Evaluating and Treating Patients with Polyarthritis of Recent Onset

Robert Meador, MD
H. Ralph Schumacher, MD

Polyarthritis of acute or recent onset represents a diagnostic and management challenge. Polyarthritis is generally defined as inflammation (ie, swelling, tenderness, warmth) at 5 or more joints detected on physical examination. A patient with 2 to 4 involved joints is said to have pauci- or oligoarticular arthritis; this finding suggests, for example, reactive arthritis, Lyme disease, or crystal-induced disease. Ancillary laboratory testing is indicated in many instances, but a thorough history and physical examination should establish the diagnosis in approximately 75% of cases.[1] Management depends on accurate diagnosis, and patients in whom early rheumatoid arthritis (RA) is diagnosed should receive prompt treatment with disease-modifying agents.

This article examines polyarthritis more fully, focusing on the evaluation and treatment of patients with polyarthritis of recent onset. After general comments on the epidemiology and diagnosis of polyarthritis, specific disorders in which polyarthritis occurs will be discussed in detail. **Table 1** lists several types of polyarthritis

CHARACTERISTICS OF POLYARTICULAR DISEASE

Although monoarthritis is widely recognized to require urgent evaluation because of the risk for septic arthritis, crystal disease, and rare tumors, patients with polyarthritis should also receive prompt evaluation and early intervention. Most polyarticular diseases are characterized by a constellation of historical and clinical findings. Although its actual prevalence is unknown, acute polyarthritis is most likely very common and, in some cases, self-limited. In a population-based cohort, only 27% of patients who presented with polyarthritis developed RA by the time of follow-up 3 to 5 years later.[2] Signs and symptoms of early arthritis may not match a textbook-defined type of arthritis, so making a definitive diagnosis can be difficult in the early days or weeks after onset.[3] Accurate diagnosis should still be pursued, however, because some diseases that present with polyarthritis may also have major associated and treatable systemic features. Infectious arthritis, in particular, can occasionally be polyarticular in nature and can be cured if patients receive immediate evaluation and appropriate treatment.

DIFFERENTIAL DIAGNOSIS IN SUSPECTED POLYARTHRITIS

Before discussing the different types of polyarthritis, it is essential to distinguish between arthritis, inflammation surrounding a joint (ie, periarticular inflammation), and other causes of extremity pain. A necessary initial step is to differentiate between the joint inflammation of arthritis and similar symptoms caused by periarticular disease. Most often, nonarthritic states do not produce the overt joint swelling typical of arthritis.[3] For example, tendonitis and related disorders may mimic polyarthritis, but the tenderness and inflammation typical of these disorders are limited to the tendon sheaths and bursae on one side of the affected joint or adjacent to the joint. Pain will often be greater with a specific motion of the joint (eg, abduction of the shoulder in cases of subacromial bursitis) rather than on any motion of the joint as occurs in arthritis. Similarly, diabetes mellitus may be associated with thickening of tendons and subcutaneous tissues that can result in painful contractures, without any primary involvement of the joints.

Diseases of the spine can cause neurogenic claudication, resulting in widespread aching in the legs brought on by standing or walking; however, an objective examination typically reveals no joint abnormalities. Likewise, vaso-occlusive diseases (eg, Buerger's disease, atherosclerosis) often produce diffuse pain, but no joint abnormalities are present and pulses are decreased. Finally, the pain of fibromyalgia is often interpreted as joint pain, but tenderness actually occurs at the muscle.

Dr. Meador is a rheumatologist, Baylor Medical Center at Garland, Garland, TX. Dr. Schumacher is the Director, Arthritis-Immunology Center, VA Medical Center, Philadelphia, PA; and a Professor of Medicine, University of Pennsylvania School of Medicine, Philadelphia, PA.

