Rheuma Facts®

A Quarterly Magazine

Serving physicians with interest in Rheumatology

10th Issue

Current News

Herpes Zoster & the Risk of Stroke in Patients with Autoimmune Diseases

January 31, 2017. By Arthritis & Rheumatology

In patients with autoimmune diseases, incident HZ was associated with as much as a twofold increased risk of stroke in the subsequent few months. In younger patients, we hypothesize that the HZ-related relative effect on stroke risk is greater than that observed in this analysis.

Given the public health implications of these observations, new urgency should be directed at increasing the rate of administering vaccinations for zoster in vulnerable populations.

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An Association of Enthesopathy with Seronegative Spondyloarthropathy

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Enthesopathy

Enthesopathy is a disorder of the entheses, which are the connective tissues between bones and tendons or ligaments. Enthesopathy occurs when these tissues have been damaged, due to overuse, injury or infection. It may also be caused by an inflammatory condition such as psoriatic arthritis, ankylosing spondylitis, sarcoidosis, or gout. Some research indicates that enthesopathy may develop as a result of an autoimmune disorder. Enthesopathy may develop in various parts of the body, including the shoulders, hips, elbows, wrists, knees, heels or feet. This condition is typically found in individuals over the age of 50, and is usually characterized by symptoms of severe pain and inflammation.

Although the location of symptoms may vary, the symptoms of enthesopathy include pain, swelling and inflammation, that most commonly occurs in peripheral joints such as foot joints, elbow and shoulder joints, or hip joints. If enthesopathy occurs in the hands or feet, it may cause the fingers or toes to swell significantly.

Enthesopathy is a disease occurring at an enthesis-the site of attachment of a ligament or tendon to bone. The term does not refer to a specific process; enthesopathies can occur in a variety of inflammatory, degenerative, traumatic, metabolic, and endocrine disorders. This report describes a patient with enthesopathy accompanying an inflammatory senonegative arthropathy associated with ulcerative colitis.

My patient a 42-year-old woman had ulcerative colitis diagnosed in 2005 after colonoscopy and biopsy. Bowel symptoms had been quiescent on a regimen of (sulfasalazine) and hydrocortisone acetate enemas; however, pain in the left leg occurred in 2007, and trochanteric bursitis was diagnosed on the basis of clinical point tenderness over the left femoral greater trochanter. In September 2010, the bowel symptoms remained quiescent but the patient again had intermittent leg

pain. A radionuclide bone scan, showed increased uptake in the left greater trochanter (the site of attachment of the gluteus minimus, gluteus medius, piniformis, obturator externus, and obturator inter-nus muscles and the iliofemoral ligament), the right inferior pubic ramus (the site of attachment of the gracilis and adductor brevis muscles), and the right anterior inferior iliac spine (the site of attachment of the rectus femonis muscle and iliofemoral ligament). A plain film of the pelvis showed cortical erosions, sclerosis at these sites as well as irregular enthesophytes adjacent and superior to the left greater trochanter. Interestingly, the film also showed fusion of the sacroiliac joints. The bone scan showed normal accumulation of radiotracer in this region, as would be expected for an inactive process.

The arthropathy and enthesopathy of ulcerative colitis fall into the group of senonegative spondyloarthopathies, along with ankylosing spondylitis, psoriatic arthritis, Reiter's disease, and other enteropathic arthropathies such as Crohn's disease. Ulcerative colitis can have manifestations indistinguishable from isolated ankylosing spondylitis, although ulcerative colitis has less of a male predominance. Sacroiliitis accompanies ulcerative colitis in 1-26% of patients. Inflammatory changes in extra articular entheses are characteristic of senonegative spondyloarthropathy, especially at sites including the iliac crest and femoral trochanter.

This patient had the range of articular and extraarticular findings seen in a typical case of ulcerative colitis and shows the utility of bone scintigraphy in imaging active disease. MRI is as best tool to diagnose sacroilitis. Bone scintigraphy can also be used to gauge response to therapy. Finally, it is important to include enthesopathy in the differential diagnosis when abnormalities shown on bone scans are confined to sites of tendon on ligament insertions.

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Corticosteroid Use in Rheumatoid Arthritis

Compiled and summarized by:
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Corticosteroids have a complicated role in treating RA*. How are researchers working to find the balance between the benefits and risks?

