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Juvenile Spondyloarthritis / Enthesitis Related Arthritis (SpA-ERA)

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1. WHAT IS JUVENILE SPONDYLOARTHRITIS/ENTHESITIS-RELATED ARTHRITIS (SpA-ERA)

1.1 What is it?

Juvenile SpA-ERA constitutes a group of chronic inflammatory diseases of the joints (arthritis), as well as tendon and ligament attachments to certain bones (enthesitis) and affects predominantly the lower limbs and in some cases the pelvic and spinal joints (sacroiliitis - buttock pain and spondylitis - back pain). Juvenile SpA-ERA is significantly more common in people that have a positive blood test for the genetic factor HLA-B27. HLA-B27 is a protein located on the surface of immune cells. Remarkably, only a fraction of people with HLA-B27 ever develops arthritis. Thus, the presence of HLA-B27 is not enough to explain the development of the disease. To date, the exact role of HLA-B27 in the origin of the disease remains unknown. However, it is known that in very few cases the onset of arthritis is preceded by gastrointestinal or urogenital infection (known as reactive arthritis). Juvenile SpA-ERA is closely related to the spondyloarthritis with onset in adulthood and most researchers believe these diseases share the same origin and characteristics. Most children and adolescents with juvenile spondyloarthritis would be diagnosed as affected by ERA and even psoriatic arthritis. It is important that the names "juvenile spondyloarthritis", "enthesitis-related arthritis" and in some cases "psoriatic arthritis" may be the same from a clinical and therapeutic point of view.

1.2 What diseases are called juvenile SpA-ERA?

As mentioned above, juvenile spondyloarthritis is the name for a group of diseases; the clinical features may overlap with each other, including axial and peripheral spondyloarthritis, ankylosing spondylitis, undifferentiated spondyloarthritis, psoriatic arthritis, reactive arthritis and arthritis associated with Crohn’s disease and ulcerative colitis. Enthesitis-related arthritis and psoriatic arthritis are two different conditions in the JIA classification and are related to juvenile SpA.

1.3 How common is it?

Juvenile SpA-ERA is one of the most frequent forms of chronic arthritis in childhood and it is more frequently seen in boys than in girls. Depending on the region of the world, it can account for about 30% of children with chronic arthritis. In most cases, the first symptom appears around the age of 6 years. Since a great proportion of patients (up to 85%) with juvenile SpA-ERA are HLA-B27 carriers, the frequency of adult SpA and juvenile SpA-ERA in the general population and even in certain families depends on the frequency of this marker in the normal population.

1.4 What are the causes of the disease?

The cause of juvenile SpA-ERA is unknown. However, there is a genetic predisposition, which in most patients relies on the presence of HLA-B27 and other genes. Today, it is thought that the HLA-B27 molecule associated with the disease (which is not the case for 99% of the population with HLA-B27) is not synthesized properly and when it interacts with cells and their products (mostly pro-inflammatory substances), it triggers the disease. Nonetheless, it is very important to emphasize that HLA-B27 is not the cause of the disease, but rather a susceptibility factor.

1.5 Is it inherited?

HLA-B27 and other genes predispose individuals to juvenile SpA-ERA. In addition, we know that up to 20% of patients with such diagnoses have first or second degree relatives with the disease. Thus, juvenile SpA-ERA

might have some family clustering. However, we cannot say that juvenile SpA-ERA is hereditary. The disease will affect only 1% of people with HLA-B27. In other words, 99% of people who have HLA-B27 will never develop SpA-ERA. Moreover, the genetic predisposition is different among ethnic groups.

1.6 Can it be prevented?

Prevention is not possible as the cause of the disease is still unknown. It is not useful to test other siblings or relatives for the HLA-B27 if they have no symptoms of juvenile SpA-ERA.

1.7 Is it infectious?

Juvenile SpA-ERA is not an infectious disease, not even in cases triggered by an infection. Moreover, not all people infected at the same time with the same bacteria develop juvenile SpA-ERA.

1.8 What are the main symptoms?

Juvenile SpA-ERA has common clinical characteristics.

Arthritis

The most common symptoms include joint pain and swelling, as well as limited mobility of the joints.
Many children have oligoarthritis of the lower limbs. Oligoarthritis means that the disease involves 4 or fewer joints. Patients developing chronic disease may have polyarthritis. Polyarthritis means that the articular involvement affects 5 or more joints. The joints most frequently affected are the knee, the ankle, the mid-foot and the hips; less frequently, arthritis involves the small joints of the foot.
Some children may have arthritis of any joint of the upper limbs, particularly the shoulders.

Enthesitis

Enthesitis, inflammation of the enthesis (the site where a tendon or ligament attaches to the bone), is the second most frequent manifestation in children with SpA-ERA. Commonly affected entheses are located at the heel, in the mid-foot and around the kneecap. Most

common symptoms include heel pain, mid-foot swelling and pain and kneecap pain. Chronic inflammation of the enthesis may lead to bony spurs (bony overgrowth) causing heel pain in many cases.

Sacroiliitis

Sacroiliitis refers to the inflammation of the sacroiliac joints, located in the rear of the pelvis. It is rare during childhood; it most frequently occurs 5 to 10 years after the onset of arthritis.
The most common symptom is alternating buttock pain.

Back pain; spondylitis

Involvement of the spine, very rare at onset, may occur later in the course of the disease in some children. The most common symptoms include back pain during the night, morning stiffness and reduced mobility. Back pain is frequently accompanied by neck and, in rare cases, also by chest pain. The disease may cause bony overgrowth and bridging joining the vertebral bodies many years after onset in a few patients. Therefore, it is almost never observed in children.

Eye involvement

Acute anterior uveitis is due to inflammation of the iris of the eye. Although it is an uncommon complication, up to one-third of patients may be affected once or several times during the course of their disease. Acute anterior uveitis presents with ocular pain, redness and blurred vision for several weeks. It usually affects one eye at a time but it may have a recurrent pattern. Immediate control by an ophthalmologist (an eye doctor) is necessary. This type of uveitis is different from the type found in girls with oligoarthritis and antinuclear antibodies.

Skin involvement

A small subset of children with juvenile SpA-ERA may already have or may develop psoriasis. In these patients, the classification as ERA is excluded and changed to psoriatic arthritis. Psoriasis is a chronic skin disease with patches of scaling skin mainly located on the elbows and the knees. The skin disease may precede the arthritis by years. In other patients, the arthritis can already exist several years before the first psoriasis rash occurs.

Bowel involvement

Some children with intestinal inflammatory disorders, such as Crohn’s disease and ulcerative colitis, may develop spondyloarthritis. ERA does not include inflammatory bowel disease as one of its components. In some children, intestinal inflammation is subclinical (without gut symptoms) and the severity of articular symptoms is greater, requiring specific treatment.

1.9 Is the disease the same in every child?

The spectrum is wide. While some children have a mild and short-term disease, others have a severe, long-term and disabling disease. Thus, it is possible that many children might have just one joint involved (e.g. a knee) for several weeks and never present the same picture or additional features for the rest of their life, while others develop persistent symptoms extending to several joints, entheses and the spinal and sacroiliac joints.

1.10 Is the disease in children different from the disease in adults?

The initial symptoms of juvenile SpA-ERA are different from those of adult SpA, but most data suggest that they belong to the same spectrum of diseases. Peripheral (limbs) joint disease is more frequent at onset in children, in contrast to the more frequent axial (spinal and sacroiliac joints) involvement in adults. Disease severity is greater in children than in adults.