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Special Article

An Approach to a Child with Arthritis

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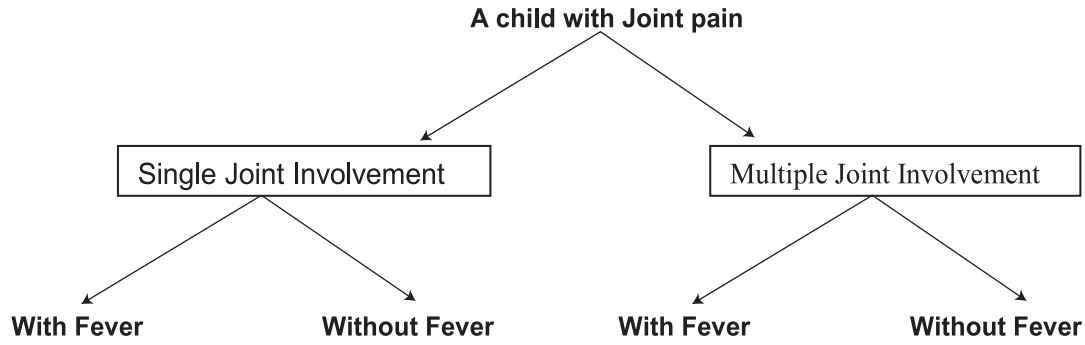
Introduction:

Musculoskeletal and joint diseases appear to be increasing and continue to be a growing childhood health problem. Confusion over terminology and a lack of awareness of these conditions have probably contributed to their under-recognition.[1] Musculoskeletal pain in children are common, affecting about 10-20 % of school children.[2] Various local and systemic, acute and chronic, benign and malignant conditions are associated with musculoskeletal pain (Table-I). A correct diagnosis is essential for appropriate management. It is important to remember that all the limb and joint pains are not arthritis and all arthritis are not painful.[3]

A child presenting with arthritis is always a diagnostic challenge even for the most experienced clinicians. Arthritis is manifested as a swollen joint or a joint having at least 2 of the following conditions: limited range of motion, pain on movement, or warmth overlying the joint.[4]



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It is known that:

1. Arthritis and arthritis like symptoms can be the presentation of systemic diseases like leukaemia, tuberculosis etc.
2. Many rheumatologic diseases have extra articular manifestations like renal, pulmonary, skin, cardiac and ophthalmic.
3. Identification of musculoskeletal emergencies (e.g. septic arthritis, systemic onset JIA) is very much important for management purpose.
4. It may not be possible to conclude a diagnosis at first visit as several rheumatologic diseases evolve over time.
5. Recognition of pattern of arthritis is very important component of diagnosis.

Arthritis in childhood is not uncommon. The pattern, presentation and duration of arthritis help differentiate between the various possible diagnoses. These patients frequently create a diagnostic dilemma because of the extremely broad differential diagnoses. The most important aspects of the diagnosis are comprehensive history taking and a detailed clinical examination. Relevant laboratory investigations can help in facilitating the diagnosis but can often also mislead the treating physician.[6] In this review article we present an approach to a child with arthritis for appropriate evaluation and diagnosis which would help to reduce morbidity and mortality from these problems in children.

Approach to a child with arthritis:

Clinical information in patient including demography, disease chronology, inflammatory nature, progression, distribution of joint involvement and extra-articular manifestations help narrow the diagnostic possibilities. A carefully conducted history and physical examination are the initial and most important steps in narrowing the differential diagnosis and guiding the diagnostic evaluation.

History Taking:

Important aspects to be emphasized in the history are as follows:

Age- Age of onset of the disease may give clues to the diagnosis. Polyarticular juvenile idiopathic arthritis (JIA) [rheumatoid factor negative], Kawasaki disease (KD) and Henoch Schonlein purpura (HSP) usually present in early childhood. In mid-childhood, psoriatic arthritis, juvenile dermatomyositis (JDM) and polyarteritis nodosa (PAN) have their peak frequencies. Enthesitis related arthritis (ERA) and systemic lupus erythematosus (SLE) typically present in late childhood or early adolescence. Rheumatoid factor positive polyarticular JIA, mimicking the clinical profile of adult RA, usually presents after the age of 10 years.

