Introduction

Musculoskeletal diseases are among the most common reasons for which medical help is sought. Anywhere between 25% and 30% of individuals will have a musculoskeletal complaint in their lifetime. A significant proportion of patients who present with musculoskeletal complaints have in fact systemic illness such as rheumatoid arthritis (RA), systemic lupus erythematosus (SLE) etc. which may be potentially life-threatening if not detected, correctly diagnosed and treated. These conditions have to be distinguished from other musculoskeletal conditions, which have no systemic component, are mechanical in origin and are referred to the orthopedic department.[3]

1. Therefore the first step in approach to a patient with musculoskeletal complaints is to separate systemic, serious, life-threatening illness from local, regional and mechanical problems.[3] Patients with musculoskeletal problems could have any of the following presenting complaints.
   • Joint pain/arthralgia.
   • Arthritis.
   • Diffuse pain.
   • Stiffness of joints.
   • Back pain.
   • Constitutional symptoms.
   • Symptoms of systemic organ, muscular or cutaneous involvement.

2. The next step in approach to a patient with musculoskeletal complaints is to find out from which structure this pain is arising from (anatomical basis). Pain could arise from the joint or from periarticular structures (articular versus non-articular). Articular structures include the synovium, synovial fluid, articular cartilage, intra-articular ligaments, joint capsule and juxta-articular bone. Non-articular (or peri-articular) structures, such as supportive extra-

Abstract

Monoarthritis can be inflammatory or non-inflammatory, and can be acute or chronic. A thorough history and physical examination can differentiate inflammatory from non-inflammatory monoarthritis. The most common causes of acute inflammatory monoarthritis are infectious arthritis, crystal induced arthritis (gout and pseudogout). Examination of synovial fluid often is essential in making a definitive diagnosis. Immunoinflammatory diseases like rheumatoid arthritis, systemic lupus erythematosus, spondyloarthritis, Behçet’s disease, and reactive arthritis can all begin as acute inflammatory monarthritis. Synovial biopsy is useful to diagnose chronic infections like tuberculosis and brucellosis. In order to arrive at a final diagnosis other organ systems should be thoroughly reviewed, because other systemic illness like sickle cell disease, thalassemia, sarcoidosis can all cause monoarthritis.

Keywords: Monoarthritis, monoarticular pain, crystal induced arthritis, gout, pseudogout

An approach to monoarthritis

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articular ligaments, tendons, bursa, muscle, fascia, bone, nerve and overlying skin, may be involved in the pathologic process. Articular disorders may be characterized by deep or diffuse pain, pain on active and passive movement and swelling (caused by synovial proliferation, effusion, or bony enlargement), crepitation, instability, or deformity. By contrast, non-articular disorders tend to be painful on active, but not passive movement, demonstrate focal tenderness and swelling away from the joint line. Moreover, non-articular disorders may rarely have synovitis, swelling, crepitus, instability, or deformity of the joint itself.

Pain caused by bone diseases can be difficult to distinguish from that from the joints. Examples of diffuse bone diseases are metabolic bone disease, multiple myeloma and multi focal osteomyelitis. In general bone diseases cause pain which is much worse at night. This category must also be considered in differential diagnosis of musculoskeletal pain.

3. Once articular origin of the pain is established, the other relevant features include the duration (acute <6 and chronic >6 weeks); the number (mono, oligo (≤3), or polyarthritis), and distribution of joint involvement, and whether the pain is inflammatory (morning stiffness >30 min, systemic symptoms, local inflammatory signs, laboratory evidence of inflammation- (elevated ESR/ CRP, thrombocytosis, anaemia of chronic disease, etc.) or non-inflammatory.

