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International Medical Research

Spring 2014 Rheumatology Newsletter I

Rheumatoid Arthritis - A Crippling Invader

Rheumatoid arthritis (RA) is a serious inflammatory arthritis and autoimmune disease, which affects one to three percent of the world's population. This disease occurs when our immune system which involves the interaction between T cells, B cells, and other immune cells, a highly complex defense network that protects our bodies from harmful invaders such as bacteria, viruses, infectious microorganisms and even cancer, goes astray, mistaking joint tissue for a foreign invader. It then attacks the thin and delicate substance which lines and protects our joints called the "synovial membrane," and causes inflammation. When the inflammatory process advances, enzymes and other chemical mediators released from white blood cells can damage cartilage, bone and ligament causing a joint to become deformed and impairing its function.

Joints most commonly affected by RA are the fingers, wrists, elbows, shoulders, knees, ankles, neck, and jaw in a symmetrical fashion. Usually, but not always, small, firm bumps called "rheumatoid nodules" appear throughout the body. Further damage to the neck and spine can create instability in the spine and weakness in the arms and legs. Furthermore, RA does not limit itself to joints alone, as it can affect your eyes, lungs, heart, blood vessels and nerves.

Although RA emerges most commonly in thirty to fifty-year-olds, it can strike at any age, even in children and the elderly. In general, the older you are when RA strikes, the milder your symptoms are likely to be. Your chances of developing RA is about one to two percent, while your odds increase to two to four percent if a sibling has RA and to twelve to fifteen percent if your identical twin has RA. The risk for a child born of a mother with RA is somewhat greater, but the possibility is so low that it is not considered a strong factor.

The female sex hormone appears to be associated with a higher risk for developing RA, which explains why women are three times more likely to be affected than men. Childbirth, breast-feeding and menopause tend to induce painful RA flare-ups, but on the other hand, symptoms tend to lessen during pregnancy. About 75% of women affected with RA, who become pregnant, notice significant improvement in joint pain and swelling even without medication, particularly at the third trimester, while 20% of women fail to improve and 5% get worse.

Even though the process is not yet fully understood, it is evidence that complex changes within a pregnant woman's immune system not only allows a fetus to survive within the uterus, but can potentially impede the inflammatory process of rheumatoid arthritis, if she has it. Interesting, most women will notice their RA flare within six to eight months after delivery, and some 10% of those during the first two weeks. Even though several studies have shown an increased risk of miscarriage for patients with RA, there is no existing evidence that RA affects fertility or a developing fetus.

How is The Diagnosis of RA Made?

If you have RA, you will feel stiff in the morning, for more than an hour, and suffer from pain and swelling in your joints. Most commonly affecting the fingers, wrists, elbows, shoulders, ankles, neck and jaw in a symmetrical (equal) fashion, rheumatoid arthritis can also affect any part of your body. Some people even experience weight loss, anemia, low-grade fever and fatigue. Frequently, patients experience a sudden worsening of joint pain and swelling called a "flare". The reasons for this is unknown, however, weather change, hormone levels, infection, and stress can aggravate RA.

To determine if you have RA, a rheumatologist would perform a physical exam in addition to routine blood tests such as a rheumatoid factor (RF) and an anti-CCP. Even though seventy to eighty percent of RA patients have RF in their blood, its presence does not automatically indicate RA, as this blood test can also suggest other disorders such as hepatitis C and Sjogren's syndrome. Moreover, thirty to forty percent of the elderly have weak or moderate positive RF results and do not have RA. However, in general, RA patients with a positive RF tend to have more severe symptoms than those with a lower level.

Other blood tests, the ESR, are conducted to determine the rate at which the red blood cells settle to the bottom of a test tube, which indicates the intensity of inflammation. The higher the ESR is, the more severe inflammation, and vice versa. Although X-ray of hands and feet may show joint space narrowing or bone damage, it can be normal at the early stage of RA. Ultrasound and MRI can detect the early change of synovium (synovitis) or even minimal bone damage.

Early Aggressive Treatment of RA is Crucial

Between five and twenty percent of people with mild RA usually experience a spontaneous disappearance of symptoms within the first two years. However, more than fifty percent of those will have a recurrence of RA of different intensity. Another five to twenty percent will have a more progressive course, more often leading to some joint deformity. Usually more than eighty percent will become partially disabled within twelve years of diagnosis and sixteen percent will become completely disabled. This is why RA is called the "crippling arthritis" and its course needs a defensive action.

