Juvenile Idiopathic Arthritis
Essential Elements of Care

MR Alam

Summary:

The chronic arthritides in childhood remain a poorly understood group of conditions. Their classification has been a source of much confusion over the years with differences in terminology used by different research groups. Childhood arthritis is an important cause of short term morbidity in children and can lead to long term joint destruction and disability. Proper diagnosis and early aggressive intervention can minimize both the short and long term morbidity of the disease, thereby improving outcome during childhood as well as in adulthood. The various sub-types of JIA with their clinical features, diagnosis and differential diagnosis have been described. An outline of current management strategies and outcome of treatment are given and potential future developments are highlighted.

(J Bangladesh Coll Phys Surg 2008; 26: 83-90)

Introduction & Nomenclature:

Juvenile idiopathic arthritis (JlA) is a relatively rare disease affecting 1 in 1000 children in UK[1]. Important changes have occurred in the last decade regarding the course of juvenile idiopathic arthritis and resultant long-term disabilities. Published studies demonstrate that at least 50 percent of all children with JIA continue with active disease as they enter adulthood. Persistent synovitis leads to joint destruction in children much sooner than previously thought, often within 2 years of the onset of disease. The long-term impacts on the ability to function and the effects of chronic disability can be profound. Additionally, juvenile idiopathic arthritis can have detrimental effects on the physical and psychological growth of a child. There may be disruption of the family unit, divorce and other psychological stresses that affect all members of the family. The above considerations have prompted pediatric rheumatologists to treat children with juvenile idiopathic arthritis early and aggressively. The current treatment goal is resolution of disease with return to normal growth, development and activities[7]. In order to do this, patients must be accurately diagnosed as early as possible and then treated persistently until their disease resolves. It is widely thought that a comprehensive team approach is associated with a superior outcome. There has been too little awareness of the major role played by modem treatment regimen in JIA where methotrexate has transformed the outlook for most children with severe disease[4, 5].

Juvenile idiopathic arthritis is the umbrella term for a group of chronic childhood arthritis of unknown causes in children below sixteen years of age & persisting for at least six weeks[2, 19, 24]. The earliest formal description of this disease was given by Sir George Frederick Still in 1897. this work was done when he was a registrar at the hospital for sick children, Great Ormond Street, London. In this initial description of 19 patients, he identified three patterns of arthritis, one of which came to be known later as Still's Disease (now known as systemic onset JIA)[67, 68]. Subsequently different classifications were given by researchers.

According to American College Of Rheumatology it is called Juvenile rheumatoid arthritis (JRA) lasting at least six weeks with several subtypes e.g.

1. Puciarticular (1 to 4 joints involved)
2. Polyarticular (5 or more joints involved)
3. Systemic JRA
4. Spondyloarthropathies

According to European League against Rheumatic Association it is called JCA (juvenile chronic arthritis) lasting at least 3 months with following subtypes

- Puciarticutar (1 to 4 joints involved)
- Polyarticular (5 or more joints,RF negative)
- Systemic JCA
- Spondyloarthropathies

Finally the term JIA (Juvenile Idiopathic Arthritis) was first proposed in 1994 & later revised in 1997 by the International league against rheumatism as compromise for the American term JRA & the European term JCA[50,51,52]. Because the American & European classification of the disease were

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Received: 17 February, 2008 **Accepted:** 20 April, 2008

confusing, it was difficult to use the term interchangeably, in an effort to improve research and treatment, ILAR has given the name J1A.However regardless of the classification, children who develop symptoms that persist for at least six weeks before the age of sixteen years are considered to have Juvenile idiopathic arthritis. The term idiopalhic means unknown cause. This classification is gaining favour among researchers and health professionals but is not yet universally used.

JlA (Juvenile Idiopathic Arthritis) is an inflammatory disorder of connective tissue, characterized by joint swelling & pain or tenderness. It may also involve skin, heart, lungs, liver, spleen, eyes. Depending on the type the disease can occur as earty as six weeks of age, but rarely does so before the age of 6 months, peak onsets are usual between the age of one & three years and between eight & twelve years. Cause remaining unclear, but genetic factor, viral, bacterial infection, trauma and emotional stress are said to be responsible.

Difficulty arises in diagnosing cases in some of the subvarieties e.g. psoriatic arthritis, enthesitis related arthritis & systemic onset varieties.

Special problems in children:

It is important to realize that the symptoms of arthritis can vary greatly. Many children particularly young ones do not complain when they have pain in joints or may not admit it when asked. Clues that a child may be having joints problem include

- Reluctance to join in physical activities
- Unusual changes in mood
- Unwillingness to use one limb particularly
- Unusually bad behavior
- The morning journey is often difficult because of early morning stiffness
- He or she may be able to move less quickly than others between classes and sometimes teachers can play important role in recognition of the condition and improvement of quality of life

Presentation & Differential Diagnosis :

With the exception of systemic variety, children with chronic arthritis usually present with pain or swelling of joints. In determining symptoms it must be remembered that age of the child will affect how symptoms are expressed and age appropriate assessment – must be used.

Arthralgia clearly distinguishes from arthritis, where there is objective evidence of abnormality on examination of joints.