Table 1. Some Types of Polyarthritis

Systemic rheumatic diseases

Rheumatoid arthritis

Systemic lupus erythematosus

Still's disease

Scleroderma

Psoriatic arthritis

Sarcoidosis

Infectious arthritides

Viral arthritis

Nongonococcal septic arthritis

Gonococcal arthritis

Crystal-induced arthritides

Gout

Pseudogout

Less common systemic diseases

Poststreptococcal reactive arthritis

Multicentric reticulohistiocytosis

Relapsing polychondritis

Whipple's disease

Malignancy

Less inflammatory diseases

Primary osteoarthritis

Osteoarthritis secondary to metabolic disease

Amyloidosis

Table 2. Some Typical Patterns of Joint Involvement

Pattern	Examples
Migratory (symptoms are present in certain joints for a few days and then remit, only to reappear in other joints)	Early phase of Lyme disease, rheumatic fever, gonococcal arthritis, Whipple's disease, palindromic onset of rheumatoid arthritis
Additive (symptoms begin in some joints and persist, with subsequent involvement of other joints.)	Systemic lupus erythematosus, rheumatoid arthritis, osteoarthritis
Intermittent (repetitive attacks of acute polyarthritis [or often oligoarthritis] with complete remission between attacks)	Polyarticular gout, pseudogout, reactive arthritis

erably less time to become limber. The presence of fever can signify infectious arthritis, systemic lupus erythematosus (SLE), or crystal-induced disease.

Physical examination features of RA and other inflammatory arthritides include synovial thickening and joint effusions with local warmth. However, swelling and effusion may also occur in types of arthritis that are not primarily inflammatory, making analysis of joint fluid essential for differentiation. In cases of OA, knee effusions can occur either abruptly or gradually, and the knees may feel warm. However, bony enlargement is more common in mechanical disorders such as OA. Tenosynovitis can be found in patients with RA, gonococcal arthritis, fungal arthritis, or gout.

Diagnostic possibilities for the polyarthritides can be narrowed by several considerations; it should be noted, however, that more than one disease can coexist (eg, OA and gout), and specific clues to the diagnosis may not be evident early in the course of the disease. The sequence of early joint manifestations is revealing. As individual joints become involved, the process may be migratory or additive. The term *migratory arthritis* implies that previously involved joints become asymptomatic as new joints become inflamed; thus, the disease appears to migrate from joint to joint. Diseases that typically present with migratory, additive, or intermittent patterns are listed in **Table 2**.

Additionally, determining patterns of joint involvement may prove helpful. For example, both RA and OA can affect proximal interphalangeal joints, but RA involves metacarpophalangeal joints as well. Moreover, in RA and other inflammatory types of polyarthritis,

APPROACH TO DIAGNOSING POLYARTICULAR DISEASE

As mentioned previously, a careful history and physical examination are key to accurate diagnosis of polyarthritis. Whereas a single descriptive finding may be essentially diagnostic for a few types of polyarthritis (eg, a positive culture in cases of gonococcal polyarthritis, the rash of psoriasis in cases of psoriatic arthritis), most polyarthritides are identified by a collection of clinical findings. In patients with objective findings at multiple joints, a crucial step is to determine whether the disease process is overtly inflammatory or more subtly inflammatory (as in cases of osteoarthritis [OA]). Disease course and treatment obviously differ radically based on the presence and severity of inflammation. Historical suggestions of inflammatory disease include severe morning stiffness, weight loss, fever, and spontaneous joint swelling.[3] In patients with inflammatory arthritis (eg, RA), morning stiffness generally lasts longer than an hour; in contrast, most patients with OA take consid-

Figure 1. Clinical photograph of a patient with early onset rheumatoid arthritis of the hands.

laboratory markers of inflammation (eg, erythrocyte sedimentation rate, C-reactive protein level) are often increased, and thrombocytosis is frequently present.