The main goal in the fight against rheumatoid arthritis is to reduce inflammation and pain and to prevent or minimize joint damage. Because most joint destruction with RA begins during the first two years of the disease, an early and aggressive treatment offers the best odds of slowing its progression and preventing joint damage.
Due to an increased understanding of rheumatoid arthritis pathogenesis, the strategic plan in treating RA has changed from using NSAIDs and corticosteroids to control symptoms, to so-called disease modifying anti-rheumatic drugs (DRAMDs), such as Methotrexate, Azulfidine, Plaquenil or Arava which could alter the inflammatory process and slow down joint damage.

Despite the powerful of DMARDs drugs, only 60-70 percent of patients respond to treatment. Xelianz (tofacitinib), a new small molecule DMARD, is proven to be even more effective than traditional DMARDs.

Biologic Agents-New Breakthrough Treatment

More recently, thanks to scientific breakthroughs in molecular biology and genetic engineering, we have a better understanding of the role of T cells, B cells, and chemical mediators in RA and other autoimmune diseases. Tumor necrosis factor (TNF), IL-6, IL-1and other cytokines are key chemical mediators that can cause inflammation and joint damage. However, if these chemical mediators are blocked, if communication between T cells and B cells is interrupted, or if B cells are eliminated, inflammation and joint damage can be impeded and even prevented.

Currently, there are five anti-TNF biologic agents that can effectively block TNF molecules: etanercept (Enbrel), adalimumab (Humira), infliximab (Remicade), golimumab (Simponi) and certolizumab pegol (Cimzia). Like anti-missiles, anti-TNF agents can lock in on a target (TNF) and block the enemy's offensive maneuvers.

There are other types of biologic agents for RA. Unlike other biologic agents, abatacept (Orencia) inhibits T cell activation and reduces joint inflammation. Rituximab (Rituxan) targets and depletes B cells. Tocilizumab (Acterma) can block IL -6. All are proved to be similarly effective as anti-TNF to control inflammation and prevent joint damage.

Furthermore, new biologic agents such as anakina, rilonacept and canakinumb can block IL-1 and are successful in treating patients with systemic onset

juvenile idiopathic arthritis. Even though RA can be debilitating, these new biologic drugs and small molecule DMARDs give us good reason to be optimistic.

RA and Osteoarthritis (OA)

In the past 5 years, Tom, a 65 year-old man, had gradually developed pain, stiffness at the base of his thumb and bony bump at the knuckles, along with brief stiffness in the morning. He also had pain in his neck and knees for many years. Did he have RA?

Over 16 million people in the United States have osteoarthritis. That means, that by the time we reach sixty, half of us will have some degree of osteoarthritis. Osteoarthritis is often referred to as a degenerative disease, and in general is the result of wear and tear on a joint due to aging, obesity, overuse, or injury. Cartilage, which is smooth and moist, becomes thin and rough, wearing itself down to the point of causing the bones to rub together, thus causing severe pain and reducing joint movement.

Most commonly, osteoarthritis affects the fingers, knees, hips, neck and lower back. If you have osteoarthritis, you may experience brief morning stiffness, pain with movement, bony growths on finger and knee joints, as well as joint "cracking" upon movement. X-ray reveals joint narrowing and bone overgrowth. RF and anti-CCP are negative. ESR is not elevated. Although cartilage breakdown may cause a little inflammation, osteoarthritis typically is not associated with inflammation and should not be treated with corticosteroids, DMARDs and biologic agents.

RA and Psoriatic Arthritis

In the past 6 months, John, a 40-year-old man, with a 10-year history of psoriasis, developed joint pain and swelling of his knuckles, ankles and toes. His back is stiff especially at night and in the morning. ESR was elevated, but RF was normal. Did he have RA?

About 95% of people with psoriatic arthritis (PsA) experience swelling of the hand, wrist, elbow, knee, ankle, foot joints, and their surrounding tendons. Such swelling gives fingers and toes a sausage-like appearance, which makes grasping an object or making a fist very painful. PsA also frequently affects tendons such as the achilles tendon (in the heel) or plantar fascia (in the sole of the foot). Patients experience pain in the heels or bottoms of feet, particularly in the morning when taking their first steps.

The other five percent of people with psoriatic arthritis have inflammation of the spinal joints. This form of psoriatic arthritis most commonly affects joints in the neck, lower back and sacroiliac joints (tailbone area). Patients suffer pain and stiffness in the neck, lower back, and buttocks that is worse at night and first thing in the morning. A common complaint with psoriatic arthritis of the spine is that patients usually are awakened at night due to an increase in pain.