Therefore a patient with arthritis (joint pain and swelling) can be classified in one of the categories as given in Table 1.[3]

Table 1: Shows a broad classification of the causes of arthritis with a focus on major causes of monoarthritis

<table>
<thead>
<tr>
<th>Acute arthritis</th>
<th>Chronic arthritis</th>
</tr>
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<tbody>
<tr>
<td>Monoarthritis</td>
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<tr>
<td>Crystal induced arthritis (gout and pseudogout)</td>
<td>Tubercular arthritis</td>
</tr>
<tr>
<td>Septic arthritis</td>
<td>Fungal arthritis</td>
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<tr>
<td>Gonococcal arthritis</td>
<td>Other infections (e.g Brucellosis)</td>
</tr>
<tr>
<td>Acute onset of inflammatory polyarthritis (like RA, SLE)</td>
<td>Immunoinflammatory arthritis</td>
</tr>
<tr>
<td>Polymyositis (e.g., acute onset of polyarthritis, reactive arthritis)</td>
<td>Crystal induced arthritis</td>
</tr>
<tr>
<td>Polymyositis (e.g., RA, psoriatic arthritis, spondyloarthritis)</td>
<td>Non-inflammatory</td>
</tr>
</tbody>
</table>

Therefore, monoarthritis which is arthritis of a single joint can either be acute or chronic or be either inflammatory or non-inflammatory.

**Acute Inflammatory Monoarthritis**

Acute inflammatory monoarthritis is a rheumatology emergency. The most important causes are infectious (septic) arthritis, acute gouty arthritis, pseudogout, reactive arthritis and initial presentation of a polyarthritis.[4] The diagnosis of septic arthritis should not be missed as delay in initiating antibiotic therapy can lead to permanent damage to the cartilage of the joint. History must include history of fever and involvement of other joints. Presence of classical signs of inflammation-red hot swollen and tender joint makes it easy to label acute inflammatory arthritis. Synovial fluid analysis is the single most important test in the emergency evaluation of acute monoarticular arthritis.[5] Synovial fluid should be sent for cell count, gram stain, bacterial culture and also examined for crystals under polarized light microscope.

a. Non gonococcal bacterial arthritis (septic arthritis) — Septic arthritis is a true rheumatology emergency because it can rapidly destroy the articular cartilage.[6] Septic arthritis may develop in a fulminant fashion with high grade fever, confusion and marked toxicity or may be subacute with little or no fever. The knee joint is the most common joint to be involved, followed by hip and less commonly are the shoulder, wrist and elbow. Patients with RA are at increased of developing septic arthritis.[7] Prior joint abnormality, prosthetic joint also significantly increases the likelihood of developing septic arthritis.[8] It is important to rule out septic arthritis in any patient of RA who presents with a red hot and swollen joint.[8] Synovial fluid typically reveal white cell count of >50,000 cells/μL. *Staphylococcus aureus* is still the most common cause of non-gonococcal septic arthritis. Other pathogens include *Streptococcus pneumoniae* and Gram-negative bacilli. Reports in the literature show an increased incidence of methicillin-resistant *S. aureus*.[9]

Treatment for septic arthritis consists of hospital admission and appropriate empirical intravenous (IV) antibiotics (also to cover for *S. aureus*) should be started once samples for gram stain and culture has been obtained to avoid joint destruction. Daily aspiration should be done for accessible joints like the knee. Orthopedic consultation should be sought
because certain joints such as shoulder and hip may require arthrotomy and open drainage. There is no role of intra-articular antibiotics.

b. Gonococcal arthritis is main cause of infectious arthritis in young persons (<40 years of age).\(^{[10]}\) The causative organism is *Neisseria gonorrhoeae* and arthritis is a consequence of bacteremia arising from gonococcal infection or, more frequently, from asymptomatic gonococcal mucosal colonization of the urethra, cervix, or pharynx. Women are at greatest risk during menses and during pregnancy and overall are two to three times more likely than men to develop disseminated gonococcal infection (DGI) and arthritis.

DGI is a syndrome of fever, chills, rash and arthritis which is migratory, with prominent tenosynovitis of the knees, hands, wrists, feet and ankles. Important findings on the skin of the trunk and extensor surface of extremities are papules that progress to hemorrhagic pustules.