Synovial fluid analysis must be performed immediately in patients with polyarthritis who are febrile or acutely ill; it is best performed at least once in any patient with a swollen joint. The analysis may be diagnostic in patients with bacterial infections or crystal-induced synovitis. In patients with other polyarthritides, synovial fluid analysis may permit the examiner to determine whether the arthritis is inflammatory or not. Synovial fluid leukocyte counts in patients with most inflammatory arthritides are seldom less than $2 \times 10^3/mm^3$.[4] In contrast, joint swelling that is part of a mechanical problem (eg, OA) produces clear fluid with fewer leukocytes (virtually always $< 0.5 \times 10^3/mm^3$). Yet, this latter amount is still greater than occurs normally, indicating that there is, in fact, some mild inflammation. Moreover, even in clearcut cases of inflammation, there are times when standard guidelines do not apply. For example, inactive or less active joints in patients with RA will produce fewer leukocytes; similarly, some effusions in cases of SLE arthritis contain few cells.

Biopsy of the synovium or other tissues may be necessary to confirm or establish a diagnosis in less common diseases presenting with polyarthritis (eg, mycobacterial or fungal infections, Whipple's disease, vasculitis).[5] Biopsy should also be considered in patients with chronic (> 6–8 weeks) nontraumatic arthritis for which the diagnosis has not been established by history, physical examination, laboratory studies, or synovial fluid analysis with culture.

TYPES OF POLYARTHRITIS
Acute Inflammatory Polyarthritis

Rheumatoid arthritis. Although classification of polyarthritis as RA requires that symptoms be present for at least 6 weeks, 10% of patients with RA first see a physician at less than 6 weeks with acute pain, swelling, and stiffness of the joints; a smaller number initially experience episodic symptoms, and 20% have a subacute onset of symptoms.

The joints most commonly affected initially are the metacarpophalangeal joints, proximal interphalangeal joints, wrists, and metatarsophalangeal joints. A photograph of hands affected by RA is shown in **Figure 1**. Most patients with RA have symmetric polyarthritis, but on rare occasions the disease may spare one hand while causing extensive damage to the other, usually dominant, hand. Typically, joint involvement is additive, with sequential involvement of groups of joints. Approximately 70% to 80% of patients with newly diagnosed RA have positive results on rheumatoid factor testing within a year of disease onset, and an additional 10% to 15% become positive for rheumatoid factor over the first 2 years of the disease.

Occasionally, patients develop extra-articular features of the disease, including episcleritis, subcutaneous nodules, and pleural effusions, early in the disease course; however, these features usually do not appear until much later. Patients with inflammatory arthritis

and with a significant number of involved joints are at high risk for functional limitation. Indeed, polyarticular arthritis, independent of rheumatoid factor, is associated with poor functional outcome when associated with recent onset inflammatory synovitis.[6] Other major predictors of poor outcome include poor functional status, a low hemoglobin level, a high platelet count, and elevated erythrocyte sedimentation rate.[7]

A recent study developed a set of diagnostic criteria to distinguish between persistent versus self-limited RA. Predictive factors for persistent RA included morning stiffness (> 1 hour), arthritis in 3 or more joint groups, bilateral compression pain in the metatarsophalangeal joints, and an IgM rheumatoid factor that is 5 IU or greater.[8]

The traditional slow, pyramidal approach to RA therapy has been challenged; earlier use of disease-modifying antirheumatic agents is now generally recommended.[9] Disability and functional loss often occur early in RA, and 50% of radiologic damage is observed within the first 2 to 6 years of the disease course, supporting the view that RA is particularly aggressive within the first few years.[10] Rheumatologists today institute 1 or more of the disease-modifying antirheumatic agents as soon as the diagnosis of RA is made.

