Gillette Children's Specialty Healthcare

A PEDIATRIC Perspective

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Juvenile Spondyloarthropathies

Inflammation in Disguise

by Evren Akin, M.D.

The spondyloarthropathies are a group of inflammatory conditions that involve the spine (sacroiliitis and spondylitis), joints (asymmetric peripheral arthropathy) and tendons (enthesopathy). The clinical subsets of spondyloarthropathies constitute a wide spectrum, including:

- Ankylosing spondylitis
- Psoriatic arthritis
- Reactive arthritis
- Inflammatory bowel disease associated with arthritis
- Undifferentiated sacroiliitis

Depending on the subtype, extra-articular manifestations might involve the eyes, skin, lungs, gastrointestinal tract and heart. The most commonly accepted classification criteria for spondyloarthropathies are from the European Spondyloarthropathy Study Group (ESSG). See Table 1.

The juvenile spondyloarthropathies — which are the focus of this article — might be defined as any spondyloarthropathy subtype that is diagnosed before age 17. It should be noted, however, that adult and juvenile spondyloarthropathies exist on a continuum. In other words, many children diagnosed with a type of juvenile spondyloarthropathy will eventually fulfill criteria for adult spondyloarthropathy.

Initially, diagnosis and classification of juvenile spondyloarthropathies is difficult. One of the reasons for the complexity in diagnosis is that inflammatory back pain and radiographic changes — which are noted as classic spondyloarthropathy symptoms in the classification tables (see Tables 1 and 2) — are rare in childhood, especially before age 9. Conversely, monoarticular or asymmetric arthritis associated with enthesitis is a common presentation (seronegative enthesopathy and arthropathy syndrome).

Because psoriasis, bowel involvement and other symptoms of spondyloarthropathy might take years to develop, children might be diagnosed initially with juvenile rheumatoid arthritis (JRA), also known as juvenile idiopathic arthritis.

To further complicate matters, up to 30 percent of children with psoriatic arthritis might have a positive antinuclear antibody (ANA) and no psoriasis upon presentation; up to 20 percent might have silent uveitis, which is indistinguishable from the uveitis associated with JRA.

Classification

Classifying juvenile spondyloarthropathies is an ongoing effort. Several classification systems have been proposed, each with its own caveat. The ESSG criteria have been validated in children, but the emphasis on inflammatory spinal pain is problematic because such a symptom is uncommon in children.

Case Study

What does spondyloarthropathy look like in a child?

A 12-year-old boy is actively involved in sports. When his right toe starts to hurt, overuse injury is thought to be the cause. The right toe eventually swells up, and he is referred to a rheumatologist to evaluate for possible gout. Over the next few weeks, his right knee begins hurting as well. At the rheumatologist's office, arthritis of the right second toe and the right knee is noted. Family history is remarkable for back stiffness in the father, which is reported as "due to sports participation."

Antinuclear antibody (ANA) and rheumatoid factor are negative; HLA-B27 is positive. While the boy is on naproxen, within several months after the onset, his right ankle also swells up. He is soon started on sulfasalazine. Again the response is less than desirable, and his provider starts him on methotrexate.

The boy's knee and ankle seem to be getting better, but he has an acute episode of redness and pain in his right eye about a year and a half into the illness. He is diagnosed with uveitis and treated with topical steroids. He then has a flare-up of arthritis in his right knee, and infliximab is added to the methotrexate and sulfasalazine. He has a dramatic response to infliximab and is able to come off the sulfasalazine and reduce the methotrexate dose to a minimum; the arthritis quickly goes into remission. Six years later, at the age of 18, he is on minimal doses of infliximab and methotrexate, but each time the medications are discontinued, he develops morning stiffness in his lower back and joint pain in his right ankle. He has not had active arthritis for three years. He continues to play competitive sports in college and is well otherwise.
(See page 2 for Case Discussion.)

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The International League of Associations for Rheumatology (ILAR) classification (Table 2) of idiopathic arthritides of childhood includes a category of enthesitis-related arthritis that is more common than back pain in children with juvenile spondyloarthropathy. Inflammatory bowel disease-associated arthritis, however, is not included. Also problematic is that the ILAR classification includes psoriasis but excludes a family history of psoriasis in its criteria.

Clinical Characteristics

It usually takes years to confirm a diagnosis of spondyloarthropathy because symptoms unfold over a long period of time. Nevertheless, the following should raise suspicion of spondyloarthropathy:

- Recurrent joint pain with a family history of psoriasis, inflammatory bowel disease, or back pain and/or stiffness at rest
- History of recurrent tendonitis, apophysitis or plantar fasciitis
- Teenage patient with monoarticular arthritis (especially of the hip) or asymmetric arthritis involving fewer than four joints (pauciarticular)
- Pauciarticular arthritis that is difficult to control with nonsteroidal anti-inflammatory drugs (NSAIDs) and methotrexate
- History of frequent trips to a chiropractor (in the teenager or teenager's parent) for back adjustments

Asymmetric arthritis of the lower extremities is typical but not the rule. Tenderness over insertion of the patellar tendon, in the Achilles tendon, and at the attachment sites of the plantar fascia around the heel and metatarsal heads would suggest enthesopathy. Tendonitis might be present. A modified Schober's test might show limited spine flexion, although it is not common at presentation. Likewise, chest expansion is usually preserved in the early disease course.

The inflammatory back pain and radiographic changes of sacroiliitis — which are hallmarks of adult-onset ankylosing spondylitis — are uncommon in children. Rarely, you might find a teenager presenting with hip pain that has sacroiliitis.