Sex - Many rheumatological disorders (e.g. SLE, polyarticular JIA) have a predilection for girls. On the other hand vasculitides like KD and PAN; spondyloarthropathies like inflammatory bowel disease and ERA are more common in boys. Systemic onset JIA have equal distribution in both sexes.[8]

Onset of disease and duration-While some arthritides may have an acute onset (e.g. septic arthritis and arthritis associated with KD/HSP) others may have a sub acute or chronic insidious course as typically seen in poly articular JIA or sarcoidosis. Polyarthritis of less than 6 weeks duration is usually seen in self limiting viral arthritides, rheumatic fever or reactive arthritis.[7] It may sometimes be prudent not to give a label in the first few weeks of the illness when the disease process is still evolving.[6]

Pain- Characteristics of the pain and/or stiffness (site, number of joints, severity, frequency, duration, pattern, and association of warmth or discoloration) frequently accompanied by loss of function which limit daily activities. Morning stiffness is a characteristic feature of inflammatory arthritis. Night pain should alert the clinician to a malignancy or an osteoid osteoma. There are some red flags signs (raise concern about inflammation, infection, malignancy or non-accidental injury) for potentially serious conditions.

Red flags signs[9] are followings:

- Fever, malaise, systemic upset (reduced appetite, weight loss, sweating)
- Bone or joint pain with fever
- Refractory or unremitting pain, persistent night-waking
- Incongruence between history and presentation (such as the pattern of the physical findings and a previous history of neglect)

Systemic enquiry: Should be focused in the presence of fever or other constitutional symptoms

(eg. weight loss, anorexia, night sweats, or nocturnal pain) as well as presence of extra-articular features (diarrhoea, urethral discharge, ocular symptoms, rash, haematuria/proteinuria, headache, convulsion)

Precipitating factors: Trauma, infections (streptococcal, enteric, viral), immunizations, drug exposures, exposure to a person with tuberculosis.

Personal or family history: Bleeding diathesis or HLA-B27–associated diseases

(inflammatory bowel disease (IBD), acute anterior uveitis, psoriasis, ankylosing spondylitis).[10]

Physical examination:

Articular involvement- Examination involves determining not only which joints are involved at any one time, but determining over time if possible, the evolution of joint involvement. Clinical approach to a child with arthritis essentially revolves around recognition of the pattern of joint involvement (Table-II). It may not always be possible to give a specific diagnostic label at the first instance. The treating clinician has to identify the following components in evolution of the disease:

• *Is the involvement articular or non-articular?*
Articular structures include synovium, synovial fluid, articular cartilage, intra-articular ligaments, joint capsule and juxta articular bone. Non –articular structures include ligaments, tendons, bursas, muscle, fascia, bone, nerve and overlying skin. Articular disorders are characterized by pain, swelling, joint line tenderness and limitation of active as well as passive movements. Associated swelling due to synovitis, joint effusion, bony enlargement, instability locking, crepitus and deformity signify articular involvement. Pain only during active movement and point tenderness are features of non-articular disorders.[12]

• *Is the involvement inflammatory or non-inflammatory?*
Inflammatory disorders could be due to infective, immune mediated or idiopathic and non-inflammatory disorders are usually mechanical in origin. Pain during physical activity and improvement with rest imply non-inflammatory or mechanical pain. Inflammatory pain is associated with morning stiffness, gelling (pain after a period of inactivity), diffuse joint swelling and tenderness. Inflammatory disorders often have systemic manifestations and are associated with elevated acute phase reactants. Non-inflammatory disorders have variable clinical findings and have no positive laboratory findings.[13]

• *Is the involvement acute or chronic?*
Joint swellings occur within hours after trauma or a bleeding diathesis. Acute arthritis (days to weeks) is a feature of infections, rheumatic fever, neoplasia, connective tissue diseases and mechanical joint pains. Chronic arthritis (> 6 weeks) is a feature of Juvenile Idiopathic Arthritis (JIA) and chronic infections such as tuberculosis.[10]

• *How many joints are affected?*

Classification of JIA is based on number of joints involved (mono-single joint, oligo-4 or less joints, and poly-5 or more joints). Acute monoarthritis is seen in infective arthritis, reactive arthritis, JIA, neoplastic diseases, trauma and mechanical disorders. Chronic monoarthritis may be tuberculous, septic or reactive in a sick child.[14] Acute polyarthritis with fever is a feature of viral arthritis, rheumatic fever, infectious endocarditis and other conditions. Chronic polyarthritis is a feature of various forms of JIA, mechanical problems and metabolic disorders.[6]

