Systemic Juvenile Idiopathic Arthritis

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KEYWORDS

• Systemic juvenile idiopathic arthritis • Juvenile idiopathic arthritis • Pediatrics
• Rheumatology • Macrophage activation syndrome

KEY POINTS

- The clinical presentation of systemic juvenile idiopathic arthritis (sJIA), often dominated by fever and systemic features, is unique in comparison to the other JIA subtypes.
- sJIA is a diagnosis of exclusion and requires adequate consideration of infectious, oncologic, autoimmune, and autoinflammatory diseases.
- Macrophage activation syndrome is a serious and potentially fatal complication of sJIA, characterized by sustained fever, organomegaly, cytopenias, coagulopathy, and high transaminases. It requires prompt evaluation and treatment.
- Newer biologic agents, particularly interleukin-1 and interleukin-6 inhibitors, are highly effective and have reduced the use of systemic corticosteroids.
- The primary care provider has a crucial role in monitoring children with sJIA for disease-related complications and medication-related adverse events.

INTRODUCTION

Systemic juvenile idiopathic arthritis (sJIA) is a very distinctive subtype of juvenile idiopathic arthritis (JIA) with unique clinical manifestations, associated complications, and therapeutic options. The full expression of sJIA is characterized by fever and arthritis, accompanied by at least one of the following: rash, generalized lymphadenopathy, hepatomegaly and/or splenomegaly, and serositis. However, the classic features are not always present at disease onset. Moreover, the symptoms and signs are nonspecific, overlapping with other inflammatory and non-inflammatory conditions. Therefore, sJIA, a rare cause of fever in children, remains a very challenging condition to diagnose, and pediatric primary care providers require a high index of suspicion to avoid unnecessary delays in establishing the diagnosis. In contrast to other JIA subtypes, children with sJIA often require hospitalization for severe systemic symptoms at onset or during flare-ups, require more intensive systemic treatment, and have higher disease-associated

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morbidity. Providers who comanage sJIA patients need to carefully monitor for associated systemic complications and for treatment-related adverse effects. In this review, the authors discuss primarily the clinical features, the differential diagnosis, complications, and management issues relevant to the pediatric primary care provider.

INCIDENCE OF SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

JIA is the most common rheumatic disease in childhood, with an estimated prevalence of 1 to 4 per 1000 children.[1,2] sJIA accounts for approximately 10% to 20% of JIA cases, with incidence rates ranging from 0.4 to 0.8 children per 100,000 children.[3]

DEMOGRAPHICS

Age

Peak age of presentation is 1 to 5 years of age. However, children can present throughout childhood and adolescence.[4]

Gender

Male and female children are affected equally, unlike other JIA subtypes.[4]

Ethnicity

sJIA occurs in children of all ethnic backgrounds.[5] A slightly higher prevalence rate has been reported in Japan and India than in the United States or Canada.[6,7]

WHEN TO CONSIDER SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

The diagnosis of sJIA should be considered in children who have unexplained, prolonged fever that spikes once or twice daily, especially when it is associated with intermittent rash, arthralgias, or arthritis.

HOW SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS PRESENTS

Classification Criteria

Widely accepted classification criteria for sJIA are based on the International League of Associations for Rheumatology (ILAR) classification criteria for JIA, which were revised in 2001 (**Box 1**).[5] These criteria require that the onset of symptoms occurs before the age of 16 years, the duration of arthritis is at least 6 weeks, and that other conditions are excluded. The term adult-onset Still disease may be considered part of the spectrum of sJIA and describes patients whose symptoms begin at the age of 16 years or older.[8] Distinct classification criteria exist for adult-onset Still disease, with the Yamaguchi criteria[9] and Fautrel's criteria[10] being the most well recognized. In contrast to the sJIA classification criteria, these criteria include arthralgia and do not require the presence of frank arthritis.

The ILAR criteria were developed to achieve consensus in identifying relatively homogeneous subgroups of JIA patients, primarily for research studies. Although not developed as diagnostic criteria, many physicians use them for this purpose. Most children with sJIA do not, in fact, meet ILAR classification criteria at initial presentation. Behrens and colleagues[4] found that only 30% met these criteria when they initially presented to a pediatric rheumatologist for assessment. Janow and colleagues[11] found that 71% of sJIA patients will eventually meet ILAR criteria during their disease course. The ILAR criteria may therefore not be sufficiently sensitive for the timely diagnosis and treatment of severe symptoms associated with new-onset sJIA. In practice, a presumptive diagnosis of sJIA is often made without arthritis being present for 6 weeks, if the symptoms