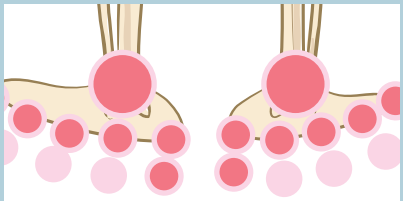
abstract



Rheumatoid arthritis is the most common etiology for inflammatory arthritis in the older population, with an estimated prevalence of 2%. An older individual with inflammatory polyarthritis usually falls into one of two categories. The first consists of patients with well-established long-standing disease, whose course is often confounded by end organ damage and toxicity related to antirheumatic drugs. The other category comprises patients with late-onset inflammatory polyarthritis, whose presentation is often nonspecific and, thus, more elusive to diagnose. Systemic lupus erythematous can also occur in the older adult; it is less prevalent than rheumatoid arthritis and is associated with multiple organ involvement, including musculoskeletal symptoms.

Key words: *rheumatoid arthritis, systemic lupus erythematosus, inflammatory polyarthritis, late-onset disease*

Inflammatory Polyarthritis in the Older Adult

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Introduction

According to the 2000 Canadian Community Health Survey, at least four million Canadians 15 years and older are afflicted with a musculoskeletal (MSK) condition.[1] Forty percent of these individuals are over the age of 65 years. Compared with people with other chronic conditions, those with arthritis experienced more pain, activity restrictions, and long-term disability. They more frequently reported contact with health care professionals in the previous year.[2]

Although noninflammatory arthritis, such as osteoarthritis (Figure 1), is the predominant etiology behind these MSK symptoms, inflammatory arthritis can also occur within this population. As inflammatory polyarthritis results in greater frequency of constitutional symptoms, joint swelling, and damage than osteoarthritis, identification and timely management of these inflammatory conditions is of paramount importance. Rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) account for a significant proportion of symmetrical inflammatory polyarthritis seen in older adults.

An older individual with inflammatory polyarthritis usually falls into one of two categories: a patient with well-established long-standing disease or a patient with a new late-onset inflammatory polyarthritis. The first group is usually characterized by patients with a high burden of damaged joints and possible clinical manifestations of treatment toxicity as a result of long disease duration. They may or may not have smouldering disease activity during their later years. Management options for persons with long-standing disease are usually more restricted due to a prior history of primary or secondary failure to traditional therapeutic modalities.

Patients with late-onset inflammatory polyarthritis are often challenging to diagnose, as the symptoms are more likely to be nonspecific and exhibit a different pattern of synovitis than those classically described for early onset polyarthritis. For instance, older RA patients are more likely to present with systemic complaints such as generalized weakness, anorexia, weight loss, fatigue, or fever, and onset of joint symptoms typically is abrupt. An additional challenge with late-onset disease is the prevalence of concomitant disease that may also mask inflammatory disease such as polymyalgia rheumatica, malignancy, and even osteoarthritis. In this review, we discuss the clinical presentation and treatment of RA and SLE, and highlight additional issues germane to treating older patients.

Rheumatoid Arthritis

Epidemiology

RA is the most common inflammatory arthritis, with an estimated overall prevalence of 1%, which increases to at least 2% in the older population.[3] Females with young-onset RA (RA onset prior to the age of 60) are two to four times as likely to be affected as males. This ratio decreases to 1.5 to 1 for females in late-onset RA (RA onset after the age of 60).[4]

Table 1: Criteria for Diagnosis of Rheumatoid Arthritis

Patient must exhibit four of the following:
• Morning stiffness lasting at least one hour
• Arthritis in three or more joints as observed by a physician
• Arthritis in the wrist or hand joints
• Symmetrically affected joints
• Rheumatoid nodules
• Rheumatoid factor positive
• Radiographic changes typical of RA, which must include erosions or bony decalcification most marked adjacent to the involved joints

Note: Symptoms must last for at least six weeks before a diagnosis of RA can be definitively given.
Source: Modified from Arnett FC et al., 1988.[5]

Diagnosis

Diagnosis of RA follows the 1987 American Rheumatism Association criteria. Criteria for RA diagnosis are shown in Table 1.