Table-II

Characteristics patterns of joint involvement in children[6,11]

Disease	Clinical presentation	Pattern	Symmetry	Axial involvement	Upper or lower limbs
Viral arthritis	Acute	Small joints	Symmetrical	No	Upper/lower
Poly articular JIA	Chronic	Large & small joints	Symmetrical or asymmetrical	No	Upper/lower
Enthesitis related Arthritis	Chronic	Large	Asymmetrical	Yes	Lower
Psoriasiasis Arthritis	Chronic	Small and large	Asymmetrical	Yes/No	Upper/lower
SLE	Chronic	Small and large	Symmetrical	No	Upper/lower
Reactive Arthritis	Acute	Large	Asymmetrical	No	Lower

• *Is there axial or peripheral joint involvement?*

Typically joint involvement can be axial (spine, centrally located joints as sacroiliac joint, sternoclavicular or manubriosternal joint), peripheral joints (in the extremities) or root joints (overlap between axial and peripheral joints e.g. shoulder and hip joint).Axial involvement is observed in enthesitis related arthritis (ERA).These joints are rarely affected in systemic diseases such as SLE. Combined patterns of involvement can be seen in polyarticular or systemic JIA. A young adolescent who has chronic low back pain and peripheral asymmetric arthritis probably has one of the spondylo-arthropathies like ERA, psoriatic arthritis, enteropathy associated arthritis or reactive arthritis.

• *Is the involvement additive, migratory or intermittent**?***

The term additive means new joint involvement over and above an already involved joint. This is seen in polyarticular JIA. Migratory involvement refer to fleeting joint pain is seen in acute rheumatic fever and intermittent arthritis in SLE or sickle cell disease. In intermittent pattern there is complete remission of signs symptoms followed by next recurrence in the same or other joints.[15]

• *Is the involvement symmetric or asymmetric?*

Inflammatory connective tissue diseases such as SLE, polyarticular JIA and viral arthritis have symmetric joint involvement. Joint involvement is asymmetric in oligoarticular JIA, psoriatic arthritis, reactive arthritis and septic arthritis. In many cases the pattern of involvement may not be discernible at beginning of illness.[5,14]

• *Is the characteristics of a particular disorder?*

Site of involvement is characteristic of many diseases, e.g. distal interphalangeal joint in psoriatic arthritis, bilateral temporomandibular joint in RF-ve polyarthrits and knee/ankle joints in reactive arthritis.[16]

• *Is the arthritis deforming or non deforming?*

Arthritis can be deforming or non-deforming. Joint deformities usually indicate a long standing or aggressive disease. Deforming arthritis is typically seen in RF +ve polyarticular JIA. Early initiation of anti-inflammatory therapy can help prevent some of these deformities. Malalignment of articular structures, soft tisue contracture associated fibrosis or ankylosis is responsible for these deformities. The arthritis associated with SLE and inflammatory bowel disease is usually non-deforming.[6,8]

• *Is there any associated enthesitis*?

Enthesitis is an inflammation at the attachment of tendons, ligaments, fascia and joint capsule attached with bone. This is an important component of ERA. Diagnosis is ERA is strongly supported by the presence of marked tenderness on the patella, at the tibial tuberosity, at the attachment of the achillies tendon, at the attachment of the planter fascia to the base of the fifth metatarsal and at the heads of the metatarsals. Enthesitis is also less commonly found at the greater trochanters of the femurs, anterior superior iliac spine, iliac crests, pubic symphysis and ischial tuberosities and seldom at enthesis of the upper extremities.[17]

Abnormalities detected on physical examination are important clues to the diagnosis of arthritis. A detailed general physical examination should include growth parameters and vital signs. The presence of fever should alert the clinician or more severe emergency conditions (eg: septic arthritis, HSP, KD). A detailed examination with a focus on rashes, palpable purpura, peeling of the skin, thickening of the skin, conjunctivitis, iritis, nail pitting, pigmentation, psoriasis, oral ulcers, nodules and hepato-splenomegaly/lymphadenopathy can provide clues to the underlying diagnosis.[13] (Table-III)