Steroids

The original corticosteroid – was considered a miracle drug when it was first used in 1949 to treat Rheumatoid Arthritis. Newer treatments for the disease have since come along, but corticosteroids – also commonly referred to as glucocorticoids – remain a powerful, if somewhat flawed, weapon in the anti-inflammatory arsenal, and there's emerging evidence they do more than just provide symptomatic relief.

A study from the Netherlands, published in 2012 in the Annals of Internal Medicine, found that adding prednisone to a methotrexate regimen early in the disease process had numerous positive effects versus using methotrexate alone, including less joint damage, less physical disability and reduced disease activity.

"The correct use of corticosteroids will help to protect the joints from future damage and will mean that some patients will not need to go on to other treatments, such as biological agents, which are more dangerous and much more expensive," says John R. Kirwan, MD, of the University of Bristol Academic Rheumatology Unit, Bristol, United Kingdom.

Dr. Kirwan suggests that therapy with corticosteroids – specifically, prednisone – in conjunction with another disease-modifying anti rheumatic drug (DMARD), should be considered the "gold standard" for early treatment of RA*. And yet, Dr. Kirwan admits some doctors avoid using corticosteroids for RA*, primarily because of concern about side effects.

The Ups & Downs of Corticosteroids:
Without a doubt, prednisone and other drugs in the class do come with a substantial number of possible side effects – most of which are dose-related.

"Some of the side effects include weight gain and thinning of the skin, which can lead to increased bruising," says Stanley Cohen, MD, clinical professor of medicine at the University of Texas Southwestern Medical School in Dallas. "There's acceleration of bone loss with higher risk of fracture, increase in blood sugar and in every clinical trial, the group of patients on prednisone always had a greater risk of infection."

Elena M. Massarotti, MD, rheumatologist and associate professor at Harvard

*Rheumatoid Arthritis

Medical School in Boston, calls the use of prednisone and other corticosteroids "the classic double-edged sword."

"There's some evidence that prednisone in low doses may improve the radiographic features of rheumatoid arthritis," Dr. Massarotti says. "The general teaching in the management of patients with rheumatoid arthritis has been to minimize corticosteroid use and preferably to eliminate it altogether."

Dr. Massarotti says prednisone's primary utility in RA is as a "bridge" drug – one which can provide relief for a short time while other, safer drugs are taking effect – or one which can be used if a patient experiences a flare. "So they might need a short course of corticosteroids to quiet symptoms down," she says.

Corticosteroids reduce inflammation because they are chemically similar to the body's natural anti-inflammatory substance, cortisol, which is produced by the adrenal glands. In RA, the inflammatory response within the joints is greatly exaggerated – such that the body's natural supply of cortisol is insufficient to relieve symptoms.

Aside from side effects, one of the dangers of using glucocorticoids is sudden withdrawal. As the body gets used to what it senses as extra "cortisol," it slows down production of the real thing. Gradually lowering the dose of the corticosteroid gives the adrenal glands time to step-up natural production, thus preventing such withdrawal symptoms as severe weakness and fatigue.

While some RA patients may be leery of corticosteroids, others embrace them – and no wonder, says Dr. Cohen. "They make the patient feel tremendously better."

Building a Better Corticosteroid

Efforts are underway to develop better and safer corticosteroids. A delayed release form of prednisone, Rayos, is now available. This preparation, taken before bedtime, releases its prednisone into the system at a time during the night when the adrenal glands are at their lowest activity. The result for patients is an improvement in early morning stiffness.

"People with RA know that symptoms are usually much worse in the mornings," says Dr. Kirwan. "This delayed release formulation has been shown to get better control of morning stiffness compared to taking corticosteroids in the morning."

Dr. Kirwan says researchers are looking for other ways to mitigate side effects of corticosteroids without sacrificing therapeutic effects. “One option is to find a new type of substance, called a SEGRA, or selective glucocorticoid receptor agonist, which only affects the inflammation action, not the metabolic one.”

Another involves creating what might be called “smart” corticosteroid injections. “The corticosteroid is attached to liposomes (basically a protective enclosure) which naturally home in on places where inflammation is happening,” he says.

As flawed as these drugs may be, clinicians and patients agree, they work.