True gonococcal septic arthritis is a monoarthritis of hip, knee, ankle, or wrist. Gonococcal septic arthritis is less common than the DGI syndrome and always follows DGI, which is unrecognized in one-third of patients. Synovial fluid, typically contains >50,000 leukocytes/L; the gonococcus is only occasionally evident in gram-stained smears and cultures of synovial fluid are positive in <40% of cases. Blood cultures are almost always negative. Treatment consists of ceftriaxone (1 g IV or intramuscular every 24 h) to cover possible penicillin-resistant organisms, until resolution of local and systemic signs. This can be followed by oral ciprofloxacin (500 mg twice daily) to complete 10-14 day course.

c. Crystal induced arthritis — Gout, which is caused by monosodium urate crystals, is the most common type of inflammatory monarthritis.\(^{[11, 12]}\) Gout occurs almost always in a man above the age of 40 years. In general, only one joint is affected initially, but polyarticular acute gout can occur in subsequent episodes. The metatarsophalangeal joint of the first toe often is involved, but tarsal joints, ankles and knees also are affected commonly. The first episode of acute gouty arthritis frequently begins at night with dramatic joint pain and swelling. The pain may be so excruciating that the patient may not even tolerate the touch of the bed clothes. Joints rapidly become warm, red and tender and there may be peeling of skin overlying the affected joint with a clinical appearance that often mimics that of cellulitis. Early attacks tend to subside spontaneously within 3 to 10 days and most of the patients have intervals of varying length with no residual symptoms until the next episode. Later attacks may be monarticular or polyarticular. Certain events may precipitate acute gouty arthritis—these include excessive alcohol intake, dietary excess, trauma and surgery.

d. Pseudogout — Calcium pyrophosphate dihydrate crystals can cause monoarthritis that is clinically indistinguishable from gout and thus is often called pseudogout. Pseudogout is most common in the knee and wrist, but it has been reported in a variety of other joints, including the first metatarsal phalangeal joint (MTP) joint. Among other crystals known to cause acute mono-arthritis are apatites, calcium oxalate and liquid lipid crystals.

### Chronic Inflammatory Monoarthritis

The causes of chronic inflammatory monoarthritis are indolent infections such as tuberculosis (TB), brucellosis, fungal infections and rare parasitic infections. Any patient who presents with the chronic inflammatory monoarthritis must undergo synovial fluid analysis especially for microbiological analysis and/or synovial biopsy must be done in order to get a correct diagnosis. Other important causes of chronic inflammatory monoarthritis are tophaceous gout and immunoinflammatory arthritis due to autoimmune conditions like spondyloarthritis (SpA), SLE or RA. By and large this category remains a diagnosis of exclusion.

a. Tubercular arthritis — Approximately 10-11% of extrapulmonary TB involves bone and joints (osteoarticular TB).\(^{[13]}\) The most common site of osteoarticular TB is the spine, followed by peripheral tubercular arthritis.\(^{[14]}\) Tubercular arthritis occurs mainly as a chronic monoarticular arthritis of a hip or knee (about 85%), but may involve other joints. The onset of tubercular arthritis is typically insidious with pain and swelling of a single joint, but signs of inflammation may be limited. Tubercular arthritis is usually due to reactivation of a hematogenously seeded focus and need not be associated with active disease elsewhere; it can also spread from adjacent osteomyelitis. The risk factors for development of osteoarticular TB and include individuals who are from low socioeconomic status, alcoholics, diabetes mellitus, HIV infection, corticosteroid therapy and other chronic illnesses.
TB of the hip usually presents with mild to moderate pain in the groin, thigh or knee. Children most commonly present with a limp. At rest the hip is usually held in a flexed and abducted posture. It is common to find atrophy of gluteal muscles and tenderness in the groin. Plain radiographs in early stage of the disease are non-diagnostic, but in later stages of the disease there can be destruction of the femoral neck, acetabulum and cold abscess. TB of the knee usually presents with insidious onset pain, swelling and stiffness. Other presentations include a limp and reduction in motion of the knee. The joint is usually warm to touch; synovitis and effusion are commonly present. Muscle spasm and synovial effusion result in flexion deformity. Plain radiographs in the early stage of disease will show soft-tissue swelling subsequently damage to the articular cartilage will result in narrowing of the joint space, irregularity of the cartilage surface and areas of destruction of the epiphysis. A high index of suspicion is necessary for early diagnosis. Yield of synovial fluid smear for acid fast bacilli is only 20-40%, while culture may become positive in up to 80% of cases.[13] Synovial fluid analysis shows elevated cell counts with no specific distinguishing features. Very low glucose levels in synovial fluid may favor the diagnosis of TB. Synovial biopsy is a must in cases of chronic monoarticular inflammatory arthritis where diagnosis is in doubt.