The musculoskeletal examination should include a review of all joints and examination of the gait but with a focus on the affected joints. The focused examination of the affected joint should include inspection of the skin for warmth, redness, swelling, and soft tissue involvement, using the contralateral side for comparison. Passive and active range of motion should be observed.[18]

A recently developed and validated tool is the pGALS (pediatric Gait, Arms, Legs, Spine), which is a simple musculoskeletal screening examination that can be performed in a few minutes. pGALS has been demonstrated excellent sensitivity to detect abnormality, quick to perform with highly acceptable to school age children and their parents.[19]

Table-III

Extra-articular signs to be looked in a child with arthritis[6,7,12,13]

System involved	Physical findings	Systemic disease
Eye	Anterior or posterior uveitis, non exudative conjunctivitis, Keratoconjuctivits	JIA, KD, Reactive arthritis, Sarcoidosis
Oral cavity	Oral ulcers , straw berry tongue , cracked lip	KD, SLE
Skin	Malar rash, discoid rash, macular rash, heliotrope rash, Gottorn's papules, palpable purpura, petechaie , Oedema of hands and feet Erythema nodosum, leg ulcers, Raynaud phenomenon , perianal desquamation slapped check appearance, genital ulcer	SLE, JDM, HSP PAN Sarcoidosis, Reactive arthritis
Nails and hair	Alopecia, nail pitting, onycholysis, clubbing	SLE, Psoriasis, IBD
Musculoskeletal	Proximal muscle weakness, muscle tenderness, muscle contracture, enthesitis, bursitis , dactylitis ankylosis	JDM, ERA, JIA
Vascular system	Gangrene, stroke	SLE, APLA
Lymphatic system	Lymphadenopathy	KD, SLE, JIA
Renal system	Nephritis, nephrotic syndrome, hypertension, urinary sediment, sterile pyuria, amyloidosis, RPGN and ESRD	JIA,KD, SLE,PAN, HSP
Central nervous system	Stroke, seizures, focal deficits, psychosis, chorea, blindness, aseptic meningitis, pseudotumor cerebri	RF, SLE, PAN, Bachet diseae
Peripheral nervous system	Mononeuritis complex, polyneuropathy	PAN, SLE , Chrugg strauss syndrome
Paranasal sinuses	Acute or chronic sinusitis	Wegener's granulomatosis
Lungs	Hilar adenopathy, pulmonary infiltrates, Pulmonary haemorrhage, pulmonary	Sarcoidosis. PAN

The components of pGALS screen are as follows:-

1. **Screening questions to enquire about:**
   a) Pain and stiffness in joints, muscles or back
   b) Difficulty in dressing oneself and
   c) Difficulty in going up and down stairs.
2. **Gait**:
   a) Observing the child walking
   b) Asking the child to walk on tip-toes and heels.
3. **Arms**:
   a) Moving hands in different directions
   b) Making a fist
   c) Touching fingertips with thumb
   d) Squeezing metatarso-phalangeal joints.
4. **Legs**:
   a) Bending and straightening knees
   b) Passive flexion and extension of hip
   c) Feel for knee effusion.

5. Spine:
Lateral flexion of cervical spine, bending forwards to touch toes, observe spine from side and behind.

Following the screening examination, the observer is directed to a more detailed examination of the relevant area, based on the 'look, feel, move' principle as in the regional examination of the musculoskeletal system.[9]

Investigations:
It is said that 80% of the rheumatological diagnosis comes from clinical history, 15% from examination and only 5% from investigation. Laboratory investigations, by themselves, have very little role in arriving at a diagnosis and one should never fall in the trap of treating the investigation rather than the patient.[20] No laboratory test can confirm the diagnosis and absence of disease marker does not exclude a disease. The laboratory can be used to provide evidence of inflammation, to support the diagnosis, to monitor toxicity of therapy and as a research tool to understand more completely the pathogenesis of the disease.[21]

a) Hematology-
Hematological abnormalities as a general rule are reflective of the extent of inflammatory disease. Normocytic normochromic anemia is found in most inflammatory conditions and the extent of anemia parallels the disease activity. Co-existent nutritional deficiency anemia can also play a role. Leucocytosis is common in children with active arthritis and in children with systemic onset JIA the leucocyte counts can be strikingly high. Poly-morphonuclear leucocytes are predominant. In contrast leucopenia suggests a diagnosis SLE. Inflammatory arthropathies are generally associated with thrombocytosis. Presence of thrombocytopenia should alert to a possibility of SLE or leukaemia.[22]

