Systemic Juvenile Idiopathic Arthritis (SJIA)
The Most Serious Form of Chronic Childhood Arthritis

Systemic juvenile idiopathic arthritis (SJIA) is a rare and serious childhood autoinflammatory disease[1]. It is called 'systemic' because the inflammation affects the whole body, including a varying number of joints. The condition, when active, is characterized by daily spiking fevers, rash, chronic pain and arthritis that may result in joint destruction, functional disability and impaired growth[1,2]. Patients can also suffer enlargement of their liver and spleen, as well as inflammation of the lining of their organs[1]. SJIA affects less than one child per 100,000[3].

The role of inflammation in SJIA

Although the exact cause of SJIA is unknown, activation of the innate immune system is involved in the inflammation associated with SJIA. Evidence for this comes from increased levels of certain inflammatory signalling molecules (cytokines) in patients with SJIA[4]. The innate immune system is normally responsible for the initial response to infection, in contrast to 'acquired' immunity that develops after initial exposure to an infection.

It is thought that raised cytokine levels can cause inflammation in several organs, leading to a range of SJIA symptoms; such as the characteristic daily spiking fever, skin rash, and effects on blood-cell levels[3]. Interleukin-1 beta (IL-1 beta) is a cytokine that is produced excessively in patients with SJIA, and has been suggested to be a cause of these symptoms[5].

Inflammation can lead to severe complications in SJIA over time

The onset of SJIA peaks around 2 years of age, but onset can also occur until 16 years of age[1]. The time-pattern of symptoms can then be monocyclic, intermittent or persistent. One study found that the majority (two-thirds) of patients had persistent SJIA – leading to the worst outcomes – which had not gone into remission over the course of an average 10 years' follow-up in 77% of cases[6].

In addition to the acute inflammatory symptoms of SJIA, patients can experience multiple severe complications. These complications include 'macrophage activation syndrome' (MAS), which is a known, potentially fatal condition associated with SJIA that is characterized by liver abnormalities, bleeding disorders, central nervous system dysfunction and multiple organ failure[7,8]. Approximately 10% of SJIA patients are diagnosed with MAS, some of whom suffer repeated episodes[2]. MAS has been observed to be fatal for between 8% and 22% of patients[7].

Patients are also at risk of joint damage, osteoporosis and, much less commonly in recent years, amyloidosis[1,4]. They can face serious developmental and psychological consequences[1]. Deaths of SJIA patients occur due to the disease itself (e.g. cardiac complications and MAS) as well as causes related to treatment (e.g. corticosteroid-related complications)[9,10].

The impact of SJIA

SJIA has a high impact on patients' quality of life and also on their families, due to both the symptoms and treatment of the condition[1,11]. Children affected by SJIA can experience disability due to arthritis that can persist well into adult life[1,12]. These patients have also been

reported to suffer problems at school, including bullying, as well as a lack of independence due to treatment requirements[12]. Transfer from pediatric to adult rheumatology services can also prove stressful for patients and their families[12], while families of patients with SJIA also bear significant costs due to transport, over-the-counter medicines and home alterations[11].

Diagnosis and treatment challenges

Diagnosis of SJIA is challenging and often delayed, since many illnesses in young children can mimic the condition, including early-stage malignancy, infections and other autoinflammatory diseases[1]. There is no specific laboratory diagnostic test for SJIA, so diagnosis it is often based on exclusion, using a variety of laboratory and physical investigations[3].

The aim of SJIA therapy is to suppress systemic inflammation and induce disease inactivity[13]. Long-term corticosteroid use in children has declined due to potentially serious adverse effects, including Cushing syndrome, growth suppression, and osteoporosis[13]. Further research in this area may lead to the development of more effective therapies[1].

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ILARPR033-06/12