Rheumatoid factor is felt to be less useful in diagnosing RA in this population, as the prevalence of autoantibodies increases with age. Anticyclic citrullinated antibody (CCP) may be a more specific marker in the diagnosis of late-onset RA, although this is not readily available in most laboratories.[6]

A major challenge in diagnosing RA in the older population is differentiating it from polymyalgia rheumatica (PMR). Both these entities have overlapping clinical features, especially when PMR presents with peripheral arthritis in the small joints. Furthermore, PMR symptoms can coexist in RA patients, which occurs in about 6.5% of late-onset RA patients.[4] A high degree of suspicion is also required to identify an individual with underlying malignancy, as this is more likely to occur in the later years.

Clinical Signs and Symptoms

The onset of RA can be acute or insidious. Joint destruction is progressive and over time a reduction in range of movement, instability of the joint, malalignment, and deformity can be seen in the affected joint. The pattern of affected joints early in RA is typically symmetric small joint involvement in the hands, feet, and wrist (Figure 2). Later stages of RA progress to involve larger joints, such as the shoulder, elbow, knees, and hip. Cervical spine involvement is also common. However, the lumbar spine is typically not involved. In late-onset RA, there is an increased frequency of shoulder involvement than in early onset RA. However, classical rheumatoid hand deformities of the proximal interphalangeal (PIP), metacarpophalangeal (MCP), and wrist are less likely to be involved.

Extra-articular features of RA include manifestations related to vasculitis (such as rheumatoid nodules, digital infarcts, episcleritis, peripheral neuropathy, palpable purpura or leg ulcers), or due to lymphocytic infiltrate (such as sicca symptoms, hypothyroidism, interstitial lung disease, splenomegaly, or lymphadenopathy).

Late-onset RA patients are more likely to have constitutional symptoms characterized by fatigue, weight loss, myalgia, lymphadenopathy, and PMR symptoms.[4] However, late-onset RA subjects are less likely to have interstitial lung disease and sicca symptoms. It has been suggested that RA is a risk factor for coronary artery disease.[7] Thus it is especially important to monitor older RA patients for cardiac symptoms as they may have comorbid cardiac illness that may be exacerbated.

Table 2: Criteria for Diagnosis of Systemic Lupus Erythematosus

Patient must exhibit four of the following:
Malar rash
Discoid rash
Photosensitivity
Oral ulcers
Arthritis, nonerosive, involving two or more joints
Serositis, either pericarditis or pleuritis
Kidney dysfunction, defined by proteinuria >3+ or cellular casts (any cell type)
CNS involvement, usually seizures or psychosis in the absence of medication or other metabolic disorders
Cytopenia, either anemia, leucopenia, lymphopenia, or thrombocytopenia
Immunologic tests positive for anti-DNA, anti-Sm, or antiphospolipid antibodies
The presence of antinuclear antibodies

Source: Tan EM, et al., 1982.[15]

Laboratory Features

RA is a clinical diagnosis with no one laboratory test to confirm the diagnosis. With respect to nonspecific laboratory features, elevation in erythrocyte sedementation rate and C-reactive protein as well as anemia of chronic disease are more likely to occur with RA in the older population. While the degree of anemia tends to correlate with the activity of underlying RA in younger RA patients, this marker is less helpful in aging adults, who are more prone to anemia from impaired nutritional absorption.

Management

Older patients with RA are best approached with a multidisciplinary team to ensure mobility and independent functional ability as long as possible. Physiotherapy and occupational therapy are key to fall prevention, a major cause of loss of independence in this age group.

The present therapeutic management of RA includes early use of methotrexate (MTX) with rapid escalation of the dose to 20 to 25 mg/week if the response is inadequate (this is generally, but not exclusively, done by specialists). This is usually followed by sequential addition of further disease modifying antirheumatic drugs (DMARDs), i.e., combination therapy (with the addition of DMARDs such as plaquenil, sulfasalazine, azathioprine or leflunomide). Some rheumatologists initiate combination therapy from the outset (usually MTX, plaquenil, and sulfasalazine) at presentation to clinic.