Treatment of tubercular arthritis is same as for other forms of TB. The intensive phase consists of administration of rifampicin, isoniazid, pyrazinamide and ethambutol for 2 months, followed by a continuation phase of rifampicin and isoniazid for 4 months. Intermittent short course chemotherapy has not been assessed in osteoarticular TB. The optimal duration of therapy is also still unsettled.[13] Hence, each patient has to be individually assessed and where relevant, treatment duration may have to be extended for a given patient.[15]

b. Fungal infections — Fungal arthritis is a rare but nevertheless an important differential diagnosis of chronic monoarthritis. It usually follows a chronic indolent course of several months that leads to delays in diagnosis and to inappropriate treatment such as intra-articular and systemic steroids. [16] Various predisposing factors that depress the immune system have been implicated in patients developing fungal arthritis. Candida species can rarely cause septic arthritis.[17] Isolated monoarthritis is caused by the direct intra-articular inoculation of fungi that inhabit the skin or as a complication of hematogenously disseminated candidiasis. Disseminated candidiasis with its accompanying arthritis is seen in patients with serious underlying disorders, IV drug abusers or after prolonged antibiotic therapy.[18] Rare cases have been reported where direct inoculation is caused by repeated injection of a joint or as a contaminant during joint surgery.[19,20] The causative organism in 80% of cases is Candida albicans and remaining cases are caused by Candida tropicalis.[21] The knee is the most commonly affected joint in most cases, though any other peripheral joint or the spine can also be affected.[21] Most cases are monoarticular and osteomyelitis is often present. Diagnosis is achieved by isolating the organism by culture of the aspirated joint fluid or bone. Treatment with amphotericin B is effective and joint destruction with loss of function occurs only in a small percentage of affected individuals.

Coccidioides immitis, Blastomyces dermatitidis and Histoplasma capsulatum are rare causes of chronic monoarthritis.[16] Arthritis due to these dimorphic fungus results from hematogenous seeding or direct extension from bony lesions in persons with disseminated disease. Infection with Sporothrix schenckii is common among gardeners and other persons who work with soil or sphagnum moss. Joint involvement is rare.[22] Articular sporotrichosis is six times more common among men than among women and alcoholics and other debilitated hosts are at risk for polyarticular infection.[23] Tenosynovitis, with or without carpal tunnel syndrome, is associated with deep inoculations. If untreated, the infection will lead to osteomyelitis.

c. Immunoinflammatory causes of chronic inflammatory monoarthritis. The SpA group of diseases consists of ankylosing spondylitis (AS), reactive arthritis, psoriatic arthritis (PsA), arthropathies associated with inflammatory bowel disease (IBD) and undifferentiated SpA.[24] A pattern of peripheral arthritis which is asymmetrical, oligoarticular and predominantly of lower limb is characteristic of this group of diseases.[24] Diagnosis of SpA in a patient with chronic monoarthritis is suggested by presence inflammatory back pain or enthesitis or dactylitis, with one SpA feature like; psoriasis,
IBD, preceding infection, HLA-B27, uveitis, inflammatory sacroiliitis on magnetic resonance imaging or plain radiographs.\[25, 26\]

