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Therapeutic advancements in juvenile idiopathic arthritis

Elizabeth A. Kessler, MD, MS [1], Mara L. Becker, MD, MSCE *

Division of Rheumatology, Department of Pediatrics, Children's Mercy Hospitals and Clinics, 2401 Gillham Road, Kansas City, MO 64108, USA

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A B S T R A C T

The treatment of juvenile idiopathic arthritis (JIA) has substantially evolved over the past two decades. Research has been conducted and is ongoing on how therapies can best be utilized either as monotherapy or in combination for enhanced efficacy. The introduction of biologic therapies that selectively target specific cytokines has changed the acceptable clinical course of childhood arthritis. In addition to the development and utilization of new therapeutic agents, the pediatric rheumatology community has made vital progress toward defining disease activity, developing validated outcome measures, and establishing collaborative networks to assess both clinical outcomes and the long-term side effects related to therapeutics for juvenile arthritis. In this chapter, we will discuss the therapeutic evolution in JIA over the past two decades. Although the largest strides have been made with biologic agents, and these newer drugs have more rigorous data to support their use, select commonly used non-biologic therapies are included, with the discussion focused on more recent updated literature.

Introduction

Juvenile idiopathic arthritis (JIA) is the most common pediatric autoimmune musculoskeletal condition, estimated to affect one in 1000 children [1]. It is classified based on age of onset, number and type of joints involved, and the presence of serologic markers, systemic signs, and symptoms. As the field has

* Corresponding author. Tel.: +1 816 234 3686; fax: +1 816 234 3082.
E-mail addresses: eakessler@cmh.edu (E.A. Kessler), mlbecker@cmh.edu (M.L. Becker).
[1] Tel.: +1 816 234 3686; fax: +1 816 234 3082.

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developed, significant work has been invested in the development of an agreed-upon classification system for juvenile arthritis worldwide. The current JIA subtypes are characterized as follows: systemic, oligoarticular, polyarticular, enthesitis-related, psoriatic, and undifferentiated arthritis [2] (Table 1). Despite this relatively rare condition with a heterogeneous disease phenotype and poorly understood pathophysiology, the treatment strategies for JIA have evolved tremendously over the past two decades.

Early treatment options for JIA were limited to nonsteroidal anti-inflammatory drugs (NSAIDs) including aspirin, corticosteroids, and non-biologic disease-modifying antirheumatic drugs (DMARDs) like D-penicillamine, gold, sulfasalazine (SSZ), and methotrexate (MTX). Historically, few treatment options were available for children with disease refractory to these medications, and the risk-to-benefit ratio for long-term corticosteroid use and many of the early DMARDs was not favorable, resulting in

Table 1
Definition of subtypes of juvenile idiopathic arthritis.[a]

Category	Characteristics
Systemic	Arthritis in ≥1 joint(s) with or preceded by quotidian fever of ≥2 weeks' duration documented for ≥3 days and accompanied by ≥1 of the following: 1. Evanescent erythematous rash 2. Generalized lymphadenopathy 3. Hepatomegaly and/or splenomegaly 4. Serositis *Exclusions*: a, b, c, d.
Oligoarticular	Arthritis in 1–4 joints during the first 6 months of disease A. Persistent – affecting ≤4 joints throughout disease course B. Extended – affecting >4 joints after the first 6 months of disease *Exclusions*: a, b, c, d, e.
Polyarticular, RF negative	Arthritis in ≥5 joints during first 6 months of disease, negative RF *Exclusions*: a, b, c, d, e.
Polyarticular, RF positive	Arthritis in ≥5 joints during first 6 months of disease, positive RF on 2 separate occasions at least 3 months apart *Exclusions*: a, b, c, e.
Psoriatic	Arthritis and psoriasis, or arthritis and ≥2 of the following: 1. Dactylitis 2. Nail pitting or onycholysis 3. Psoriasis in a first-degree relative *Exclusions*: b, c, d, e.
Enthesitis-related	Arthritis and enthesitis, or arthritis or enthesitis with ≥2 of the following: 1. Presence of or history of sacroiliac joint tenderness and/or inflammatory lumbosacral pain 2. Presence of HLA-B27 antigen 3. Onset of arthritis in male >6 years old 4. Acute anterior uveitis 5. AS, ERA, sacroiliitis with IBD, Reiter's syndrome, or acute anterior uveitis in a first-degree relative *Exclusions*: a, d, e.
Undifferentiated	Arthritis that fulfills criteria for no category or ≥2 categories
Exclusions	
	a. Psoriasis or history of psoriasis in the patient or first-degree relative b. Onset of arthritis in an HLA-B27-positive male >6 years old c. AS, ERA, sacroiliitis with IBD, Reiter's syndrome, or acute anterior uveitis in a first-degree relative d. Positive RF on two separate occasions at least 3 months apart e. SJIA in the patient

RF, rheumatoid factor; HLA-B27, Human Leukocyte Antigen B27; AS, ankylosing spondylitis; ERA, enthesitis-related arthritis; IBD, inflammatory bowel disease; SJIA, systemic JIA.

[a] Modified from the International League of Associations for Rheumatology [2].