NSAIDs are frequently used for symptomatic relief. A conscious effort is made to minimize the use of corticosteroids. If the combination DMARDs are not successful in controlling the patient's symptoms, antitumour necrosis factor (TNF) agents are then added to the regimen. The anti-TNF agents, which include monoclonal antibodies (infliximab and adalimumab) and receptor antagonists (etanercept), are quite effective in up to 80% of subjects with RA. All the anti-TNF agents appear to be more effective with the use of concomitant MTX therapy.

With respect to pharmacotherapy in the older adult, those receiving NSAIDs are at higher risk of adverse events, especially gastrointestinal bleeding and renal function impairment.[9] These effects are amplified when the patient is taking anticoagulant therapy or diuretics, or has comorbid peptic ulcer or renal disease. NSAIDs have drug-drug interactions with warfarin, beta-blockers, ACE inhibitors, diuretics, phenytoin and digoxin, all of which are commonly used medications in the older population.[10]

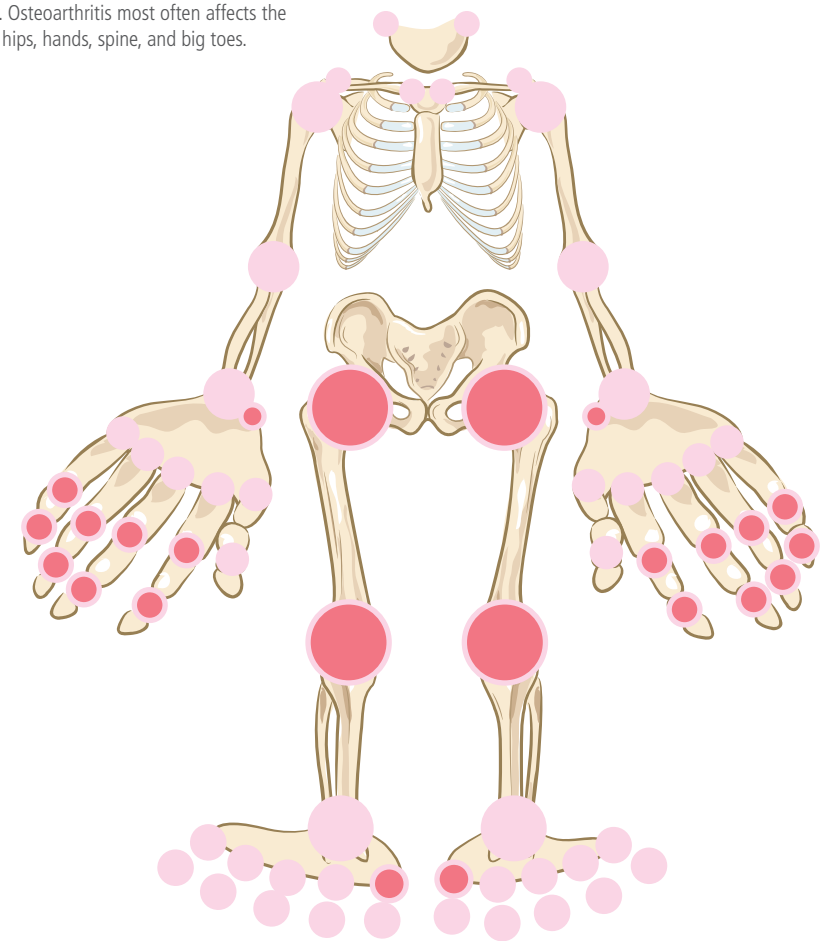
DMARD treatment requires close monitoring of renal and hepatic functions, and low doses should be maintained if possible. Methotrexate clearance is correlated with creatinine clearance, and doses must be adjusted in older adults according to renal function. Sulfasalazine has increased risk of gastrointestinal toxicity in this population, and enteric coated tablets should be used.[11]

The biologic agents show great promise in young- and late-onset RA. However, additional care must be exhibited when prescribed to older adults, as their natural infection resistance is lower, and many have been exposed to tuberculosis.