RA and Inflammatory Bowel Disease

Tim, a 35-year-old man with a history of Crohn's disease, suffered with frequent abdominal cramping and bloody diarrhea. Additionally, during the past few months, he has experienced joint pain and swelling in his left knee and ankles, which he has observed to be linked to his bowel condition. What kind of arthritis he had?

There are two distinct forms of inflammatory bowel associated arthritis: one involving the arm and leg joints called peripheral arthritis, and the other involving the spine called spondylitis. Peripheral arthritis, the more common of the two, tends to be a sign of bowel inflammation, often showing up just before bowel symptoms or flare ups occur, and subsiding when bowel inflammation improves (either spontaneously or as a result of treatment). Normally involving large joints, such as the knee or ankle, few joints are affected at the same time and they eventually improve without causing joint damage. While peripheral arthritis is best treated by controlling bowel inflammation, its prognosis is good.

In contrast, spondylitis tends to be present for even years before bowel symptoms appear. Patients experience back pain and stiffness, particularly in the morning. Unlike peripheral arthritis, spondylitis seems to be associated, in more than half the cases, with the gene called HLA-B27, but not the activity of bowel inflammation.

Even though the treatment of psoriatic arthritis (PsA) and inflammatory bowel related arthritis is similar to rheumatoid arthritis (RA), spondylitis has relatively poor response to MTX and other DMARDs but excellent response to biologic anti-TNF agents. In generally, they test negatively for rheumatoid factor, a blood test that is commonly positive with RA. The pattern of joint involvement is also different.

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Juvenile Idiopathic Arthritis

Kathryn, an active and healthy nine year old girl, loved to swim and play soccer. One day, she started complaining about her knees, and soon, they became swollen, warm and painful. Every morning, when Kathryn would wake up, she felt very stiff until she began moving around. Finally, Kathryn was diagnosed to have juvenile idiopathic arthritis (JIA, also called juvenile rheumatoid arthritis).

JIA is not an uncommon disease. Approximately 50,000 to 200,000 children within the United States develop JIA, usually between the ages of three and thirteen. JIA consists of three distinct types of arthritis: polyarticular, pauciarticular and systemic.

About 20 percent of children with JIA have polyarticular arthritis: poly (many) articular (joints) arthritis (inflammation). Usually, polyarticular JIA involves five or more joints symmetrically, meaning both right and left, and is quite similar to adult rheumatoid arthritis. Often, the small joints of the hands are affected, as well as the knees, ankles, hips, feet, neck and jaw. Roughly half of the children affected with polyarticular arthritis will test positive for rheumatoid factor (RF), which can identify, as in adult RA, those who will not do well. Children with a positive RF may also have a greater risk of developing a more chronic, progressive form of the disease, which may cause joint damage. Polyarticular JRA affects twice as many girls than boys.

Pauci (few) articular arthritis, the most common form of JIA, affects over 50 percent of children with arthritis, mostly girls. Joint involvement occurs asymmetrically, meaning a single joint on one side of the body usually in the knees, elbows, wrists, and ankles. Children with pauci-articular JIA usually test positive for anti-nuclear antibodies (ANA), antibodies in the cell's nucleus, which can make them more susceptible to iridocyclitis and chronic uveitis, two types of potentially serious inflammatory eye conditions. Boys with pauci-articular JIA have a different disease pattern than girls. They generally do not have ANA, therefore are less likely to develop eye disease and their arthritis tends to affect the joints of the spine and hips. Furthermore, boys seem to have the genetic marker HLA-B27, which suggests an early form of ankylosing spondylitis (HLA-B27 arthritis).

The least common form of JIA is systemic, meaning involvement of the whole body, not just one part: internal organs as well as joints. This type of JIA affects both boys and girls equally and while systemic remission is possible, joint involvement does seem to persist. Additional symptoms may include fever, inflammation of the heart (myocarditis) or its outer lining (pericarditis) or lungs (pleurisy), anemia (low red blood count), or enlarged lymph nodes or spleen.

The treatment of JIA relies on an early and correct diagnosis to minimize symptoms and to control the disease process. A treatment course should be formatted around your child's specific symptoms and type of arthritis. Usually, medication such as DMARDs or biologic agents, exercise, eye, dental care, and healthy eating habits are the treatment options available for good results.

Next Issue:

- NSAIDs and Corticosteroids
- Disease-modified Anti-rheumatic Drugs (DMARDs)
- Biologic Agents
- Small molecule DMARDs

RESEARCH TREATMENT EDUCATION