Celecoxib is a Safe Treatment for Arthritis

Lara C. Pullen, PhD

Compiled and summarized by:
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A non-inferiority study has found moderate doses of the selective cyclooxygenase (COX-2) inhibitor celecoxib comparable to ibuprofen and naproxen with regards to cardiovascular safety.

"Celecoxib is at least as safe as, if not safer than, commonly used non-selective NSAIDs [non-steroidal anti-inflammatory drugs], such as ibuprofen and naproxen," writes investigator Daniel Solomon, MD, MPH, a professor of rheumatology at Harvard Medical School, in an email to The Rheumatologist. "These findings held up in the overall PRECISION study populations, as well as key subgroups, such as osteoarthritis vs. rheumatoid arthritis, low-dose aspirin users vs. non-users and those with prior cardiovascular events vs. those with only cardiovascular risk factors."

Steven Nissen, MD, cardiologist at the Cleveland Clinic in Ohio, and colleagues published the results of the Prospective Randomized Evaluation of Celecoxib Integrated Safety vs. Ibuprofen or Naproxen (PRECISION) trial Dec. 29 in The New England Journal of Medicine. The investigators designed the trial in response to concerns about the safety of celecoxib. Specifically, another selective COX-2 inhibitor, rofecoxib, was withdrawn from market in 2004 due to evidence of adverse cardiovascular effects. Its withdrawal was associated with controversy, and in its wake, regulatory restrictions have limited the dose of celecoxib, the last remaining selective COX-2 inhibitor, to 200mg daily for most patients.

"Although the primary purpose of the trial was to assess cardiovascular outcomes, we also adjudicated gastrointestinal [GI] and renal outcomes to provide a comprehensive safety evaluation," explain the authors in their discussion. "To compare the three drugs, we constructed a two component composite of two adjudicated outcomes - clinically significant gastrointestinal events and iron-deficiency anemia of gastrointestinal origin." Celecoxib treatment resulted in lower rates of gastrointestinal events than did either comparator drug.

"The major clear advantage of celecoxib is that users had fewer GI bleeds," emphasizes Dr. Solomon, who was involved in the study. "As well, there was a reduced risk of renal events comparing celecoxib with ibuprofen."

Noninferiority Trial

The study included 24,081 patients with rheumatoid arthritis or osteoarthritis who were randomly assigned to receive either celecoxib, naproxen or ibuprofen for a mean treatment duration of 20.3 ± 16.0 months. The study was performed at 926 centers in 13 countries between October 2006 and June 2014. The patients were evaluated for a mean follow-up period of 34.1 ± 13.4 months. Adherence (31.2%) and retention (72.6%) were lower than in most clinical trials that assess cardiovascular outcomes.

The noninferiority trial required that prespecified criteria be met in two populations: intention-to-treat population and on-treatment population. In the intention-to-treat analysis, the primary outcome (cardiovascular death, nonfatal myocardial infarction or nonfatal stroke) occurred in 2.3% of the patients in the celecoxib group, 2.5% of patients in the naproxen group and 2.7% of patients in the ibuprofen group. In the on-treatment analysis, a primary outcome event occurred in 1.7% of patients in the celecoxib group, 1.8% of patients receiving naproxen and 1.9% of patients receiving ibuprofen. Thus, when celecoxib was compared with either naproxen or ibuprofen, it met all prespecified noninferiority requirements (P<0.001 for non-inferiority in both comparisons).

"We also included a broader outcome-major adverse cardiovascular events-as a secondary composite outcome to provide greater power to detect differences among the three treatments," write the authors in their discussion. "Fewer major adverse cardiovascular events occurred in the celecoxib group than in the ibuprofen group, but the difference did not reach significance in the intention-to-treat population (P=0.06). The rate of death from any cause was lower in the celecoxib group than in the naproxen group, although the difference did not reach significance (P=0.052)."However, the rate of nonfatal myocardial infarction was higher in the ibuprofen group than in the naproxen group (hazard ratio, 1.39; 95% confidence interval, 1.01 to 1.91; P=0.04).

The investigators also found that the rate of hospitalization for hypertension was significantly lower in the celecoxib group than in the ibuprofen group (hazard ratio, 0.60; 95% confidence

interval, 0.36 to 0.99, P=0.04). However, there was no significant difference between the rates of hospitalization for hypertension between the celecoxib group and the naproxen group.