Figure 1:
Typical Joint Distribution for Osteoarthritis

clinical signs

In osteoarthritis, the surface of the joint is damaged and surrounding bone grows thicker. Osteoarthritis most often affects the knees, hips, hands, spine, and big toes.



Systemic Lupus Erythematosus

Epidemiology

Systemic Lupus Erythematosus (SLE) is a prototypic autoimmune disorder that predominantly affects females of child-

bearing age and is involved with inflammation in multiple organ systems.

In the U.S., incidence of SLE has been estimated to be 15–124 cases per 100,000.[12] This incidence varies according to age and gender. Between the ages of 15–45 years, the female-to-male ratio is around 12:1. This ratio drops with age, though women are still at higher risk of developing the disorder. The female predominance is reduced to 4.4:1 in late-onset SLE, defined as the onset of SLE after the age of 50.[13]

Clinical Signs and Symptoms/ Diagnosis

SLE can affect multiple organ systems and often has a varied and dynamic course. There are 11 criteria used to help diagnose SLE at which four must be present. Often early symptoms are nonspecific, and the disease is frequently incipient for many years. The diagnostic criteria for SLE are presented in Table 2. These criteria are intended to separate SLE from other disorders and do not include many other common symptoms, such as fatigue, fever, weight loss, lymphadenopathy, and vasculitis. Thus, SLE can affect virtually any organ.

Lupus arthritis is usually characterized by a symmetrical polyarthritis of the small joints of the hands, the wrists, and the knees. Although the clinical presentation may resemble RA when viewed by a plain radiograph, the inflammatory synovitis tends not to be erosive.

Overall, late-onset SLE appears to be a milder disease than early-onset SLE. In a recent pooled analysis of 714 cases in the literature, late-onset SLE was characterized by higher occurrence of serositis and pulmonary involvement and lower occurrence of malar rash, photosensitivity, palpable purpura, alopecia, Raynaud's phenomenon, neuropsychiatric manifestations, renal involvement, and lymphadenopathy.[14] With respect to laboratory features, the analysis noted higher frequency of rheumatoid factor positivity, whereas antiribonucloprotein, anti-Sm, and serum complement abnormalities were less likely to occur when compared to young SLE patients.

Numerous studies have noted that the severity of SLE usually declines over time.[14] This decline in severity may be primarily attributed to less frequent kidney involvement (proteinuria, renal insufficiency, diffuse proliferative glomerulonephritis) in late-onset SLE. Because of the disease process this has led to less treatment with high-dose corticosteroids and immunosuppressive agents. Finally, although there is a reduced 10-year survival in late-onset SLE patients when compared to their younger counterparts, this is due to the consequences of aging rather than SLE related factors. Thus, overall, late-onset SLE tends to be a milder disease entity than young-onset SLE.

