Little Reduction Seen

Work Disability *from page 1*

al and work disability, as well as a patient self-report questionnaire that included questions about work status at the time of the first RA symptoms, current work status, and the questions, "Are you work disabled because of RA?" and "If so, since when?" she noted.

At the time of first symptoms, 68% of the patients were working and of these, 35% reported that they subsequently became work disabled because of RA, Dr. Sokka reported in a press conference.

Of the 1,650 patients whose RA symptoms began in the year 2000 or later and who continued to work after their diagnoses, the probability of continuing to work for 2 years was 80%, based on a Kaplan-Meier analysis, and the probability of continuing to work for 5 years was 68%, she said.

Although the rates of work disability were similar between richer and poorer countries, the median HAQ levels among subjects who remained working were significantly lower in patients from countries with a per capita gross domestic product (GDP) less than $11,000 USD, compared with those from countries with a per capita GDP higher than $24,000 USD, according to Dr. Sokka.

In the richer and poorer countries, respectively, the mean disease activity scores (DAS28) were 3.7 and 5.2, and the mean HAQ levels were 0.75 and 1.3.

"There was not much difference in work disability rates in patients from countries with low or high GDP—about one-third of patients from both of these country groups who were diagnosed during this millennium told us that they had become work disabled 5 years after onset of disease—yet when we looked at how the patients who continue working are doing in their daily lives in terms of disease level, it's clear that people from poorer countries are continuing to work despite more active disease," Dr. Sokka said in an interview with RHEUMATOLOGY NEWS.

"Although this might be explained partly by differences in the way patients are treated between countries—the clinic structure, how actively patients are being treated, how doctors feel about RA therapies—as well as issues such as patient compliance and patient education, the differences are likely due to society-level influences that are beyond the scope of rheumatologists."

The study findings were "surprising and disappointing," according to Dr. Sokka.

"We hoped that advances in RA drug therapies during this decade would translate into reduced work disability. The fact that it hasn't tells us that we still have a lot of work to do," she noted.

The goal of treatment is to achieve remission, "but we also have to look at other outcomes," said Dr. Sokka.

"Work disability is the most costly consequence of rheumatoid arthritis, so we also should be looking at maintaining and improving work ability in these patients."

The QUEST-RA study was funded by Abbott Laboratories. ■

To see a video interview with Dr. Sokka, go to www.youtube.com/watch?v=CYnu39RniVc.

Retreatment With Rituximab Promoted Clinical Response

BY DIANA MAHONEY

COPENHAGEN — Rheumatoid arthritis patients who do not respond to initial treatment with rituximab can be re-treated successfully with a second course of the B-cell–depleting, monoclonal anti-CD20 antibody after 6 months, Dr. Edward Vital reported at the European Congress of Rheumatology.

The findings are particularly important because rituximab is often used as a treatment of last resort after the failure of other therapies, such as anti–tumor necrosis factor agents and methotrexate, "and approximately one-third of patients fail to achieve an adequate response to initial treatment with the drug," said Dr. Vital of the Leeds Institute of Molecular Medicine at the University of Leeds (England).

Although it had previously been presumed that RA patients who failed initial rituximab therapy had B-cell–independent disease, the new data suggest that is not the case, said Dr. Vital.

To determine whether nonresponders to initial rituximab therapy might have disease that is potentially still amenable to B-cell–depletion therapy, and to assess the impact of re-treatment, Dr. Vital and his colleagues assessed the B-cell status and treatment response of 104 RA patients treated with standard doses of rituximab. All of the patients were positive for rheumatoid factor and/or anti–cyclic citrullinated peptide antibodies. Of the 104 patients, 38 did not respond to initial therapy, based on change in clinical status as measured by Disease Activity Score 28 and EULAR criteria.

A comparison of baseline blood and synovial B-cell parameters showed no difference in erythrocyte sedimentation rates or C reactive protein levels between nonresponders and responders. But nonresponders had significantly higher numbers of memory and pre-plasma cells at baseline, along with more synovial B cells, Dr. Vital reported. Additionally, using highly sensitive rare-event fluorescence-activated cell sorting (RE-FACS), the investigators identified incomplete B-cell depletion in 90% of the treatment nonresponders, he said.

Of the nonresponders, 25 underwent retreatment 6 months later, "when their B-cell numbers were significantly lower than they were at baseline of their first treatment cycle," Dr. Vital reported. Among the re-treated patients, 72% responded clinically (defined as a moderate or better EULAR response) to the therapy at 6 months. Of these, 32% had a good response and 16% were in remission—response rates that are comparable to those observed among treatment-naive patients, he said.

