Juvenile Idiopathic Arthritis or Growing Pains: Catching Arthritis Early

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Joint pain is a common complaint in childhood. Chronic joint pain should be investigated to differentiate the more benign entities, such as growing pains and Osgood–Schlatter disease, from childhood arthritis. Juvenile idiopathic arthritis is the most common rheumatic disease in children. When diagnosed and treated early, long-term outcomes can be favourable. Treatment delay can lead to functional limitations and morbidity. In the last 25 years, new treatments have become available for arthritis; access to these medications for childhood arthritis remains limited due to the exclusion of paediatric patients in clinical trials.

Keywords

Arthritis, biologics, children, chronic arthritis, disease-modifying antirheumatic drug (DMARD), joint pain, juvenile idiopathic arthritis, magnetic resonance imaging (MRI)

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Why do we need to identify arthritis?

In children, joint pain occurs frequently; it is usually associated with activities or accidental falls and is generally short-lived. A small proportion of children have more persistent joint pain, and in this group, it is important to distinguish between benign causes such as growing pains or more concerning entities such as childhood arthritis. Childhood arthritis can have an insidious onset and, in contrast to adults, children are highly adaptable to functional limitations. It is not uncommon for parents to miss subtle swelling or decreased range of motion of a joint, leading to delays in presentation to healthcare professionals. Left untreated, childhood arthritis can lead to morbidity with lifelong consequences. Early recognition and treatment are important to prevent long-term accrual of irreversible damage.

Differential diagnosis of joint pain

Timing of the occurrence of pain can be a great contributor to help distinguish what might be the cause. Childhood arthritis leads to early morning stiffness and pain, which usually improves during the day and with activity. Some children report morning stiffness for only a few minutes, while others experience this for hours or throughout the day. Mechanical pain is absent in the morning and becomes more apparent during the day or with certain activities. Night-time pain is more typical for growing pains or malignancies. Growing pains are typically seen in children between the ages of 3 and 12 years with intermittent symptoms.[1] The hallmark of the pain is that it tends to occur at the end of the day or during the night and does not continue into the morning.[1] Pain symptoms can persist for months and can be disruptive to the family. The location of the pain is generally at the front of the thighs, calves and behind the knees bilaterally.[1] Limping or limited mobility is not associated with growing pains but can be seen in mechanical issues such as patella-femoral malalignment, Osgood–Schlatter disease and Sever's disease.[2,3] These issues often occur during growth spurts and can lead to acute and chronic issues. Although often thought to be benign and transient, a recent long-term study out of Denmark reported ongoing knee problems in those with Osgood–Schlatter disease in their youth.[2] Childhood arthritis, also known as juvenile idiopathic arthritis (JIA), is usually associated with swelling, warmth, redness or limited range of motion of the affected joints. Often, there will be a recent fall or injury that contributes to the delay in diagnosis, as these incidents can be common red herrings for children presenting with joint pain.

Juvenile idiopathic arthritis

Misconceptions

There are a number of myths and misconceptions surrounding the diagnosis and treatment of JIA. One of the most common misconceptions is that arthritis only affects adults. Despite arthritis becoming more common as one ages, there are different types of arthritis that can affect anyone at all stages of life, including young children and adolescents. JIA is a chronic inflammatory disease defined by the International League of Associations for Rheumatology (ILAR) criteria as arthritis in

one or more joints that begins before the 16th birthday and persists for at least 6 weeks with exclusion of other known conditions.[4] JIA is the most common inflammatory joint disease of childhood, with an estimated global incidence between 1.6 and 23 cases per 100,000 children.[5] JIA is a diagnosis of exclusion, where infection, trauma, malignancy or other rheumatologic diseases must be ruled out, where this in itself may also delay diagnosis. Unfortunately, many paediatric rheumatologists are located in urban cities working in academic hospitals, where patients living in rural areas would have more difficulty having access to these specialists. Another misconception is that joint pain is the only presenting symptom, whereas JIA encompasses at least seven distinct categories with varying symptoms, which can include fever, rash, fatigue, lymphadenopathy, multi-organ involvement and eye inflammation. Lastly, one misconception which, if believed, can cause worse outcomes for patients with JIA is that they cannot or should not participate in sports or other physical activity due to the risk of further damage to their joints. Studies have shown that patients with JIA are less active and more easily fatigued compared with their peers.[6–8] They are also twice as likely to have decreased bone density compared with their peers.[9,10] Inactivity in these patients can lead to deconditioning, disability, reduced quality of life and the potential for morbidity and mortality in adulthood.[11] Studies have shown that regular exercise can alleviate pain in patients with JIA and improve the quality of life for those with chronic diseases.[12,13] Adult rheumatoid arthritis studies have shown that exercise can increase muscle strength and have positive effects on increased bone mineral density.[14] Debunking many of these misconceptions and educating primary care providers as well as families is an essential component in improving care for these patients.