Systemic lupus erythematosus. Arthralgias and arthritis are the most common presenting manifestations of SLE. Whereas the acute inflammatory polyarthritis of SLE may involve any joint, the small joints of the hands, wrists, and knees are most commonly involved in a symmetric fashion, much as they are in RA. Subcutaneous nodules may occasionally form and be difficult to distinguish from the nodules of RA. In contrast to RA, however, the arthritis associated with SLE is rarely erosive or destructive of bone. Although joint deformities are unusual, patients who have SLE with chronic arthritis can develop ulnar deviation and swan-neck deformities of the hands (known as *Jaccoud's arthropathy*). Systemic features of SLE are helpful in reaching a diagnosis.

Synovial fluid from patients with SLE arthritis is usually only mildly inflammatory. Laboratory analysis further reveals positive results on antinuclear antibody testing, and there may be diminished complement levels. Lupus erythematosus cells may occasionally be seen in synovial fluid.[11]

Primary pharmacologic management of SLE involves drugs that suppress end-organ inflammation or interfere with immune function. The type and severity of clinical manifestations should guide treatment. Hydroxychloroquine is widely used for rashes and arthritis in patients with SLE. Oral corticosteroids, on the other hand, are usually the first agent administered for vital organ disease. Moreover, aggressive management of hypertension, infections, seizures, hyperlipidemia, osteoporosis, and other comorbid conditions that commonly occur in patients with SLE is required.

Still's disease. Still's disease can occur in children or adults and is characterized by rheumatoid factor–negative polyarthritis in association with features of a systemic inflammatory disease. Often, the systemic features of the illness overshadow the polyarthritis. The most striking features are fever, evanescent rashes, sore throat, adenopathy, and leukocytosis. Still's disease may present with joint involvement in a manner similar to RA. Treatment of the arthritis can be similar to treatment in cases of RA, but corticosteroid administration may be needed more often.

Scleroderma. Arthralgias and morning stiffness are relatively common early features of scleroderma and may antedate skin changes. Erosive polyarthritis is less common, although cases of erosive RA have been described in patients with scleroderma.[12] The tethering effects of later skin thickening can lead to hand deformities and joint ankylosis; these deformities may mimic true arthritis.[13] Tendon friction rubs may develop in patients with systemic sclerosis as a result of inflamed and fibrinous tendon sheaths. Treatment of scleroderma remains difficult, with no proven effective agents.

Psoriatic arthritis. In contrast to RA, psoriatic arthritis is seronegative, meaning that the rheumatoid factor is typically absent. Although monoarthritis and oligoarticular arthritis are common initial manifestations, symmetric polyarthritis involving the small joints of hands, feet, wrists, ankles, knees and elbows is the most common pattern of this disorder. The arthritis may be indistinguishable from RA, but there is a higher frequency of distal interphalangeal or sacroiliac joint involvement. Enthesitis (ie, inflammation at the insertion of a ligament, tendon, or articular capsule into bone) and dactylitis (sausage-shaped digits) are common features of psoriatic arthritis. Patients who have symmetric polyarthritis and psoriasis but lack the characteristic clinical features or radiologic changes (eg, sacroiliitis) of psoriatic arthritis and have positive results on rheumatoid factor testing most likely have coincidental RA. Recognition of psoriatic plaques is important, because psoriasis precedes arthritis in two thirds of cases.[14]

The general management principles for patients with psoriatic arthritis are the same as for those with RA, meaning that treatment depends on the type of the joint disease (axial versus peripheral) and the severity of joint and skin involvement. Nonsteroidal anti-inflammatory drugs (NSAIDs) are effective as therapy in most patients and should be tried first. Methotrexate is effective for

both skin disease and peripheral arthritis in patients with oligo- or polyarticular disease.

Sarcoidosis. The multisystem disorder of sarcoidosis can be accompanied by arthritis in 15% of cases. When arthritis is part of the initial presentation, it typically involves the ankles, knees, or wrists. Typically, 4 to 6 joints are involved. Löfgren's syndrome is a particular manifestation of sarcoidosis marked by the triad of acute arthritis, erythema nodosum, and bilateral hilar adenopathy. In contrast to what occurs in RA, the duration of acute arthritis in sarcoidosis averages several weeks, ranging from a few days to 3 months.

