Celiac Disease Related to Autoimmune Disorders

BY SHARON WORCESTER

EXPERT ANALYSIS FROM THE CONGRESS OF CLINICAL RHEUMATOLOGY

DESTIN, FLA. – Consider screening for celiac disease in children with juvenile idiopathic arthritis, arthromyalgias, and myositis, advised Dr. Alexa B. Adams.

Celiac disease has a strong association with numerous autoimmune disorders. Untreated celiac disease poses serious health consequences, such as short stature, failure to thrive, osteopenia/osteoporosis, and enteropathy-associated T-cell lymphoma. Early diagnosis and treatment could obviate or reduce the need for the more aggressive treatments that are typically prescribed for these associated autoimmune disorders, said Dr. Adams, a pediatric rheumatologist and pediatrician at Cornell University, New York.

The identification and treatment of celiac disease in the setting of autoimmune disorders also appear to have the potential to alter the course of subsequent autoimmune disease, she said.

A link between celiac disease and juvenile idiopathic arthritis (JIA), for example, is well established. Several studies have demonstrated an increased prevalence of celiac disease among children with JIA, and cases of celiac disease in association with juvenile spondyloarthropathies and with pauciarticular, polyarticular, and psoriatic arthritis also have been reported. Furthermore, data show that a gluten-free diet can improve the musculoskeletal symptoms that are associated with celiac disease.

The mechanisms for the association between JIA and celiac disease are unknown, but may be related to ongoing intestinal permeability in untreated celiac disease, Dr. Adams said, adding that she advocates screening for celiac disease in all JIA patients.

She described a case involving a 6-year-old boy who presented with pain and swelling of the knee as well as morning stiffness. He had previously been treated for Lyme disease, and he had a 2-year history of headaches, behavioral problems, and poor growth, compared with his identical twin.

Based on physical and laboratory examinations (serology was negative for celiac disease) and after the young patient was referred to pediatric infectious disease and neurology specialties where he underwent lumbar puncture and brain MRI, the treatment focused on possible central nervous system Lyme disease. Although his joint complaints were resolved, he had persistent headaches, poor growth, and worsening transaminitis.

The boy tested negative for infectious and autoimmune hepatitis. An abdominal ultrasound showed fatty infiltration of the liver. Ultimately, the child was referred to a pediatric gastroenterologist. Work-up, including duodenal biopsy, showed findings that were consistent with celiac disease, and a gluten-free diet was initiated.

"On a gluten-free diet, the child's headaches resolved, he had no recurrence of joint pain, he was growing and gaining weight, and he had no further behavioral issues," Dr. Adams said.

An early diagnosis of celiac disease in a JIA patient and early initiation of a gluten-free diet can prevent unnecessary treatment with NSAIDs, disease-modifying antirheumatic drugs, and anti–tumor necrosis factor agents. The patient can also avoid unnecessary imaging and joint injections.

Associations between celiac disease and adult rheumatoid arthritis/seronegative arthritides also exist, but are not as robust as that seen between celiac disease and JIA.

The coexistence of adult RA and positive celiac antibodies – including EmA (endomysial antibodies) and gliadin IgA – has been well described, but an association with biopsy-proven celiac disease has not borne out, Dr. Adams said.

The same is true in adult spondyloarthropathy.

It is possible that there are age-related differences in gluten tolerance or in the pathogenesis of arthritis and/or gut permeability that can explain the age-related differences, but this remains unclear, she noted.

As for celiac disease and myositis, the associations are well documented in both the pediatric rheumatology and pediatric gastroenterology literature, and also (although only more recently) in the adult literature.

Interestingly, a high prevalence of the DQAI*0501 allele is found in both diseases, Dr. Adams noted.

Because treatment of inflammatory myositis often requires significant use of glucocorticoids and sometimes additional immunosuppressive therapy, screening for celiac disease should be considered in myositis patients, she said, describing two cases involving young girls who were diagnosed with myositis and polymyositis, respectively. Both failed to respond adequately to prednisone/methotrexate, and both are doing well now on only a gluten-free diet after being diagnosed with celiac disease on biopsy.

