft, nontender, nondistended, no rebound or guarding. No hepatosplenomegaly or masses. **GU:** unremarkable. **RECTUM:** normal externally. **EXTREMITIES:** Well perfused, without edema, cyanosis or clubbing. No peripheral joint swelling. **SKIN:** no eczema or rash.

LABS FROM VISIT TO HIS PEDIATRICIAN: CBC with differential normal, urine culture: negative, Ca 10.4; P; 4.4, Alk P. 330; growth hormone: normal; parathormone: normal; Antigliadin IgG 35 (normal less 20), antigliadin IgA 20, (normal less than 20), anti-tissue transglutaminase IgA 1 (normal less than 7), total IgA: not performed, Chemistry 14 normal.

Based on his lab results, an EGD with intestinal biopsy was obtained and the pathology report stated that the duodenal mucosal showed signs of chronic diffuse inflammation with the presence of some villi

QUESTIONS:

1. What is the most likely reason for this patient's symptoms?
2. What additional labs would you do?
3. How would you interpret the histological findings?
4. How the family history can help assisting with this patient's diagnosis?

Case #2

A.F. is a 45 years old female that was referred to our clinic with a history of chronic diarrhea (6-8 bowel movements/day) and 20 pounds weight loss. No decrease in appetite. Family history revealed that a maternal cousin has been recently diagnosed with celiac disease. No history of recent traveling or other cases of diarrheal diseases in the immediate family. Her 25 years old sister is affected by seasonal allergies.

PHYSICAL EXAMINATION: GENERAL: A.F. is in no acute distress. **NUTRITION:** weight 41 Kg; height 161 cm. **HEENT:** Sclerae anicteric. Moist mucous membranes. No oropharyngeal lesions. **NECK:** Supple. No adenopathy or thyromegaly. **LUNGS:** Clear to auscultation bilaterally. **CHEST:** Tanner III breasts. **HEART:** S1 and S2. Regular rate and rhythm. No murmur, gallop or rub. **ABDOMEN:** Soft, nontender, nondistended, no rebound or guarding. No hepatosplenomegaly or

masses. GU: unremarkable. RECTUM: normal externally. Rectal vault empty. EXTREMITIES: Well perfused, without edema, cyanosis or clubbing. No peripheral joint swelling. SKIN: diffuse eczema on the trunk and arms.

LABS FROM VISIT TO HIS PEDIATRICIAN: CBC with differential normal, stool culture for enteric pathogens and O&P negative, urine culture: negative, Antigliadin IgG 35 (normal less 20), antigliadin IgA 2, (normal less than 30), anti-tissue transglutaminase IgA 1 (normal less than 7), total IgA: not performed, Chemistry 14 normal.

Based on his symptoms and lab results, an EGD with intestinal biopsy was obtained and showed blunted villi with infiltration of the lamina propria with neutrophils and eosinophils. No increase in intraepithelial lymphocytes was detected.

QUESTIONS:

1. What is the most likely reason for this patient's symptoms?
2. What additional labs would you do?
3. How would you interpret the histological findings?
4. Do you agree the way the patient was approached?

Case #3

W.S. is a 66 year old female who was diagnosed with celiac disease 2 years ago with a biopsy which showed Marsh grade IIIb pathology in the distal duodenum. She was diagnosed as part of a family screening following the diagnosis of her brother six months before her diagnosis. W.S. claimed that she had no symptoms, however, she elected to embrace a gluten-free diet, eliminating all pasta, cereal, cookies, cakes and breads from her diet. After six months on the diet, she started to experience joint pain, fatigue, and occasional headaches. Her bowel movements are about 3 times per day characterized by the passage of soft stools. No weight loss or fever reported. She is having recurrent oral aphthous ulcerations about twice per month. She also has an occasional rash, which "looks like chicken-pox" and is very itchy, on her arms, knee, and elbows.

PHYSICAL EXAMINATION: GENERAL: W.S. is in no acute distress, but appears depressed. NUTRITION: appropriate nutritional status. HEENT: Sclerae anicteric. Moist mucous membranes. No oropharyngeal lesions. Dental enamel defects on upper and lower incisors. NECK: Supple. No adenopathy or thyromegaly. LUNGS: Clear to auscultation bilaterally. HEART: S1 and S2. Regular rate and rhythm. No murmur, gallop or rub. ABDOMEN: Soft, nontender, nondistended, no rebound or guarding. No hepatosplenomegaly or masses. GU: unremarkable. RECTUM: normal externally. EXTREMITIES: Well perfused, without edema, cyanosis or clubbing. No peripheral joint swelling. SKIN: presence of starching lesions at the elbows and knees, with a few vesicular eruptions.

LABS AT DIAGNOSIS: Antigliadin IgG 118 (normal less 25), antigliadin IgA 222, (normal less than 30), antiendomysial antibody positive at a titer of 1:36, tissue transglutaminase IgA 40 (normal less than 4), total IgA level 253 (normal 21-440), Chemistry 14 normal, CBC with differential normal, except CMV at 68.

QUESTIONS:

- 1 What is the most likely reason for this patient's symptoms?
- 2 How can you measure compliance with the gluten-free diet?
- 3 Which other co-morbid conditions might explain her symptoms?

- 4 What additional labs would you do?
- 5 When would you repeat her small bowel biopsy?

REFERENCES

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