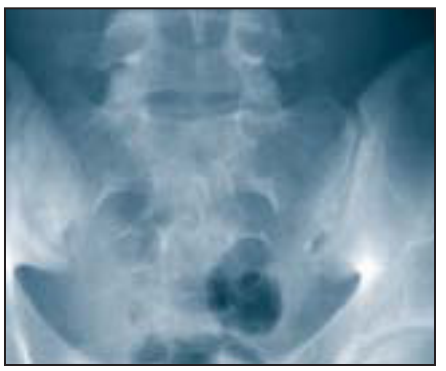
IMAGING 360°

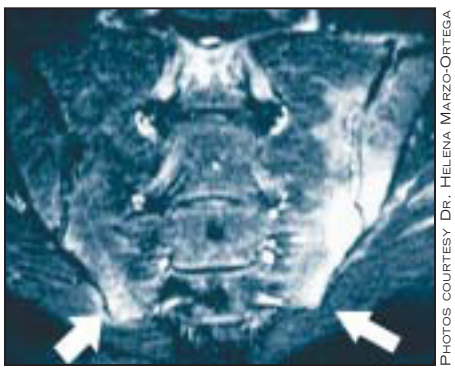
Ankylosing Spondylitis

Magnetic resonance imaging and other advanced imaging modalities have a long way to go before they become accepted parts of the diagnostic work-up for ankylosing spondylitis. History, physical examination, and conventional radiography form its existing diagnostic criteria.

Dr. Helena Marzo-Ortega is a consultant rheumatologist at the University of Leeds (England). She has been studying the use of MRI in the diagnosis and treatment of AS. Here are her thoughts on what roles different imaging modalities can play in better diagnosing and managing AS.



X-ray fails to show abnormalities in an HLA-B27-positive patient with AS.



PHOTOS COURTESY DR. HELENA MARZO-ORTEGA

MRI shows bone marrow edema (white arrows) in the same patient.

X-Ray

With x-ray, which is the imaging tool used by the main AS classification, only abnormalities affecting the bone structure can be seen. This means that "it may take up to 8-10 years of symptoms before somebody develops changes that are picked up by conventional x-ray," Dr. Marzo-Ortega noted.

Still, x-ray has a place in AS. "Young patients, who [make up] most of our population, may not [present as soon as] pain starts. It usually takes them a few months, and sometimes years, to come in," she said. The first line of investigation with such patients could be an x-ray because if positive, the diagnosis of AS can be made.

MRI

MRI is mainly used in the research setting. The strength of MRI is its ability to reveal abnormalities in the synovium, the soft tissues, and the entheses, said Dr. Marzo-Ortega.

MRI picks up inflammation and bone edema, which may be identified in about 80% of patients. "This means that there are still another 20% of cases, where we are left with a negative MRI and uncertainty about the diagnosis," she said.

AS diagnosis is based on involvement of the sacroiliac joint. "The majority of patients will have the sacroiliac joints affected before the spine."

Most research done to date using MRI in AS has looked at the sacroiliac joints to see if there are any signs of active inflammation. However, MRI equipment, limited by its reliance on the commonly used T1.5 magnets, is not sensitive enough to reveal such changes.

"The SI joints are very small and the abnormalities happen within the bone marrow. … It's really the bone marrow that we're looking at." A positive MRI would indicate inflammation within the bone marrow.

The use of biologics requires patients be followed with x-ray according to the treatment guidelines in both the United States and Europe, which follow the New York criteria.

"However, we all know that we're not prepared to wait 8-10 years so we can make the diagnosis and then treat the patient." Instead, if the MRI is positive, "we follow criteria, as recently proposed by the ASAS [Assessment in Ankylosing Spondylitis] international working group. This allows for the diagnosis of axial SpA (or preradiographic AS) to be made if sacroiliitis is found by any imaging method with at least one clinical parameter, or if there is HLA-B27 positivity plus at least two clinical parameters," Dr. Marzo-Ortega noted.

Data from a study following AS patients for 8 years show that "the MRI signal determines the development of radiographic structural damage. It is the intensity of the signal that matters. … The more severe the edema, the greater the chance to develop radiographic sacroiliitis at a year's time [Arthritis Rheum. 2008;58:3413-8].