b) Acute phase reactants-
The most important acute phase proteins that increase during inflammation are C-reactive protein (CRP), fibrinogen, haptoglobin, ceruloplasmin, compliment component C3. In clinical practice, ESR and CRP measurement are the two common tests used for assessment of degree of inflammation. CRP is a reliable marker of inflammation as it rises early (within 24 hrs), significantly and falls rapidly on resolution of inflammation.[23] In systemic onset JIA, vasculitis and bacterial infection, CRP level can increase 100-500 times. In SLE patients CRP level are generally not elevated significantly but elevated level of CRP in lupus might be indicative of active infection. It is essential to note that ESR is an indirect measure of acute phase reactants. Increased plasma level of fibrinogen gives rise to an increased ESR. In a child with joint pain elevated ESR suggests inflammatory disease in contrast to mechanical problems. ESR more than 100 can be seen in systemic onset JIA, vasculitis and sepsis.[22,23]

c) Urine analysis and Biochemistry
Significant urinary abnormalities are uncommon in cases of JIA but urine analysis forms an essential part of investigation a child with suspected SLE or vasculitic syndrome.

Renal failure is not a usual feature of JIA and presence of abnormal renal function test should alert to possibility SLE, vasculitis and drug toxicity. Mild liver function abnormalities (raised SGPT) are common in JIA but presence of significant abnormality should raise doubt about drug toxicity (particularly MTX)[24], macrophage activation syndrome (in case of systemic onset JIA) or of an alternative diagnostic possibility.

d) Serology (Autoantibodies)
Autoantibodies are useful markers for the diagnosis of various autoimmune diseases and sometimes for monitoring disease activity. Autoantibody used for screening should have high sensitivity where as antibody used for diagnosis should have high specificity.

Rheumatoid Factor (RF) are autoantibodies directed against the Fc fragment of immunoglobulin G molecule. RF positivity is uncommon in a child less than 7 years age and typically associated with polyarticular JIA. In JIA RF positivity is common in children with late age of onset, erosive disease, unremitting course and poor functional outcome.[25]

Anti-nuclear antibodies (ANA) are antibodies directed against various nuclear components. It is usually detected by immunofluorescence (IF) method, utilizing monolayers of Hep-2 cells. ANA is usually present in 10% in normal populations, 98% of children with SLE, 70-80% of children with oligoarticular JIA, 60-80% of children with scleroderma and 60% of children with JDM. Presence of ANA is associated with increased risk of uveitis in oligoarticular JIA patients. [23]

Anti-double stranded DNA (ds-DNA) is very specific (95%) but not as sensitive (70%) for SLE making it useful in the diagnosis of SLE when positive. It might have a pathogenic role in SLE nephritis and commonly associated with disease activity in lupus nephritis. Anti-sm antibodies are positive exclusively in SLE patients in 10-40% of patients.

e) Imaging

X-ray of the involved joint: Shows widening of joint space if effusion is present. Joint space narrowing with erosions of the articular surfaces is characteristically seen in JIA patients. Perthe's disease, avascular necrosis of hip and tubercular hip are also identified on a plain X-ray. Radiorraphy is low cost highly available modalities which can detect also joint sub-laxation, malalignment and ankylosis.[14,27]

Ultrasound of the joint: helpful both for diagnosis of effusion and synovitis particularly in shoulder and hip , where plain films are insensitive. It can also help us to guide diagnostic aspiration or injection in the joints. MRI demonstrates joint anatomy, shows early changes in cartilage and soft tissues, and with gadolinium contrast allows detection of synovitis. It is also useful in detecting effusion, erosions, pannus, and peri articular changes.[28]

Conclusion:

Arthritis in a child could be a benign self-limiting illness, but sometimes might be a serious chronic illness resulting in significant morbidity and /or mortality. Several musculoskeletal conditions like septic arthritis, HSP, Kawasaki disease needed emergency management. In spite of broad differential diagnosis, an organized approach including careful history taking and physical examination is very much essential for correct diagnosis. Laboratory evaluation is performed to support the clinician's impression. Serious and/or potentially life-threatening infectious, malignant, or orthopedic conditions need to be identified, and may require surgical or medical management.

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