Peripheral arthritis in AS predominantly involves the lower extremities, especially the knee.\[27,28\]

Reactive arthritis commonly presents with monoarthritis of ankle or knee. History of preceding infection either urethritis can be elicited in 40% cases. Synovial fluid will not show any organism.\[29\]

Other immunoinflammatory systemic diseases that may be associated with chronic monarticular arthritis are RA, SLE, Behçet’s disease. Therefore since indolent infections like TB, brucellosis and fungal infections constitute a major portion of chronic inflammatory monoarthritis synovial fluid microbiology and/or biopsy must be performed to get the actual diagnosis.

**Acute Non-inflammatory Monoarthritis**

The causes of acute non-inflammatory monoarthritis would include trauma, bleeding in to the joint (hemarthrosis) and palindromic rheumatism.

Trauma to a joint can lead to internal derangement, hemorrhrosis, or fracture. Such patients should be evaluated with plain radiographs and referred to the orthopedic surgeon. Penetrating injuries from thorns, wood fragments, or other foreign materials can cause non-inflammatory monoarthritis.\[30,31\] There are case reports of foreign body in the joint (foreign body synovitis) presenting like septic arthritis.

**Hemarthrosis**

The most common causes of hemarthrosis is congenital disorders such as hemophilia.\[32\] Hemophilia is a sex-linked recessive genetic disorder characterized by the absence or deficiency of factor VIII (hemophilia A, or classic hemophilia) or factor IX (hemophilia B, or Christmas disease). Spontaneous acute hemarthrosis occurs commonly with both types of hemophilia. Recurrent spontaneous accumulation of blood in to the joint can lead to a deforming arthritis.\[32\] Hemarthrosis is not common in other disorders of coagulation such as von Willebrand disease, factor V deficiency, warfarin therapy, or thrombocytopenia.

Hemarthrosis occurs when the child begins to walk and run. The joints most commonly affected are the knees, ankles, elbows, shoulders and hips. In the acute stage of bleeding the joint is warm, swollen and tender. The patient holds the affected joint in flexion and guards against any movement. Blood in the joint is resorbed over a period of a week or longer and pain, swelling and tenderness decreases. Recurrent hemarthrosis result in chronic arthritis, where swelling persists and deformity of the joint develops.

The diagnosis of hemarthrosis should be considered in a young male who presents with recurrent swollen and painful joint, which gradually improves on its own overtime. The treatment of hemarthrosis consists of immediate infusion of factor VIII or IX at the first sign of joint or muscle hemorrhage. Pain relief with paracetamol or Cox-2 inhibitors should be given, non-selective nonsteroidal anti-inflammatory drugs are generally avoided because of theoretical risk of potentiating the bleeding.

**Chronic Non-inflammatory Monoarthritis**

Under this heading is single joint osteoarthritis (OA), osteonecrosis, neuropathic joint and pigmented villonodular synovitis (PVNS).

a. OA is the most common type of arthritis. Worldwide estimates indicate that 9.6% of men and 18% of women >60 years have symptomatic OA.\[1\] It is a heterogeneous group of disorders with shared clinical features that bind the group together. OA can be primary or secondary based on the presence or absence of an obvious cause. It can be localized or generalized based on the distribution between joints and numbers of joints involved. Knee OA is very common and is often associated with disability.\[33\] Symptomatic hip OA is one-third as common as disease in the knee.

The two cardinal symptoms of OA are joint pain that worsens with use and difficulty initiating joint movement after inactivity (also known as gelling of the joints).