JIA is diagnosed by presence of chronic persistent arthritis of at least 6 weeks duration on children or adolescences – who are under the age of 16 years. The diagnosis of JIA also requires exclusion of other diseases, which may present in a similar manner. As JIA is an exclusionary diagnosis, it is important to be familiar with the alternative diagnosis. The required six-week duration of arthritis is an important 1st step in excluding common conditions such as viral arthritis, trauma, Henoch-Schonlion purpura and rheumatic fever.

Orthopedic conditions such as “Legg-Calve Perthes” disease must be excluded which may have similar presentations.

Septic arthritis needs to be considered when there is monoarticular arthritis accompanied by fever, severe pain and exquisite tenderness.

Perhaps one of the most concerning aspects of diagnosis of JIA is the recognition that some childhood malignancies such as leukemia and haematoblastoma may present with musculo-skeletal pain or arthritis. Elevated ‘lactate dehydrogenase’ is the only test that can differentiate malignancy from JIA.

Chronic childhood rheumatic diseases like Systemic Lupus Erythomatosus; Mixed Connective Tissue Diseases; Juvenile Dermatomyosities are important differential diagnoses.

Children with growing pains have nocturnal lower extremity pain that can be relieved by comfort such as massage.

The most common subtype of JIA is oligoarthritis (1-4 joints), which may lead to polyarticular variety in course of time. One of the recognized associations of JIA is chronic frequently asymptomatic iritis. Children with involvement of 5 or more joints in the 1st 6 months are classified as polyarticular type. Generally polyarticular type tends to be symmetrical.

Systemic variety is the least common subtype. This type of arthritis is considered while fever has been present for at least 2 weeks with rash. Serositis, anemia of chronic disease, lymphadenopathy, hepatosplenomegaly all may be seen. Leucocytosis and thrombocytosis are commonly seen.

A careful history should distinguish between mechanical, inflammatory and non-organic joint pain. Examination will confirm objective evidence of join inflammation. Once a diagnosis of arthritis has been reached, the length of history and the exclusion of other causes of arthritis (e.g. infection, connective tissue disorder) will lead to a diagnosis of JIA.

Radiological and laboratory investigations are not necessary in making a diagnosis of JIA. Investigation may be useful in ruling out other pathology, determining the disease subtype and assessing disease activity in some children.

Diagnosis:
Diagnosis of JIA remains a clinical one & essentially one of exclusions in addition to pattern recognition. There are no clinical, laboratory or radiologic tests that are pathognomonic for this disease.

Laboratory investigations –
ESR: May be normal in oligoarthritis and polyarticular arthritis, but is usually very high (>60 mm/hr) in systemic onset disease. If high in patients with oligoarthritis, consider infection, underlying spondyloarthropathy (e.g., IBD, Reiter's syndrome), or malignancy.

WBC: Should be normal in oligoarthritis and polyarticular juvenile arthritis. Elevated WBC with a left shift is sometimes seen in systemic onset juvenile arthritis, including leukemoid reaction (>30,000). Remember that a normal peripheral WBC and smear cannot exclude the diagnosis of leukemia.

Platelet Count: Usually normal, except in active systemic onset juvenile arthritis, where it may be elevated (>500,000). If platelet count is low, consider malignancy).

Other investigations should be done only to exclude other diagnosis.

Ensuring the correct diagnosis is essential for further management. The misdiagnosis of non-organic joint pain as arthritis will cause immense difficulties to the child and family and may be very difficult to undo. A delay in correctly diagnosing a child with JIA will lead to a delay in the child receiving appropriate therapy that may result in long-term sequele.

Management:
Management of JIA includes multidisciplinary approach like rheumatologist, physician, pediatrician, physical medicine specialists, teachers, social workers, psychologists etc. drug treatment includes NSAIDs, DMARD, steroid. The aim of modern treatment for JIA is rapid induction of disease control to prevent joint damage, to maximize joint function & to achieve a normal joint function for patients.

Methotrexate in JIA:
Weekly methotrexate is an established treatment in pediatric rheumatology & its efficacy shown by different randomized control trials[4, 5, 7, 33]. Among DMARDs, methotrexate has transformed the outlook for children with JIA. Most of the evidences from uncontrolled clinical trails suggested that methotrexate is an effective agent for treating active JIA. A more recent randomized controlled double blind crossover multi center study by woo, et. al looked at the effectiveness and safety of orally administered methotrexate in extended oligoarticular & systemic arthritis. This study used methotrexate at dose of 15 to 20 mg/m^2/week. A significant improvement occurred in three of five variables (ESR, physicians and patient's global assessment). (The study by Giannini et al forms the basis of current use of methotrexate in pediatric rheumatological practice). This was a six month randomized, double blind controlled multi center study of 127[43, 44. 45, 46] children with resistant JIA (Mean age 10.1 years, mean disease duration 0.5-1 years). 63% of the group treated with 10mg/m^2/week improved compared with 32% of those treated with 5 mg/m^2/week & 36% of placebo group.

Mechanisms of action of methotrexate:
Methotrexate is a folate analogue with an amino (NH_2) & methyl (CH_3) group. It binds dehydrofolate (DHFR) with high affinity and inhibits synthesis of thymidylate and purine, which are essential compound of DNA.