Caution Advised When Diagnosing Behçet’s

A R T I C L E S  B Y  S H A R O N  W O R C E S T E R

EXPERT ANALYSIS FROM THE CONGRESS OF CLINICAL RHEUMATOLOGY

DESTIN, FLA. – A conservative approach is best when it comes to making a diagnosis of Behçet’s disease, Dr. Kenneth Calamia said at the meeting.

Although oral and genital ulcers are common in the disease, they also are a common manifestation of many other conditions, and it is important to consider the other possible causes first.

The importance of a Behçet’s diagnosis doesn’t have anything to do with ulcers – it has to do with the risk or presence of serious manifestations, including vascular disease, central nervous system manifestations, and uveitis, said Dr. Calamia of the department of medicine at the Mayo Clinic in Jacksonville, Fla.

“You don’t want to (needlessly) give a patient the baggage of that diagnosis,” he said, noting that in patients diagnosed with Behçet’s, everything will be attributed to the disease for the rest of their lives.

In the United States and Europe, true Behçet’s is quite rare (about 0.3–7.5 cases/100,000 population), compared with places like Turkey and other “Silk Road” areas, which have a very high prevalence (100–370 cases/100,000 population). In those areas, more severe forms are much more prevalent, and the benign mucocutaneous symptoms that comprise most of the cases in the United States are referred to as American Behçet’s, Dr. Calamia said.

The term “Behçet’s syndrome” also can be used to describe the types of cases typically seen in the United States, but in many cases, the diagnosis is actually “complex aphthosis,” he said, adding that Behçet’s treatment principles can nonetheless be used to help patients with this condition.

Complex aphthosis is a term used by oral dermatologists to help classify types of recurrent aphthous stomatitis. As opposed to simple aphthosis, which is characterized by episodic, short-lived lesions that are few in number, recur three to six times per year, and tend to affect nonkeratinized mucosa, complex aphthosis lesions can be continuous, numerous, large, slow-healing, and debilitating.

Keep in mind that both simple and complex aphthosis can be associated with menstruation, sprue, inflammatory bowel disease, HIV, hematologic disorders (such as cyclic neutropenia, IgA deficiency, myelodysplasia/myeloproliferation), various deficiencies (B vitamins, folate, iron, and zinc), and smoking cessation, Dr. Calamia said, explaining that smoking tends to increase keratinization, which protects against ulcers, and that protection is lost when a patient quits.

In a study conducted by an oral dermatologist several years ago, only 9% of 269 patients with severe complex aphthosis – 16% of whom also had genital ulcers – had a Behçet’s diagnosis, he noted.

Some other diagnoses in the cohort included 25% with Behçet’s, 16% with recurrent aphthous stomatitis, and 5% with mucosal disease in 6%, smoking discontinuation in 4%, and drug-related ulcers in 3%.

“(Complex aphthosis) is the diagnosis I prefer in those who have mouth and genital ulcers, but nothing else to support a diagnosis of Behçet’s,” he said.

Consider the other possible causes of the ulcers, and also consider the differential diagnoses for recurrent aphthous stomatitis, which include recurrent intraoral herpes simplex virus, Wegener’s granulomatosis, Crohn’s disease, pyostomatosis vegetans, erythema multiforme, lichen planus, mucous membrane pemphigoid, and pemphigus vulgaris, he said.

A diffuse, widespread, and chronic presentation, which is not characteristic of recurrent aphthous stomatitis or Behçet’s disease, can help differentiate between those conditions and those differential diagnoses, he said.

Dr. Calamia disclosed that he has received research support from Genentech and Celgene, and has served on an advisory board for Centocor.

IgG4-Related Systemic Aortitis Responds to Rituximab

EXPERT ANALYSIS FROM A SYMPOSIUM SPONSORED BY THE AMERICAN COLLEGE OF RHEUMATOLOGY

CHICAGO – Rituximab is showing promise as an effective treatment for IgG4-related aortitis, a condition which has only recently been described.

In one patient, serum IgG4 level of 1,560 mg/dL, treatment with rituximab resulted in a decrease to 390 mg/dL within 2 months. Currently the patient’s serum IgG4 level is 26 mg/dL (normal is below 135 mg/dL), Dr. John H. Stone reported.

Remarkably, the treatment appears to affect only IgG4 and not other IgG subclasses, suggesting that the agent may be targeting the specific immune response, Dr. Stone said.

The IgG4-related aortitis patient who had been treated with steroids but could not tolerate the side effects – and whose IgG4 levels increased when the steroids were discontinued – rituximab had an equally abrupt effect. At 1 month folowing rituximab treatment, her IgG4 levels had fallen to 31 mg/dL. And in a 68-year-old man who previously responded to steroids, but who flared and was being treated with various disease-modifying antirheumatic drugs, serial rituximab treatments decreased his IgG4 level with each dose until it normalized.

Ten patients with aortitis, including seven with IgG4 elevation, have been treated with rituximab as part of this series, and IgG4 levels declined quickly in all seven, while all other IgG subclasses remained stable, he said.

IgG4-related aortitis was first described in 2009 by Dr. Stone and his colleagues, who published on the case of a 67-year-old patient who developed dissection of the ascending aorta in the setting of IgG4-related disease, thereby linking IgG4-related systemic disease with this newly recognized subset of noninfectious aortitis, and adding to a growing list of conditions, such as autoimmune pancreatitis, that are associated with IgG4-related systemic disease.

At surgery, a transmural lymphoplasmacytic infiltrate was detected in the aorta, and on immunohistochemistry...
The findings prompted a review of prior cases of aortitis at Massachusetts General Hospital, where a large number of aortic surgeries are performed. It was found in a 2008 study from Japan, 4 of 10 cases involving the descending aorta stained intensely for IgG4.

The investigators found that 36% of the overall group relapsed. Further examination, the relapse rate was 43% for those in the zero glucocorticoid target dose group, compared with 14% in those allowed to continue glucocorticoids – approximately a threefold increase. Even for those who discontinue glucocorticoids, timing is important. When the investigators divided patients in the zero target group into those who had to reach zero within 12 months (the early zero group) and those who were allowed to reach zero after 12 months (the late zero group), there was a 48% relapse rate for the early zero group, compared with a 29% rate for the late zero group.

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