Acute sarcoidosis has been mistaken for juvenile RA, especially in children younger than 4 years.[15] However, most affected persons are in their third or fourth decade of life, with a slight female predominance. Sarcoidosis occurs most frequently in African Americans and northern Europeans. The most common extrathoracic manifestations are cutaneous and ocular involvement. In chronic sarcoidosis, granulomas can infiltrate phalangeal and other bones.

Treatment depends on the specific manifestations. For example, therapy for Löfgren's syndrome can begin with administration of NSAIDs but may need to be changed to administration of corticosteroids. Colchicine may be effective for acute sarcoidosis arthropathy.

Infectious Arthritis

Viral arthritis. Arthropathy caused by human parvovirus B19 infection produces an RA-like polyarthritis in adults. Patients with acute arthritis should be asked if they have been exposed to a child with a rash, especially on the cheek. Polyarthritis also has been reported in patients with rubella, mumps, and other viruses. Although self-limited, symptoms of viral arthropathies resemble those of acute RA, with morning stiffness, symmetric involvement of the hands and wrists, and, occasionally, positive results on rheumatoid factor testing. A similar type of arthritis may precede the signs of hepatitis B viral infection and is often accompanied by an urticarial rash.

HIV infection should be considered in cases of acute polyarthritis, because arthritis may be an initial manifestation of the disease. HIV infection also may be associated with reactive arthritis and psoriatic arthritis, and an unusually painful polyarthritis has been described in association with HIV infection. Case reports have described extensive polyenthesitis and adjacent osteitis on imaging studies.[16] Another presentation of viral arthritis associated with HIV infection resembles SLE arthritis, with fever, hematologic abnormalities, and proteinuria.

Nongonococcal septic arthritis. Most articular bacterial infections involve a single joint, but 15% to 20% of cases are polyarticular.[17] In patients with polyarticular septic arthritis, the knees are most commonly involved. Potential risk factors for nongonococcal polyarticular septic arthritis include age greater than 50 years, RA as an underlying disease, and disease of staphylococcal origin. Septic polyarthritis should be considered even when the clinical picture is not florid (ie, when patients have only low-grade fevers and normal leukocyte counts). Nor should the simultaneous involvement of distant joints rule out infection. Indeed, the frequency of underlying rheumatic disease and its treatment may further confuse the clinical presentation.[17] Joints suspected of harboring infection should be aspirated, including those previously affected by the concurrent rheumatism. Mortality rate of polyarticular septic arthritis is 30% to 40%, compared with 4% to 8% for monarticular septic arthritis.[17]

Infection in patients with RA is polyarticular in nearly half of cases, and periarticular signs (eg, infected adjacent bursa, spontaneous drainage, sinus tract formations) are common presenting manifestations. The primary sources of infection in RA patients are infected rheumatoid nodules, infected calluses of the foot, lung infection, and urinary tract infections.[18]

Intravenous drug abuse accounts for a third of cases of septic arthritis, and many of these patients are HIV-positive. Polyarticular infection may occur; the joints predominantly affected are of the axial skeleton (ie, sternoclavicular, costochondral, hip, shoulder, vertebrae, symphysis pubis, sacroiliac joint), but peripheral joints are also involved. An elevated erythrocyte sedimentation rate and leukocytosis are present in more than half of these patients, but radiographic abnormalities are present in fewer than a third. Technetium Tc 99m bone scans are usually abnormal and especially helpful in evaluating joints of the axial skeleton. Infective endocarditis, a common condition among intravenous drug abusers, often has rheumatic manifestations, but septic polyarthritis is rarely seen in such cases.[19]

The initial selection of antibiotics to treat bacterial arthritis is directed by the clinical setting, including age, history, extra-articular foci of infection, comorbidity factors, and findings from Gram staining of the synovial fluid. The initial antibiotic regimen should be adjusted when culture identifies the causative organism and then adjusted again when sensitivities of the causative organism are known. However, acute nongonococcal septic arthritis cannot be treated successfully by antibiotics alone. The joint must be aspirated to drain intra-articular pus.