"The results were consistent with much of the observational data and some of the prior trials, so the findings were not surprising," explains Dr. Solomon. "But, they were very helpful for rheumatologists and their patients [because] we can now have greater confidence in the relative safety of different NSAIDs."

The authors note that their study addresses only the relative safety of these three drugs and does not specifically address the safety of the many other NSAIDs on the market.

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Answer of Photo Quiz of 9th Issue

Answer

- Raynaud's Phenomenon

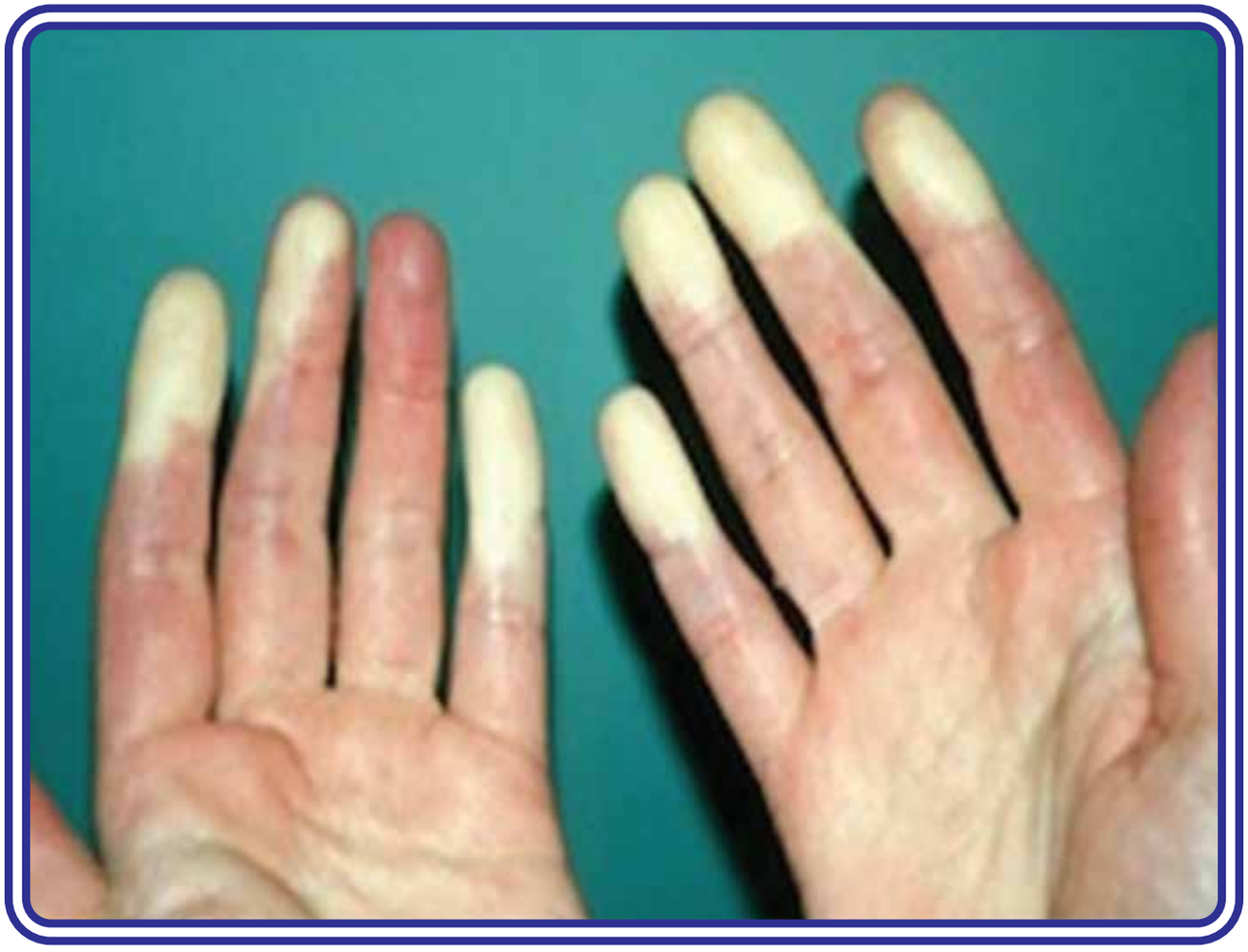

Photo Quiz

Question

What is the diagnosis for the given picture?