The findings have had an immediate impact on clinical practice at the Leeds Teaching Hospitals. "From these results, we have immediately changed our practice regarding how we treat these patients. Now all patients who fail the first cycle of rituximab get a second cycle of treatment," Dr. Vital said.

"The next question to consider is whether patients who have predictors of poor response could be treated more intensively from the outset, possibly with a different dose of rituximab, which is something we are currently investigating," he noted. Dr. Vital disclosed a financial relationship with Roche, which provided free study drugs for 45 patients. The study was funded by the U.K. National Institute for Health Research. ■

To watch an interview of Dr. Vital, go to www.youtube.com/watch?v=YfEX2UxSlps.

JOINT DECISIONS

Histiocytoid Sweet Syndrome

At first glance, it appeared that a straightforward diagnosis was in order, said Dr. Paul A. Krusinski at the annual meeting of the Noah Worcester Dermatological Society.

"We thought it looked pretty good for Sweet syndrome," he said, referencing the patient's characteristic fever and joint pain. "Often, Sweet syndrome has a prodrome associated with it and she had her—quote—sinus infection," he said.

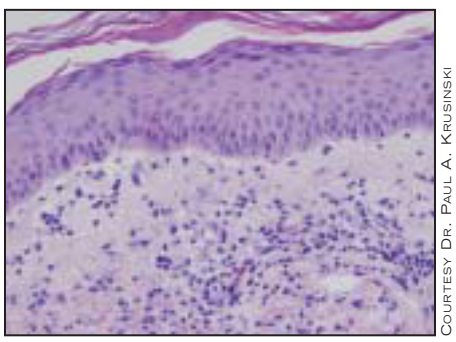
A second differential diagnosis was drug hypersensitivity reaction, noted Dr. Krusinski, professor and director of the division of dermatology at the University of Vermont, Burlington.

Histologically, edema could be seen in the upper papillary dermis. A perivascular infiltrate was evident in the dermis. At higher power, however, the Sweet syndrome diagnosis seemed less likely. "When you get a little closer, you say, 'Where are the polys [polymorphonuclear neutrophils]? Where are the neutrophils?' " he said. In their place appeared to be large histiocytes.

A dermatopathology report on an initial biopsy specimen identified "a moderately dense dermal inflammatory infiltrate that is of mixed composition but predominated by mononuclear cells," and went on to note that "only rare neutrophils are present, thus militating against Sweet syndrome." Immunostaining was positive for CD68 and myeloid precursors.

Classic Sweet syndrome, first described in 1964, is characterized by its female predominance, abrupt onset, fever, painful erythematous plaques or nodules, and abnormal laboratory values such as elevated erythrocyte sedimentation rate and positive C-reactive protein, just as in this case.

Neutrophilic infiltrate conventionally heralds classic Sweet syndrome, either in the absence of vasculitis or, rarely, with secondary vasculitis. Three subtypes are classically described, including idiopathic Sweet syndrome associated with other inflammatory diseases, cases related to hematologic malignancies, and cases associated with solid malignant neoplasms.



COURTESY DR. PAUL A. KRUSINSKI

Histology shows dense dermal inflammatory infiltrate of mononuclear cells.

A literature review revealed a study from Spanish researchers detailing 41 cases of a previously undescribed entity: histiocytoid Sweet syndrome. In this series, 26 women and 15 men aged 29-79 years had lesions typical of Sweet syndrome but failed to meet conventional histopathologic criteria for the disease (Arch. Dermatol. 2005;141:834-42).

Biopsies showed dense, bandlike infiltrate in the superficial dermis and middermis that was predominated by large mononuclear cells with "eccentric" nuclei and irregular contours. Few neutrophils, lymphocytes, or small histiocytes were present. Moderate to intense superficial dermal edema was present and there was no appreciable vasculitis.

Findings align with the monocytic histiocytic lineage, with positive staining for CD15, CD43, CD45, CD68, MAC-386, HAM56, and lysozyme.

The authors of a recent article detailing six clinically and microscopically diverse cases thought to be Sweet syndrome, drug eruptions, erythema nodosum, or Wells's syndrome hypothesized that histiocytoid neutrophilic dermatoses and panniculitides are "variations on a theme" and proposed three new disease classifications: Sweetlike neutrophilic dermatoses, histiocytoid; subcutaneous Sweet syndrome, histiocytoid; and histiocytoid neutrophilic dermatosis, unspecified (Am. J. Dermatopathol. 2007;29:334-41).

The case patient had age-appropriate cancer screening, with negative results, and responded well to prednisone 40 mg daily followed by a tapering of the drug.

Dr. Kathryn Schwarzenberger was the physician at the University of Vermont who made the diagnosis.

—Betsy Bates