MRI has a role to play in the evaluation of therapies for AS. In this disease, inflammation may lead to erosive disease but it may also lead to new bone formation, which may result in spinal fusion. "We don't really know what the relationship between inflammation and new bone formation is. Even if we use very potent agents, such as tumor necrosis factor [TNF]-alpha blockers that can control inflammation, we're not really sure whether that's making any big impact on new bone formation as an outcome," said Dr. Marzo-Ortega. MRI could be used to follow patients treated with TNF-blockers to understand what effect the drugs have on erosions and new bone formation.

CT

Computed tomography has a place in the diagnosis of AS, particularly established disease, because it has the ability to detect erosions at an early time, compared with conventional radiograph, said Dr. Marzo-Ortega. The main problem with CT is radiation exposure. "So it won't be something that we would be doing on a daily basis."

However, "there is a place for it when we have an x-ray that shows sort of borderline changes. Then we do a CT to confirm that it's definitely established abnormalities. … We're looking for erosions, we're looking for sclerosis, we're looking for ankylosis to establish changes."

Ultrasound

"Ultrasound does not have a role in spinal diseases as yet. There are no data to suggest that it is good for visualizing any structures in the spine," Dr. Marzo-Ortega said.

Where ultrasound does have a role is in evaluating peripheral joints. "There is definitely a place in spondyloarthritis/ankylosing spondylitis to look for enthesitis in the peripheral joints, and also—as in rheumatoid arthritis—to assess bone damage or synovitis." So when patients present with axial and peripheral disease, ultrasound can be useful to look for subclinical or entheseal disease in the peripheral joints. ■

By Kerri Wachter

RA, Inflammatory Bowel Overlap Still a Clinical Challenge

BY NANCY WALSH

FORT LAUDERDALE, FLA. — Despite greater understanding of genetic influences and phenotypic manifestations, and the availability of multiple immunomodulatory medications, inflammatory bowel disease continues to pose significant clinical challenges.

Why is IBD of particular interest to rheumatologists? According to Dr. Sunanda Kane, there appear to be several shared mechanisms for inflammation, and there are certainly patients with "overlap" syndromes who have significant rheumatologic abnormalities along with intestinal inflammation.

Trying to understand the common threads—rather than focusing on the differences—of both conditions will ultimately help more patients, she said.

There is mounting evidence of a genetic link between rheumatoid arthritis and inflammatory bowel disease. The STAT4 polymorphism has been found to be associated with increased susceptibility to IBD and rheumatoid arthritis (Arthritis Rheum. 2008;58;9:2598-602).

Further research suggests a link between Th17 cells and interleukin-23. Th17 cells have been implicated in the pathogenesis of rheumatoid arthritis. These cells are found in high numbers in joints with RA-induced inflammatory destruction. Their production is dependent on growth factor IL-23. Findings from animal models show that IL-23 also plays a role in gut inflammation, and loss of IL-23 was associated with a loss of inflammation. Although it remains to be seen whether gut inflammation is totally dependent on Th17, it seems clear that IL-23 plays a significant role there (Ann. Rheum. Diseases 2008;67[suppl. 3]:iii26-9)

"Classically, in inflammatory bowel disease we talk about ulcerative colitis and Crohn's disease, but sometimes there is so much overlap it's hard to tell the difference," said Dr. Kane of the Mayo Clinic, Rochester, Minn. "We don't fully understand what causes Crohn's and colitis, but we do know that the normal gut is always mildly inflamed. It has to be, because this is what 'tastes' the environment and determines what's friend and what's foe," she said at a meeting sponsored by RHEUMATOLOGY NEWS and Skin Disease Education Foundation.

Genetic studies revealed genes that predispose to an inability to downregulate gut inflammation, such as the NOD2/CARD15 gene, located at chromosome 16q12.

This gene's product is similar to disease-resistance proteins in plants, and is related to immune response to bacteria. Mutations in this gene are associated with Crohn's disease through abnormal activation of downstream inflammatory cell signaling, she explained.

Diet, smoking, and stress all can contribute to worsening of disease, as can the use of antibiotics—particularly penicillin and the other "–illins"—and nonsteroidal anti-inflammatory drugs, she said.

"There is a 30% increased risk of disease flare with regular NSAID use in IBD, so when patients have extraintestinal manifestations or concomitant rheumatologic conditions, we gastroenterologists really have to partner with the rheumatologists to make sure they use drugs other than NSAIDs," she said.

Treatment also remains challenging, despite the availability of immunomodulating drugs. Infliximab, adalimumab, and certolizumab have been used successfully, but etanercept and onercept have not been superior to placebo, and ulcerative colitis has worsened in patients treated with rituximab for other conditions.

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