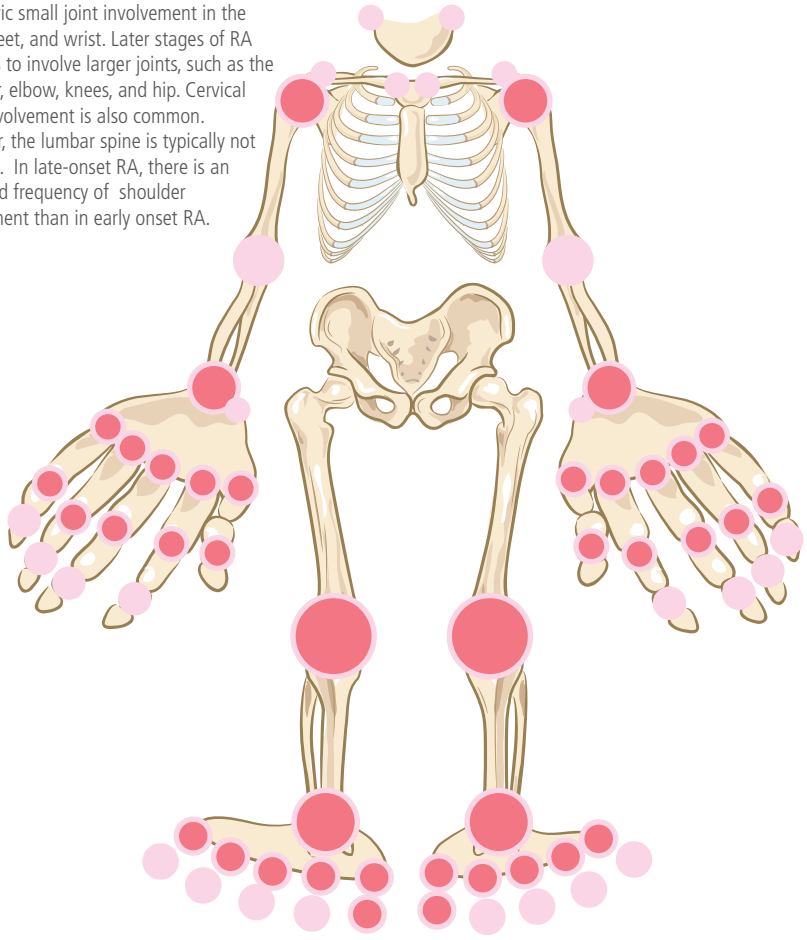
Treatment

Treatment of SLE varies depending on the severity of symptoms and the organ systems involved. An organ-specific approach is used to manage SLE. The management of inflammatory arthritis may just require NSAIDs or low-dose corticosteroids whereas cutaneous disease, such as discoid lupus, may be treated with topical corticosteroids or with antimalarial agents such as hydroxychloroquine. Long-term corticosteroids are the principle treatment modality for the management of SLE. High doses are

Figure 2:
Typical Joint Distribution for Rheumatoid Arthritis

clinical signs

The pattern of affected joints early in rheumatoid arthritis (RA) is typically symmetric small joint involvement in the hands, feet, and wrist. Later stages of RA progress to involve larger joints, such as the shoulder, elbow, knees, and hip. Cervical spine involvement is also common. However, the lumbar spine is typically not involved. In late-onset RA, there is an increased frequency of shoulder involvement than in early onset RA.



Key Points

Issues related to rheumatoid arthritis (RA) in the older adult

A.) Those with well-established, long-standing RA often manifest:
- Cumulative joint damage
- History of multiple DMARD use
- Clinical manifestations related to treatment toxicity

B.) For those exhibiting new onset of RA, clinicians will note:
- Atypical pattern of synovitis—example: predilection for shoulder involvement
- Increased constitutional symptoms
- Symptoms may resemble polymyalgia rheumatica and possibly malignancy
- Patients may have multiple comorbidities complicating management
- RF, ANA not as specific

usually reserved for significant renal and CNS disease. Small to moderate doses are used to treat the serositis and inflammatory arthritis.

The older population is more prone to developing corticosteroid toxicity, especially osteoporosis and glucose intolerance. Several common conditions among older adults are also side effects of long-term corticosteroid use, and thus their risk of adverse events is much higher. Osteoporosis, glaucoma, fragile skin, memory impairment, and increased risk of infection due to impaired immune function are all side effects of corticosteroid use.[10] Short-term side effects of high-dose steroids are weight gain, fluid retention, and insomnia, all of which have increased morbidity in aging individuals by adding strain to already weakening joints, kidney function, and mental acuity. Long-term high-dose corticosteroid use can result in peptic ulcer disease, worsening of hypertension, hyperglycemia, atherosclerosis, elevated serum lipids, and psychosis.[10] In older patients with cardiac comorbidities, these long-term effects are concerning, and patients with poor glycemic control must be vigilant with blood sugar testing to ensure proper dosing of diabetes medications. Thus, all efforts are made to minimize the dose of steroids in this population, including the concomitant use of DMARDs.

Conclusion

In conclusion, inflammatory polyarthritis is common in the older population. The diagnosis of such patients is often more elusive as "classic" symptoms are often less likely to occur. The management of these patients is confounded by end organ damage, treatment toxicity, and other comorbid illness. Thus a high index of suspicion is required for the diagnosis and the management plan should be carefully developed.

No competing financial interests declared.

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