Imaging of Juvenile Idiopathic Arthritis

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KEYWORDS

• Juvenile idiopathic arthritis • Juvenile spondyloarthropathies • Radiography • Ultrasound • MR imaging • MR imaging scoring system

KEY POINTS

- Multimodal imaging analysis plays a key role in the diagnosis and treatment monitoring of juvenile idiopathic arthritis (JIA).
- A concrete knowledge of normal joint anatomy throughout pediatric age groups is important.
- A reproducible, accurate, and established scoring system for use in international routine clinical care for monitoring and predicting long-term response to therapeutic interventions is still to be developed for any joints on MR imaging.

INTRODUCTION

JIA is an umbrella term covering several distinct categories that share common features.[1]

The term JIA replaced, in the 1990s, the older terms, juvenile rheumatoid arthritis (used commonly in the United States) and juvenile chronic arthritis (preferred in Europe). As defined by the International League of Associations for Rheumatology (ILAR), JIA diagnosis relies on the presence of arthritis that persists for at least 6 weeks, begins before the age of 16 years, and is of unknown origin.[2] The classification, established in Durban in 1997 and revised in Edmonton in 2001, defines different subtypes characterized by their clinical, demographic, and genetic features, translating into different responses to treatment (**Box 1**).

Modern multimodal imaging, including conventional radiographs (CRs), ultrasound (US), and MR imaging, plays a key role in the diagnosis, follow-up, and treatment monitoring of JIA. Unlike imaging of rheumatoid arthritis and other inflammatory joint conditions in adults, extensively studied in the past 2 decades, the available literature for JIA is more limited, and consensus articles about the role of imaging of the different manifestations of JIA have been published only recently.

The European League Against Rheumatism and the Pediatric Rheumatology European Society have recently published a consensus article with recommendations to guide radiologists and clinicians in choosing the best imaging technique for each particular clinical setting.[3] Specific scoring system for each joint may contribute to make the staging and the follow–up more reproducible.

EPIDEMIOLOGY OF JUVENILE IDIOPATHIC ARTHRITIS

Based on the current classification established by the ILAR in 2001, the incidence of JIA in European children is approximately 3 to 15 individuals per

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Box 1
International League of Associations in Rheumatology classification criteria for juvenile idiopathic arthritis

1. Systemic
2. Oligoarthritis
   a. Persistent
   b. Extended
3. Polyarthritis (RF negative)
4. Polyarthritis (RF positive)
5. Psoriatic arthritis
6. ERA
7. Undifferentiated arthritis
   a. Fits no other category
   b. Fits more than 1 category

100,000 individuals younger than 16 years.[4] Chronic arthritis seems worldwide in distribution, but the reported incidence and prevalence vary considerably throughout the world. Ethnic differences have been reported to have a significant influence on JIA epidemiology, whites being more affected than African American and Asian individuals.[5,6]

Age at disease onset and gender ratio depends on clinical subset. In most published series of patients with JIA, the female/male ratio is of 2/1 to 3/1, although equal gender ratios have been reported in certain ethnic groups, such as Indian and black South African children.[5] JIA onset occurs at approximately 6 years of age in patients with polyarticular disease in both genders, whereas young patients with oligoarticular disease have a mean age of approximately 4 years in girls and 10 years in boys.[7] Gender has a high influence in determining some features of JIA. As an example, oligoarticular JIA has a female preponderance as high as 8:1 in children younger than 8 years, mainly in a subset of patient with antinuclear antibodies positivity and associated iridocyclitis.[8]

PATHOGENESIS

The etiology and pathogenesis of JIA are unclear but thought to be the result of a combination of genetics and environmental factors. Twin and family studies suggest a role of genetic factors in the predisposition to JIA. Numerous associations between HLA alleles and JIA categories have been reported in multiple populations. Although the juvenile spondyloarthopathies or enthesitis-related arthritis (ERA) is strongly associated with the HLA-B27, other associations have been described for both HLA or non-HLA susceptibility loci with some JIA categories, in particular, *HLA-DRB1:01* and *PTPN22* or *STAT4* variants with oligoarticular or RF-negative polyarticular JIA, shared epitope encoding *HLA-DRB1* with RF-positive polyarticular JIA. Some alleles that predispose to the risk of category might be also protective against another JIA category.[9]

In combination with genetic factors, environmental triggers are also described as involved in the pathogenesis of JIA. Infectious viral or bacterial agents are mainly considered potential triggers. It has been reported an interaction between the immune system and microbiome which may play a role in the autoimmunity or contributing in the development of JIA.[10]

JIA is an immune-mediated disease. In a majority of JIA subset, errors of adaptive immunity (mistakes by antigen-specific T and B cells) initiates an inflammatory response because a defect in normal self-inhibitory mechanisms. Conversely, systemic JIA could be considered an autoinflammatory disorder involving pathways associated with innate immunity. Several cells types, including monocytes/macrophages, T lymphocytes or B lymphocytes, or specific cytokines, such as tumor necrosis factor (TNF)-α, interleukin-6, and interleukin-1, play an important role in the pathophysiology of JIA. Therapeutic advances with biologics agents are known to be efficient for specific categories of JIA, suggesting a specific role of these cells or cytokines in the disease with a different way. Polyarticular and oligoarticular JIA are better responders to TNF-α blocking agents compared with systemic JIA, where anti–IL-6 or anti–IL-1 blocking agent is more efficient. Further insights into the disease pathogenesis will be provided by the continuous advances in understanding of mechanisms related to the immune response and inflammatory process implicated in JIA.

CURRENT CLASSIFICATION

1. The most frequent clinical subtype of patients with JIA is oligoarthritis (27%–60%).[4] By definition, the oligoarthritis subtype involves fewer than 4 joints within the 6 months of onset of the disease. It occurs typically in very young girls and is often associated with the presence of antinuclear antibodies. The patients of this subtype are at increased risk of asymptomatic uveitis and should be monitored closely to detect it early. Most patients in this group are first referred for an episode of arthritis of the knee. The second most frequent clinical