Treatment

Recent advancements in the treatment of JIA have allowed shifts in clinical practice, focusing on earlier and more targeted interventions improving long-term outcomes for these patients. The 2021 treatment guidelines for patients with JIA by the American College of Rheumatology (ACR) recommend early use of disease-modifying antirheumatic drugs (DMARDs) as well as biologic DMARDs, some first-line treatment options for certain JIA subtypes.[15] However, despite these guideline changes and treatment advancements, some studies have reported that 37–63% of patients with JIA continue to have active disease into adulthood.[16–18] With this, the transition from paediatric to adult care is a vulnerable time for patients, as inadequate transition between health systems is associated with loss of follow-up, higher risk of abruptly stopping treatment, more flares in the disease and increased disability.[19,20] In addition, many patients with JIA are reclassified using adult terminology after transition, with many reclassified to rheumatoid arthritis or ankylosing spondylitis.[21] Reasons for this may be due to increased access to treatment options, as well as being able to use validated disease activity scores, as the childhood disease activity scores may no longer apply in adulthood.[22] There continue to be obstacles to the successful transition of these patients, such as the lack of specific treatment guidelines for adult patients with JIA and minimal adolescent-specific training of paediatric and adult rheumatologists.[23,24]

Limitations to treatment

It is known that low- and middle-income countries have resource constraints that contribute to the reduced availability of biologic medications for patients.[25] A 2009 study involving 25 countries across Europe and the USA looked at the association between gross domestic product (GDP) per capita and disease activity scores in rheumatoid arthritis patients, which showed that patients living in low GDP per capita countries had higher disease activity scores.[26] Another study looking at 46 European countries investigating access to biologic DMARDs and synthetic DMARDs showed that access to these medications was dependent on a country's socio-economic status, with lower income countries having minimal, if any, access to reimbursed biologic therapy.[27] This, in combination with varying regulatory agencies reviewing drug approvals, further widens the gap between access to these important medications across the globe. In addition, to receive approval from these regulatory agencies, many require substantial and specific high-quality evidence for the drug's use in paediatric patients with JIA, where many patients now have to wait until the age of 18 to receive the numerous medications adult patients have access to. Unfortunately, the majority of the clinical trials for these specialized medications exclude paediatric patients and only include adult patients. To advocate for drug approval, the results of these studies are extrapolated for use in children. This can be problematic as children are not just 'small adults', where there are specific differences in disease, physiology, drug metabolism, dosing (many medications are weight or body surface area specific) and the unknown possible side effects on growth and development in these patients.

Challenges and future directions

Despite advances in treatment and awareness of JIA, there continue to be ongoing challenges and the need for future exploration to improve care. There have been a number of paediatric-specific clinical trials that have been completed for well-known biologic treatments; however, the need for ongoing paediatric studies is essential to continue to advocate for up-to-date treatment options for this population. Global registries, including the Paediatric Rheumatology International Trials Organisation (PRINTO) and the Childhood Arthritis and Rheumatology Research Alliance (CARRA), which collect data on disease presentation, progression and treatment, have played a large role in improving our understanding of paediatric rheumatologic diseases. Previous studies have shown that patients with JIA experience symptoms of depression and anxiety at a higher rate than healthy children.[28] Their family members also experience higher rates of depression and anxiety symptoms, which may also impact their child's mental health and pain.[28] There has been a shift in focus towards prioritizing the mental health of patients with JIA with early screening and intervention.[29] There continue to be advances in genomics and digital health tools in the use for patients with JIA in hopes of achieving more personalized medicine.[30] A focus on identifying biomarkers used for prediction, disease-activity monitoring and treatment response will also hopefully allow early intervention and improved efficiency in diagnosis. Given the overall burden of this disease, it shows the importance of ongoing advocacy for those with JIA, to raise awareness, encourage research funding and support services for these children and their families.

Conclusion

Arthritis can present in childhood, and if there is persistent pain specifically associated with morning stiffness, further investigations and referral to a paediatric rheumatologist are indicated. Availability of treatment options has increased significantly in the last 25 years; however, most treatments are not approved for use in childhood arthritis as trials only include adult patients. Some medications will only be available to children with JIA after they turn 18 and are relabelled rheumatoid arthritis or ankylosing spondylitis. Advocacy for early and equitable access to biologic medications is ongoing and will hopefully lead to better access to these medications for one of our most vulnerable and important populations – children. ❑

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