Gonococcal arthritis. Unlike what occurs in cases of nongonococcal septic arthritis, 70% of patients with gonococcal arthritis initially experience polyarthralgia or polyarthritis that is often more migratory, compared with RA.[20] Only 25% of patients with disseminated infection have urogenital symptoms, whereas 67% or more report tenosynovitis, fevers, and dermatitis; purulent polyarthritis occurs in 10% of these patients. Young women are more commonly affected by gonococcal arthritis than are young men, and they typically develop infection around the time of menstruation and pregnancy. Risk factors for gonococcal arthritis include high-risk sexual practices and congenital complement deficiencies. A high index of clinical suspicion, careful culturing of samples (from blood, endocervix, urethra, pharynx, skin, synovial fluid/tissue, rectum), and appropriate antibiotic therapy will rapidly control and prevent more serious complications of disseminated gonococcal infection.[20]

Crystal-Induced Arthritis

Gout. Crystal-induced arthritis is generally monarticular in the early stages of arthritis. On occasion, it may first present as acute polyarthritis that is often accompanied by fever. The early stages of gout are characterized by recurrent episodes of often dramatic and painful attacks of joint swelling, with severe attacks sometimes lasting 1 to 2 weeks. Early in the acute intermittent stage, episodes of acute arthritis are infrequent, and intervals between attacks sometime last for years. If untreated, gout can develop into an acute or chronic polyarthritis associated with tophaceous nodules. Tophi of gout can be distinguished from RA nodules by aspiration and identification of monosodium urate (MSU) crystals. Examination of synovial fluid for the crystals can confirm gouty arthritis. The serum uric acid level is usually elevated at some time in the course of gout but is not always increased at times of acute arthritis.

Crystal deposits in joints can be destructive as well as painful. Treatment, therefore, has 2 objectives: (1) to relieve the pain of the acute attack, thus restoring normal function; and (2) to prevent the accumulation of crystals that can lead to joint damage.[21] Therapy with colchicine, NSAIDs, and corticosteroids is effective for management of acute attacks. The treatment of hyperuricemia in patients with recurrent or chronic gout implies a long-term commitment of daily therapy and behavioral change. The goal of chronic treatment with allopurinol or uricosuric agents is consistent maintenance of a serum urate level that is less than 5.0 mg/dL to allow solubilization of crystalline urate. Recent studies have indicated that avoidance of diuretic therapy, weight gain, or alcohol consumption can lead to a decrease in episodes of gouty arthritis.[22]

Pseudogout. Symptoms of calcium pyrophosphate dihydrate (CPPD) deposition can mimic those of gout, but the causative crystal is CPPD rather than MSU. Although monoarthritis is the most common presentation, oligoarticular and polyarticular disease has been described. Knees, metacarpophalangeal joints, and wrists are most often involved, leading to confusion with RA. The attacks tend to be less painful and take longer to reach peak intensity compared with gout attacks. The presence of intracellular CPPD crystals confirms the diagnosis of pseudogout. CPPD crystals tend to be blunt or square, whereas MSU crystals are needle-shaped or pointed; moreover, CPPD crystals are weakly positively birefringent under polarized light microscopy, whereas MSU crystals are strongly negatively birefringent.[23]

Although most cases of pseudogout are associated with aging, some cases in younger persons may result from metabolic etiologies. Thus, the diagnosis should be suspected in persons with suggestive symptoms, even if they are younger than 55 years. A strong association with hyperparathyroidism, hemochromatosis, hypomagnesemia, hypophosphatasia, and previous local trauma or surgery exists. Attacks can most often be managed with administration of NSAIDs.