The joint affected by OA generally has evidence of mild to — moderate firm swelling around the joint line due to osteophytes at the joint margin, palpable crepitus and restricted range of motion with pain at the end of the range. Other common findings on clinical examination are weakness and wasting of the muscles acting on the joint, tenderness around the joint and deformities and instability of the joints are seen in late stages.

b. Neuropathic arthropathy — Joint disease secondary to neuropathy was first described by Jean Marie Charcot, hence it also known as Charcot arthropathy.
It was most commonly described in association with tertiary syphilis, however nowadays it most commonly occurs due to diabetic neuropathy. Other causes of neuropathic arthropathy are spinal cord diseases such as syringomyelia, spina bifida, spinal cord injuries. The loss of pain sensation, proprioception and abnormal muscular reflexes that modulate joint movement leads to repeated trauma, resulting in progressive cartilage and bone damage. Neuropathic arthropathy may present as an acute or subacute monoarthritis with swelling, erythema and variable amounts of pain in the affected joint. Chronic presentation often mimics OA. The most important clinical findings in neuropathic arthropathy are the presence of a significant sensory deficit and a degree of pain that is less than would be expected considering the amount of joint destruction evident on radiographs.

The pattern of joint involvement depends on the location of the neurologic impairment and may involve small as well as large joints. In diabetes, the foot is most commonly involved. Patients with syringomyelia typically demonstrate upper extremity involvement.

c. Osteonecrosis also known as avascular necrosis is characterized pathologically by presence of dead bone can present like arthritis. The most common site for involvement is the femoral head. Other sites are knee, ankles, shoulders and elbows. The most common risk factor for osteonecrosis is glucocorticoid use. An important scenario is development of pain of the groin, typically a deep, throbbing pain in a patient with rheumatic illness who is on glucocorticoids. This pain which is worse at night is usually intermittent and of gradual onset, occasionally appears abruptly. Osteonecrosis is often seen in RA, SLE, systemic vasculitis and other rheumatic illness, the major risk factor being glucocorticoid therapy. Other causes include fracture, dislocation, radiation injury, pregnancy, sickle cell disease, coagulopathies, hemoglobinopathies, organ transplantation, myeloproliferative diseases etc.

d. Pigmented villo nodular synovitis (PVNS) is a rare non-inflammatory proliferative disorder of the synovium with deposition of pigment in the tissue. The etiology is unknown. The term PVNS was introduced in 1941 by Jaffe, Lichtenstein and Sutro to describe a ‘yellow-brown tumor-like tenosynovial lesion’. The typical patient is 20-40 years old male who complaints of a traumatic swelling of a single joint. The knee is involved 80% of the time. The synovial fluid is almost always gross red or bloody. Diagnosis is established by biopsy of the synovium, which is defined by the presence of giant cells, foamy cells and hemosiderin deposits in synovial tissue.

Conclusions and Pearls for Diagnosis

- Pain and swelling (arthritis) of a single joint requires prompt evaluation to identify septic arthritis, crystal induce arthritis and acute onset of inflammatory polyarthritis.
- Acute inflammatory monoarthritis is infection unless proved otherwise.
- Synovial fluid analysis is the most important investigation in the evaluation of both acute and chronic monoarthritis.
- Septic arthritis can rapidly destroy the joint if not detected and promptly treated.
- Septic arthritis can be superimposed on gout and pseudogout.
- Gonococcal arthritis is seen in a young person.
- Serum uric is often normal during an acute attack of gout; diagnosis of gout requires the demonstration of intracellular monosodium urate crystals in the joint fluid under polarized light microscope.
- RA, SLE, IBD associated arthritis, PsA, Behçet’s disease and reactive arthritis can all begin as acute inflammatory monoarthritis.
- Other systemic diseases associated with acute inflammatory monoarthritis are sarcoidosis, sickle disease, hemoarthrosis due to hemophilia and arthritis associated with chronic viral infections.
- Tuberculosis and other indolent infections should be considered in the differential diagnosis of chronic inflammatory monoarthritis. Synovial biopsy must be performed to get the diagnosis.
- Osteonecrosis, OA, neuropathic joint and PVNS should be considered in the differential diagnosis of chronic non-inflammatory monoarthritis.

References