Screen for celiac disease in patients with vague musculoskeletal complaints who don't respond to treatment. These are the patients with whom "you just don't know what to do," she said, adding that these are the patients who don't clearly have arthritis, whose symptoms are out of proportion to findings on examination, whose symptoms impact their participation in sports or other activities, and who fail to respond well to a number of treatments. Often these patients will be diagnosed with fibromyalgia – a diagnosis that is unusual in young patients and should raise concern about possible other causes, she added.

Given the consistent findings associating celiac disease with certain autoimmune disorders, and the safety and effectiveness of the gluten-free diet that is used to treat celiac disease, screening deserves consideration in these patients, she concluded.

Dr. Adams serves as a speaker for Abbott Pharmaceuticals. She had no other relevant disclosures. ■

Systemic Link Needs Further Study

An association between celiac disease and systemic autoimmune disease has been reported, but is less established than the association between celiac disease and nonsystemic autoimmune disorders, Dr. Adams said.

Reports of a link between celiac disease and systemic lupus erythematosus (SLE), for example, are limited to case reports, and at this point should be "taken with a grain of salt," she said.

However, it does appear that in children the celiac disease diagnosis typically precedes the SLE diagnosis, whereas the converse is true in adults.

Also, reports of SLE following celiac disease despite histologic normalization of the celiac disease on biopsy suggest that the treatment of celiac disease via a gluten-free diet does not modify the disease course in SLE, as it appears to do in cases of arthritis and myositis (J. Clin. Gastroenterol. 2008;42:252-5), Dr. Adams said.

There does, however, appear to be a fairly strong association between celiac disease and Sjögren's syndrome.

A 2003 report said Sjögren's syndrome is present in up to 15% of patients with biopsy-proven celiac disease, and demonstrated that anti-tTG (tissue transglutaminase, a marker for celiac disease) is more prevalent in Sjögren's syndrome than in other systemic rheumatic diseases (J. Rheumatol. 2003;30:2613-9).

Systemic sclerosis and morphia have also been reported in association with celiac disease, Dr. Adams said.

The strongest associations between celiac disease and systemic autoimmune disease are with adult idiopathic diabetes mellitus, autoimmune thyroid disease, Addison's disease, and polyendocrinopathies, she added.

More data are needed to define the prevalence of celiac disease in various subtypes of systemic autoimmune disease, she concluded.

Ocular Toxicity Rare in Patients Taking Hydroxychloroquine

BY SHARON WORCESTER

FROM A SYMPOSIUM SPONSORED BY THE AMERICAN COLLEGE OF RHEUMATOLOGY

CHICAGO – Hydroxychloroquine-related ocular toxicity is rare, but does occur and should be considered in any treated patient complaining of blurred vision, Dr. Alvin Wells said at the symposium.

He described a case involving a 21-year-old woman who was referred for rash and color changes of her hands and feet. She had a weakly positive antinuclear antibody (ANA) titer, and there was concern about possible lupus.

The patient's chief complaint was redness of the face in the presence of cold fingers and toes.

On physical examination she was found to have significant mild erythematous rash on the face and chest, and mild Raynaud's changes of the digits without ulceration or loss of digital pulp. Her laboratory study findings were completely normal except for an ANA titer of 1:640.

The patient was started on hydroxychloroquine at a standard dose of 200 mg twice daily along with 10 mg nifedipine every Monday, Wednesday, and Friday nights. A follow-up visit was scheduled for 8 weeks, but within 10 days she called in complaining of headaches and blurred vision.

Although ocular toxicity is more common with chloroquine, it does occur with hydroxychloroquine as well, and the effect is dose dependent, said Dr. Wells, who is director of the rheumatology and immunotherapy center at Duke University Medical Center in Durham, N.C.

Risk increases with doses greater than 6.5 mg/kg. This patient, who weighed only 110 lbs, was receiving a dose of about 8 mg/kg, he said.

The risk is also increased in those with higher body mass index and those with diabetes.

Affected patients may present with corneal deposits, and retinopathy may also occur. Blurred vision is the most common complaint, and examination of the macula will reveal a "bull's eye maculopathy," Dr. Wells said.

The effects are reversible upon discontinuation of the drug in 95% of cases, he noted.

Affected patients should have a baseline evaluation within 1 year (and preferably within 6 months), and if it is normal, they should be evaluated yearly thereafter, he recommended.

Dr. Wells reported that he has received consulting fees or other remuneration from Abbott, Amgen, Bristol-Myers Squibb, Genentech, Pfizer, and UCB. ■