Less Common Systemic Diseases Involving Arthritis

Poststreptococcal reactive arthritis. Poststreptococcal reactive arthritis should be considered as a diagnosis in adults who have otherwise unexplained polyarthritis. The latency period from streptococcal infection to onset of arthritis often ranges from 4 days to 6 weeks. Arthritic symptoms typically can have a more protracted course than the 3 weeks described for acute rheumatic fever, but they usually resolve after symptomatic treatment.[24]

Multicentric reticulohistiocytosis. The most common presentation of multicentric reticulohistiocytosis is a painful destructive polyarthritis resembling RA, for which affected persons may be mistakenly treated[25]; this symmetric polyarthritis resembles that of RA when the proximal interphalangeal joints are affected and that of psoriatic arthritis when the distal interphalangeal joints are involved. Joint manifestations precede the appearance of skin lesions in most patients, but the appearance and location of skin nodules, including pearly deposits at the base of the nails, can establish the diagnosis. Onset is insidious and is characterized by polyarthritis, skin nodules, and (in many cases) xanthelasma. Underlying malignancies have been reported.[26] Treatment may be difficult, requiring

in some instances administration of both methotrexate and cyclophosphamide.

Relapsing polychondritis. Polyarthritis is the second most common presenting symptom at onset of relapsing polychondritis.[27] Typically, the arthropathy is migratory, asymmetric, and nonerosive—unlike RA—and involves large and small joints of the peripheral or axial skeleton. This diagnosis should be suspected if chondritis of the ears, nose, or trachea evolves. Administration of corticosteroids is usually effective, but corticosteroid-sparing agents may be needed.

Whipple's disease. Whipple's disease is a chronic bacterial infection, usually affecting middle-aged men, that has a wide range of clinical manifestations. The most common recognized symptoms are weight loss and diarrhea, but in 75% of cases, these symptoms are preceded by polyarthritis lasting a mean of 6 years.[28] In most patients, results of periodic acid-Schiff staining of specimens from a proximal small bowel biopsy reveal inclusions within the macrophages, corresponding to bacterial structures. The polyarthritis may have a palindromic or relapsing course, although chronic destructive polyarthritis and spondyloarthropathy have also been repeatedly reported.[28] Treatment involves long-term use of antibiotics, especially tetracyclines.

Malignancy. Polyarthritis can be the presenting symptom of an occult malignancy. The association between polyarthritis and occult malignancy is suggested by the occasional close temporal relationship (average, < 10 months) between the onset of a seronegative arthritis and the diagnosis of malignancy. Other clinical features suggesting an underlying malignancy include late age at onset of arthritis, asymmetric joint involvement, explosive onset, predominance of lower extremity involvement, and absence of rheumatoid factor or nodules. Recent-onset arthritis that is reminiscent of RA may be an early manifestation of an occult malignancy.[29]

Osteoarthritis and Other Less Inflammatory Types of Polyarthritis

In OA and other polyarticular afflictions marked by fewer signs of inflammation, symptoms result in large part from mechanical effects. In contrast to more overtly inflammatory arthritis, pain is worse during and after use of the affected joints, with minimal pain at rest and morning stiffness that usually lasts less than 30 minutes. As joints are moved through range of motion, coarse crepitation may occur, and bony osteophytes may be palpable.

Primary osteoarthritis. Results of tests for inflammation, such as measurement of erythrocyte sedimentation rate, are usually normal in cases of OA, unless there is coincidental inflammation elsewhere. However, C-reactive protein (CRP) level may be slightly elevated in severe primary OA. A positive test for rheumatoid factor is usually less valuable diagnostically, because primary OA and rheumatoid factor both increase in frequency with advancing age. Radiography is helpful in establishing the diagnosis, as symptomatic OA nearly always is accompanied by radiographic changes. However, despite radiographic evidence, OA many not be responsible for symptoms in all persons, and gout, CPPD deposition, RA, and polymyalgia rheumatica can also occur in patients with OA.

