

New Multiple Sclerosis Lesions Accrue Seasonally

BY JEFF EVANS

FROM NEUROLOGY

Disease activity on MRI in multiple sclerosis patients is most likely to occur and is most intense in the spring and summer, according to a retrospective, observational study of a 3-year period in Boston.

Although the rates of clinical attacks and new contrast-enhancing lesions were not associated with significant seasonal differences, new T2 lesions developed in

VITALS

Major Finding: The point estimates for the rate of new T2 lesion accrual per day in MS were higher in the spring (0.024) and summer (0.030) than in the fall (0.010) or winter (0.016).

Data Source: A retrospective, observational study of brain MRI scans in 44 MS patients during 1991-1993.

the spring and summer at nearly twice the rate as in the fall and winter. This finding “may raise concerns for design and analysis of clinical trials with MRI outcome measures. If left unaccounted this effect could bias longitudinal assessment both at the individual as well as group level,” wrote Dominik S. Meier, Ph.D., of Brigham and Women’s Hospital, Boston, and colleagues.

The findings agreed with previous studies that measured the seasonality of clinical markers in Japan, Sweden, and the United States (Ohio and Arizona). Another three studies that examined MRI markers across the seasons had biased inclusion criteria or poor longitudinal follow-up, according to the investigators.

They matched meteorological data with clinical data from 44 patients who underwent 939 brain MRI scans during 1991-1993. The cohort included 13 patients with chronic progressive MS and 31 with relapsing-remitting MS. They had a mean age of 38 years, a mean disease duration of 8 years, and a mean Expanded Disability Status Scale score of 3.9.

Each patient had eight weekly scans, followed by eight scans every other week and six monthly examinations. No patient received disease-modifying therapy (Neurology 2010;75:799-806).

In the study, 31 patients developed 310 new T2 lesions, whereas 13 patients had no new lesions. In 42 patients, imaging detected a mean of 22 new contrast-enhancing lesions per patient. Clinical attacks during this period were recorded on 51 occasions in 24 patients, with a mean of 2.1 per patient.

The distribution of disease activity across the seasons was distinctly higher in the spring and summer even after applying several different methods of correcting for individual disease severity.

Point estimates for the rate of new T2 lesion accrual per day were higher in the spring (0.024) and summer (0.030) than in the fall (0.010) or winter (0.016).

Disease activity also was strongly correlated with warmer temperature and greater solar radiation, but not precipitation.

Patients with chronic, progressive MS tended to have an earlier and more pronounced high-activity period but lacked the peak of activity in August found in relapsing-remitting patients.

The findings did not change significantly in a separate analysis that excluded 18 patients who had been treated with brief bouts of steroids.

The findings could have an impact on MS clinical trials. The magnitude of an effect of the spring and summer on disease activity is likely affected by factors such as genetic affinity, disease phenotype, and geographic location, which “will have particular implications for multicenter trials that pool data from geographically distant locations,” the investigators wrote.

They also noted that biases may arise in studies that use prescreening MRI or

in trials with crossover arms, depending on the timing of the trial arms.

Many of the investigators involved in this study disclosed that they had received research support from the National Institutes of Health and the National Multiple Sclerosis Society, as well as research support, speaker honoraria, or served on scientific advisory boards from MS drug manufacturers, including Biogen Idec, Genentech, EMD Serono, and Teva Pharmaceutical Industries. ■

MRI Variation Is a Concern

Evidence for environmental factors in the pathogenesis of multiple sclerosis has accumulated ever since Dr. John F. Kurtzke’s pioneering epidemiological work in the 1960s. Epstein-Barr virus infection, smoking, and vitamin D status have all been shown to exert effects on MS risk. There also have been reports of seasonal variations in disease activity measured as relapse rate and occurrence of optic neuritis, with higher incidence of both in spring and summer. Several studies have shown a correlation between month of birth and MS risk, again with the highest risk in spring and summer.

Dr. Meier and colleagues report further evidence for a seasonal effect on disease activity and MS using serial MRI examinations. They elegantly show that disease activity, measured as new T2 lesions over

time, varies over the year with a peak in spring and summer. They also show strong associations with solar radiation and daily temperature, but not precipitation. The levels of vitamin D in serum might be the causal link between season and disease activity, but this assumption remains to be proven.

What is of great concern, however, is that MRI variables, a common measure of disease activity and thus treatment efficacy, seem to be influenced by season. This could bias trials aimed at assessing the effect of drugs on disease activity and need to be considered when designing future studies.

JONATAN SALZER, M.D., is a doctoral student in the department of pharmacology and clinical neuroscience at Umeå (Sweden) University. He has no relevant disclosures.



VIEW ON THE NEWS

Multiple Fibromyalgia Symptoms Require Multiple Therapies

BY SALLY KOCH KUBETIN

FROM A SEMINAR ON RHEUMATOLOGY

SANTA MONICA, CALIF. – Exercise and cognitive-behavioral therapy complement rather than replace pharmacology in the management of fibromyalgia, according to Dr. Philip J. Mease.

Findings from several studies have shown that such nonpharmacologic treatments may lessen the primary symptoms of fibromyalgia while helping to correct some maladaptive behaviors, mood disturbances, and deconditioning.

Not all nonpharmacologic therapies are equally effective. The literature suggests that aerobic exercise, cognitive-behavioral therapy, and patient education all lessen pain and improve function. The same benefits are not reported with strength training, acupuncture, biofeedback, balneotherapy, and hypnotherapy, Dr. Mease said at the meeting, sponsored by Skin Disease Education Foundation (SDEF) and the University of Louisville.

This year the American College of Rheumatology published diagnostic criteria for fibromyalgia that shifted the emphasis from tender point examination and

focused instead on the other symptoms that cause misery in these patients, such as sleep disturbance and fatigue (Arthritis Care Res. 2010;62:600-10).

Specifically, the diagnostic criteria are composed of two parts: a widespread pain index (WPI) that establishes the absence or presence of pain in up to 19 body areas but does not require the physician to press on those areas, and the symptom severity (SS) scale, that grades the patient’s fatigue, sleep, and cognition and the patient’s overall symptom burden.

Data show that 20% of patients with rheumatoid arthritis have scores indicating concomitant fibromyalgia.

DR. MEASE

These criteria, although already published, are considered preliminary and are being tested in clinical settings to confirm their reliability.

Data from recent, unpublished research out of the National Data Bank of Rheumatic Diseases show that 20% of patients with rheumatoid arthritis have scores that indicate concomitant fibromyalgia and 10% of patients

with osteoarthritis have scores consistent with fibromyalgia, according to Dr. Mease. He noted that these findings confirm the observation that fibromyalgia often coexists with other chronic pain conditions.

In addition to the recognized role for nonpharmacologic therapies, there has been a sea change in pharmacologic management of fibromyalgia. “I am intrigued by the emergence of a better understanding of the neurobiologic basis of central pain, central fatigue, and central dyscognition as they relate to fibromyalgia,” Dr. Mease said.

There have been data from clinical trials of agents targeting some of the neurobiologic pathways that are proving to be better than placebo in lessening some of the symptoms of fibromyalgia, said Dr. Mease, a rheumatologist at the University of Washington, Seattle, as well as director of the division of rheumatology research at the Swedish Medical Center there.

Findings from functional MRI studies have shown that, even at rest, the brain of patients with fibromyalgia has increased connectivity within multiple brain networks that may explain both the patients’ experience of spontaneous pain and fluctuations in pain that are unrelated to activity (Arthritis Rheum. 2010;62:2545-55).

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