The pattern of psoriatic arthritis generally resembles JRA. The ANA might be positive. The arthritis of psoriasis might precede the rash by years. Uveitis might be present but asymptomatic;

Case Discussion

This case study showcases the most common presentation of juvenile spondyloarthropathy — enthesopathy followed by arthritis. The patient had vague joint pain in his lower extremities, which were initially attributed to sports. Elusive joint pain with subtle exam findings are typical of enthesopathy. The most common sites are at the insertion of the patellar tendon, in the Achilles tendon and at the attachment sites of the plantar fascia around the heel and the metatarsal heads.

The patient presented with two swollen lower-extremity joints, which easily could have been mistaken for juvenile rheumatoid arthritis (JRA). It took several years for associated symptoms typical of spondyloarthropathy to unravel. Uveitis is commonly acute and painful in patients with spondyloarthropathy as opposed to asymptomatic silent inflammation in idiopathic JRA. The negative antinuclear antibody would not allow one to exclude JRA initially, but the disease course, the positive HLA-B27, and the acute uveitis left little doubt eventually.

It is common that family history is overlooked because the family attributes the inflammatory back pain in the parent to injury sustained years ago, to sports activity, or to a worn-out mattress. Inflammatory back pain is worse at night, rather than during activities (which would be more typical of mechanical causes). Most parents won't even mention plantar fasciitis (which is enthesopathy) or Achilles tendonitis, unless specifically asked. Also, psoriasis might be described as "eczema," and mild cases of inflammatory bowel disease might be labeled by the family as irritable bowel syndrome.

Table 1

European Spondyloarthropathy Study Group (ESSG)
Classification Criteria for Spondyloarthropathy

Inflammatory spinal pain **OR** synovitis (asymmetrical or predominantly in the lower limbs) plus any one or more of the following:

- Positive family history
- Psoriasis
- Inflammatory bowel disease
- Alternate buttock pain
- Enthesopathy
- Sacroiliitis

Table 2

International League of Associations for Rheumatology (ILAR)
Classification Criteria for Enthesitis-Related Arthritis
(a subgroup of juvenile idiopathic arthritis)

Arthritis and enthesitis, **OR** arthritis plus at least two of the following, **OR** enthesitis plus at least two of the following:

- Sacroiliac joint tenderness and/or inflammatory spinal pain
- Presence of HLA-B27
- Family history in at least one first-degree or second-degree relative of medically confirmed HLA-B27-associated disease
- Anterior uveitis that is usually associated with pain, redness or photophobia
- Onset in a boy after age 8

Exclusions:

- Psoriasis confirmed by a dermatologist in at least one first-degree or second-degree relative
- Presence of systemic arthritis

therefore, regular eye exams are necessary. Family history of psoriasis, presence of dactylitis and other nail findings is helpful in differentiating from JRA.

Inflammatory bowel disease in children might start out with arthritis or arthralgias months or years before bowel inflammation becomes clinically evident. Isolated hip arthritis; longstanding, vague gastrointestinal complaints; growth failure; difficult-to-control arthritis; and anemia might all help in diagnosing. None of these signs and symptoms, however, are specific. Screening antibodies for inflammatory bowel disease have high, false positivity in children, and pediatric gastroenterologists generally do not recommend the tests.

Laboratory Tests

There are no pathognomonic blood tests for spondyloarthropathies. Erythrocyte sedimentation rate might be elevated though it is nonspecific. The negative ANA and rheumatoid factor ("seronegativity"), in combination with positive HLA-B27 in a child with asymmetric arthritis and enthesitis, would be helpful. However, less than 5 percent of people who are HLA-B27 positive ever develop seronegative spondyloarthropathy, so diagnosis should not rely solely on this finding. Other laboratory tests are mentioned above in the context of certain subtypes.

Treatment

Medications and exercise programs are the mainstays of therapy. NSAIDs might be helpful to a degree, especially if there is inflammatory back pain. Sulfasalazine can work well for peripheral arthritis, but it is not as effective for axial disease. Methotrexate is a good option, although it might not induce remission on its own. Steroids are used sparingly, mostly as intra-articular injections. The combination of these conventional medications is often inadequate in controlling spondyloarthropathy. The discovery and use of biological agents that inhibit the tumor-necrosis factor (TNF) alpha molecule, however, have advanced the treatment of spondyloarthropathies in recent years. Anti-TNF alpha agents also are approved for use in Crohn's disease and psoriatic arthritis.

Etanercept (Enbrel), infliximab (Remicade) and adalimumab (Humira) are in this group and work in the majority of patients. They have improved short-term outcomes in ankylosing spondylitis and psoriatic arthritis dramatically. Whether they change the long-term disease course and outcome is not yet known. Regular exercises for stretching the spine are important to keep spinal mobility in patients with ankylosing spondylitis.

Prognosis

Patients might have long periods of remission, although "outgrowing" spondyloarthropathy is not an expectation. The majority of children who start out with enthesitis-related arthritis will eventually develop ankylosing spondylitis. It is difficult to accurately estimate prognoses because the spectrum of spondyloarthropathy is so wide. At least in one study, disease duration of longer than five years was found to be a negative prognostic factor, predicting more disability.

Author's PROFILE

Evren Akin, M.D., is a pediatric rheumatologist at Gillette Children's Specialty Healthcare in St. Paul, Minn. She sees patients with juvenile arthritis and related conditions.

Akin is an adjunct faculty member at the University of Minnesota School of Medicine and a member of the University's division of pediatric rheumatology. She received her medical degree from the medical faculty of Istanbul University in Turkey. She completed a one-year research fellowship at Beth Israel Hospital in Boston, and completed her internship and residency in pediatrics at Massachusetts General Hospital, Harvard Medical School. Akin then completed a postdoctoral fellowship in pediatric rheumatology at Tufts University's Floating Hospital for Children in Boston.

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