Although OA of the hands is usually thought of as a chronic disease, it may present subacutely. In women, this form of primary OA typically develops within a few years of menopause. For 1 to 2 years, the joints may intermittently become warm and tender; after this time, the mild inflammation subsides, and osteophytes of Heberden's and Bouchard's nodes develop symmetrically in multiple distal and proximal interphalangeal joints, respectively. Hips and knees are also often involved in OA; knee joints with effusions should be aspirated to confirm the absence of crystals or the lower leukocyte counts typical of OA.

Treatment of primary OA involves emphasis on mechanical measures as well as therapy with analgesic agents and NSAIDs. Intra-articular administration of corticosteroids or hyaluronic acid may temporarily relieve joint pain and swelling, allowing the joint to become more usable.[30] A specific exercise program can play a significant role in improving range of motion and decreasing pain.[31]

Osteoarthritis secondary to metabolic diseases. Patients with hemochromatosis may have polyarticular OA involving the metacarpophalangeal joints, especially the second and third. However, virtually any joint can be involved and can be a clue to the underlying disease. The pathogenesis of the arthropathy is not yet well understood. Treatment is empirical and often unsatisfactory. Phlebotomies, although valuable to treat or prevent other features of hemochromatosis, do not predictably benefit the arthropathy.[32] All first-degree relatives (> 10 years old) should be screened every 2 to 5 years for the disease by measuring a transferrin saturation.

Hypothyroidism is associated with symmetric, highly viscous noninflammatory effusions, frequently in joints with preexisting OA. Acromegaly often occurs in the hips and spine, where there is bone and cartilage overgrowth.

Wilson's disease (ie, hepatolenticular degeneration) is a rare metabolic disorder in which deposition of copper leads to dysfunction of the liver, kidneys, and brain.

The associated arthropathy is characterized by a mild premature OA of the wrists, metacarpophalangeal joints, knees, or spine. A few patients have acute or subacute polyarthritis that resembles RA. Life-long penicillamine chelation therapy can prevent virtually every manifestation of the disease.

Alkaptonuria, a rare disorder transmitted by a recessive mode of inheritance, results from a complete deficiency of the enzyme homogentisic acid oxidase. A progressive degenerative polyarthropathy develops, predominantly in large joints; symptoms usually appear in the fourth decade of life. Numerous therapies, including administration of ascorbic acid and diets low in protein, phenylalanine, and tyrosine, have been attempted; to date, no therapy has proved beneficial.

Amyloidosis. In cases of amyloidosis, an insoluble proteinaceous material is deposited in the extracellular matrix of tissue, causing low-grade polyarthritis. Amyloidosis can present with a clinical picture suggesting seronegative RA.[33] Clues to this diagnosis include the lack of inflammation and frequent hip and shoulder involvement with periarticular amyloid infiltration, which leads to enlargement of the pelvic or shoulder girdle. Synovial fluid analysis can be helpful in detecting amyloid deposits. Amyloid may be primary or secondary to any chronic inflammatory disorder, whether infectious, neoplastic, or rheumatic. A distinct form occurs during chronic dialysis. Treatment focuses on controlling the underlying inflammatory or neoplastic disorder. For organ failure, some studies show that melphalan and prednisone enhance survival. Patients with end-stage renal disease have undergone dialysis and renal transplantation with reasonable responses.

SUMMARY

Correct early diagnosis of acute and recent-onset polyarthritis is vital. The erosive damage of RA occurs earlier in the disease course than previously realized, and more specific therapies to minimize damage are becoming available. Also, arthritis may be the initial clue to a serious systemic disease. Determining whether a single, several, or many joints are affected and learning the patterns of involvement can narrow the diagnostic possibilities. Joint fluid aspiration and synovial fluid testing provide much information and should be performed at the initial evaluation, if possible. The presence or absence of fever, rash, and exposure to infectious organisms can further direct diagnostic studies and treatment.   **HP**

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